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Effect of fluid strategy on stroke volume, cardiac output, and fluid responsiveness in adult patients undergoing major abdominal surgery: a sub-study of the Restrictive *versus* Liberal Fluid Therapy in Major Abdominal Surgery (RELIEF) trial

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Abstract

Background: We designed a prospective sub-study of the larger Restrictive *versus* Liberal Fluid Therapy in Major Abdominal Surgery (RELIEF) trial to measure differences in stroke volume and other haemodynamic parameters at the end of the intraoperative fluid protocols. The haemodynamic effects of the two fluid regimens may increase our understanding of the observed perioperative outcomes.

Methods: Stroke volume and cardiac output were measured with both an oesophageal Doppler ultrasound monitor and arterial pressure waveform analysis. Stroke volume variation, pulse pressure variation, and plethysmographic variability index were also obtained. A passive leg raise manoeuvre was performed to identify fluid responsiveness.

Results: Analysis of 105 patients showed that the primary outcome, Doppler monitor-derived stroke volume index, was higher in the liberal group: restrictive 38.5 (28.6–48.8) *vs* liberal 44.0 (34.9–61.9) ml m^{-2}; $P=0.043$. Similarly, there was a higher cardiac index in the liberal group: 2.96 (2.32–4.05) *vs* 2.42 (1.94–3.26) L min^{-1} m^{-2}; $P=0.015$. Arterial-pressure-based stroke volume and cardiac index did not differ, nor was there a significant difference in stroke volume variation, pulse pressure variation, or plethysmographic variability index. The passive leg raise manoeuvre showed fluid responsiveness in 40% of restrictive and 30% of liberal protocol patients (not significant).

Conclusions: The liberal fluid group from the RELIEF trial had significantly higher Doppler ultrasound monitor-derived stroke volume and cardiac output compared with the restrictive fluid group at the end of the intraoperative period. Measures of fluid responsiveness did not differ significantly between groups.

Clinical trial registration: ACTRN12615000125527.

Keywords: cardiac output; fluid responsiveness; fluid therapy; goal-directed fluid therapy; oesophageal Doppler ultrasound; passive leg raise

Editor's key points

- The previous Restrictive *versus* Liberal Fluid Therapy in Major Abdominal Surgery (RELIEF) trial showed evidence for harm in the restrictive i.v. fluid group compared with the liberal group.
- This prospective sub-study of included patients that had oesophageal Doppler cardiac output monitoring analysed intraoperative differences in haemodynamic parameters between these groups.
- Analysis of 109 patients showed that the liberal fluid group had significantly higher Doppler ultrasound

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monitor-derived stroke volume and cardiac output compared with the restrictive fluid group.
- Although modest, these differences may explain the lower rate of acute renal injury in the liberal fluid group, and suggest the importance of haemodynamic monitoring on postoperative outcomes.

The Restrictive *versus* Liberal Fluid Therapy in Major Abdominal Surgery (RELIEF) trial evaluated the effect of perioperative i.v. fluid therapy volumes in 3000 adult patients at higher risk of complications undergoing major abdominal surgery. Participants were randomly assigned to a restrictive (zero fluid balance) or liberal (higher fluid volume) fluid strategy intraoperatively and for the first 24 h after surgery.[1] Disability-free survival up to 12 months after surgery was similar in both groups, but those assigned to the restrictive group had increased acute kidney injury. The predominant maintenance fluid was a balanced crystalloid solution, such as Hartmann's solution. There was a clinically significant difference in the volume of fluid administered; intraoperatively, the median fluid volumes were 6.5 and 10.9 ml kg^{-1} h^{-1} ($P<0.001$) in the restrictive and liberal groups, respectively.

We undertook a prospective sub-study to measure the haemodynamic consequence of the two fluid regimens intraoperatively. Reducing salt and i.v. fluid volume can improve recovery after surgery compared with fluid overload.[2,3] Additionally, a fluid volume load not in the context of hypovolaemia can lead to excess redistribution of i.v. fluid out of the intravascular space and can trigger mechanisms leading to capillary leak.[4] Conversely, fluid restriction may reduce optimal delivery of oxygen, which is important in reducing morbidity associated with fluid imbalance and oxygen debt.[5–7] Amidst the difficult balance of i.v. volume prescription, the perioperative haemodynamic consequences of fluid restriction and liberal fluid therapy remain unclear.[2,3]

There are now many commercial devices that can estimate stroke volume or cardiac output in a minimally invasive manner.[8] Secondly, respiratory variations in pulse pressure, stroke volume, and plethysmographic waveform can predict fluid responsiveness.[9] Finally, a passive leg raise (PLR) manoeuvre has very good predictive value for fluid responsiveness.[10] All these components are recommended as important considerations for titration of i.v. fluid perioperatively and are incorporated in the design of this study to provide a mechanistic basis for observed outcomes published from the RELIEF trial. Our hypothesis was that patients assigned to the liberal fluid group of the RELIEF trial would not have a significantly different stroke volume compared with the restrictive group at the end of the intraoperative fluid protocol.

Methods

We obtained consent prospectively as a pre-planned sub-study of the RELIEF trial (ethics approval number HREC/12/Alfred/58) and registered before recruitment (ACTRN12615000125527). Patients were enrolled before randomisation at three participating centres. Enrolment was contingent on the availability of a study investigator proficient in the haemodynamic protocol and specifically in the use of the oesophageal Doppler ultrasound monitor. Inclusion criteria included any patients eligible for enrolment into RELIEF. Specific exclusions included patients in whom an oesophageal probe could be placed (oesophageal or gastric surgery or oesophageal varices) or an unexpected contraindication to a PLR, such as raised intracranial pressure or severely reduced hip mobility. Patients in whom the anaesthetists intended to use cardiac output monitoring for goal-directed fluid management were excluded, as the main aim of this study was to observe differences between restrictive and liberal fluid arms of the RELIEF trial protocol. The anaesthetic team did not have access to the cardiac output parameters intraoperatively, and the team was instructed to adhere to the RELIEF liberal and restrictive protocol.

Haemodynamic measurements for the sub-study were performed at baseline before surgery and at the end of surgery. To ensure equal fluid volumes between the two groups at the first baseline haemodynamic measurement, the RELIEF trial fluid protocol was varied slightly. Patients assigned to the liberal group had half their protocolised induction bolus of crystalloid (5 ml kg^{-1}) deferred until after the completion of the first haemodynamic measurement to ensure both groups had similar i.v. fluid volumes at baseline. The deferred bolus was given shortly after induction of anaesthesia. No other changes were made to the fluid protocol. As the minimally invasive haemodynamic monitors are not available for use on the surgical wards, this sub-study was only designed to look at the effect of the intraoperative component of the RELIEF fluid protocol, which otherwise extended to 24 h post-surgery.

At the start and end of the intraoperative fluid protocol, a PLR manoeuvre was performed to determine the fluid responsiveness of patients to a reversible transfer of blood from the legs to the central blood volume compartment, measured using the oesophageal Doppler monitor. It has been estimated that a PLR can increase cardiac output by 6% or 0.19 L min^{-1} after 1 min with a greater increase of 11% or 0.6 L min^{-1} in patients with hypovolaemia.[11] Whilst a semi-recumbent PLR manoeuvre is commonly performed in critical care and recommended to mobilise the splanchnic circulation to effect a larger shift in blood volume, this is not feasible intraoperatively, and a review of PLR manoeuvres did not show a reduction in predictive ability in the supine position.[10]

The oesophageal Doppler monitor CardioQ-ODM+™ (Deltex Medical Ltd, Chichester, UK; software version 3.x) measures blood flow velocity in the descending thoracic aorta with stroke volume index (SVI_D) and cardiac index (CI_D) calculated and averaged over 5 beats using a velocity–time integral, an estimation of aortic cross-sectional area and a correction factor that transforms measured descending aortic blood flow into an estimate of global cardiac output.[12] Arterial-pressure-derived parameters were also obtained using the Liljestrand and Zander pulse pressure wave analysis algorithm built into the CardioQ-ODM+.[20] The arterial pressure signal transduced from an arterial cannula in the patient was transmitted to the CardioQ-ODM+ via a slave cable from the anaesthetic monitor, and allowed derivation of arterial-pressure-waveform-derived SVI (SVI_p), CI (CI_P), stroke volume variation (SVV_p), and pulse pressure variation (PPV). Plethysmographic variability index (PVI) was obtained using the Masimo Radical-7® monitor (Masimo SET®; Masimo Corp., Irvine, CA, USA) with a pulse oximeter probe placed on a finger.[13]

Haemodynamic study protocol

Immediately after induction of general anaesthesia with neuromuscular block and positive-pressure ventilation, the

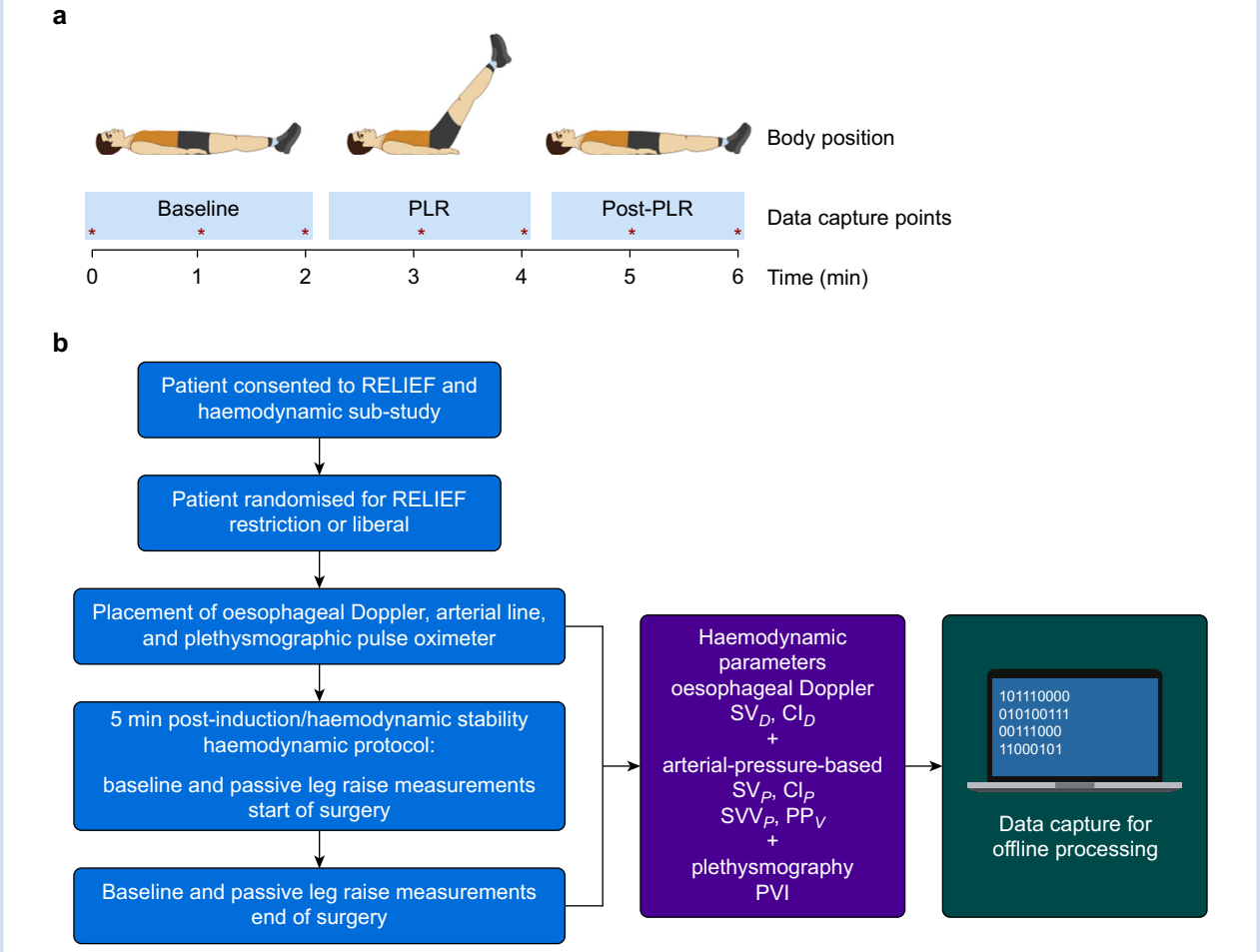

Fig 1. Haemodynamic protocol incorporating a passive leg raise manoeuvre. (a) Haemodynamic variables were recorded during a 6-min protocol at the start and end of surgery. At the 0-, 1-, and 2-min mark, the baseline measurement was taken and analysed as an average. Leg raise was applied from supine to 45 degrees after the 2-min mark. The 'legs up' measurement was taken at 3 and 4 min with the average used for analysis. The legs were placed supine after the 4-min mark. The 'legs down' measurement was taken at the 5- and 6-min marks with the average used for analysis. (b) Data capture and digital recording flow diagram. Haemodynamic parameters were obtained using the oesophageal Doppler monitor CardioQ-ODM+ (Deltex Medical Ltd, Chichester, UK), the Liljestrand and Zander pulse pressure wave analysis algorithm, and Masimo Radical-7 monitor (Masimo Corp., Irvine, CA, USA). CI_D, cardiac index Doppler; CI_P, cardiac index arterial pressure; PLR, passive leg raise 45 degrees; PPV, pulse pressure variation; PVI, plethysmographic variability index; RELIEF, Restrictive Versus Liberal Fluid Therapy in Major Abdominal Surgery; SVI_D, stroke volume index Doppler; SVI_P, stroke volume index arterial pressure; SVV_P, stroke volume variation.

investigator placed an oesophageal Doppler monitor probe. The CardioQ-ODM+ was connected and monitoring started after registration of patient details and optimisation of the Doppler waveform. There were two PLR manoeuvres; the first was after induction of anaesthesia and before surgical incision, and the second was at the end of surgery before emergence and tracheal extubation.

The monitoring protocol consisted of three baseline measurements in the first 2 min in the supine position, two measurements in the next 2 min with the legs lifted at 45 degrees, and two measurements in the next 2 min with the legs down in the supine position (Fig. 1). The protocol was designed to detect changes in cardiac output from a PLR within an acceptable time interval and in a supine position, which is practical and has been shown to be able to predict fluid responsiveness.[14] A safe and stable arterial pressure without need for vasoactive drug administration and stable anaesthesia depth was required for the haemodynamic protocol. Ventilator tidal volume during the protocol was increased, where practical, to 8 ml kg^{-1} to a maximum of 800 ml.

Statistical analysis

The primary hypothesis was to detect a difference in SVI (SVI_D) as measured with the oesophageal Doppler monitor between the two treatment groups, restrictive and liberal, at the end of the intraoperative fluid protocol. We calculated a sample size of at least 47 patients in each group to detect a difference in SVI of 20% (alpha 0.05; power 0.80) from a baseline average of 43 (14) ml m^{-2}, which was observed in a recent trial of goal-

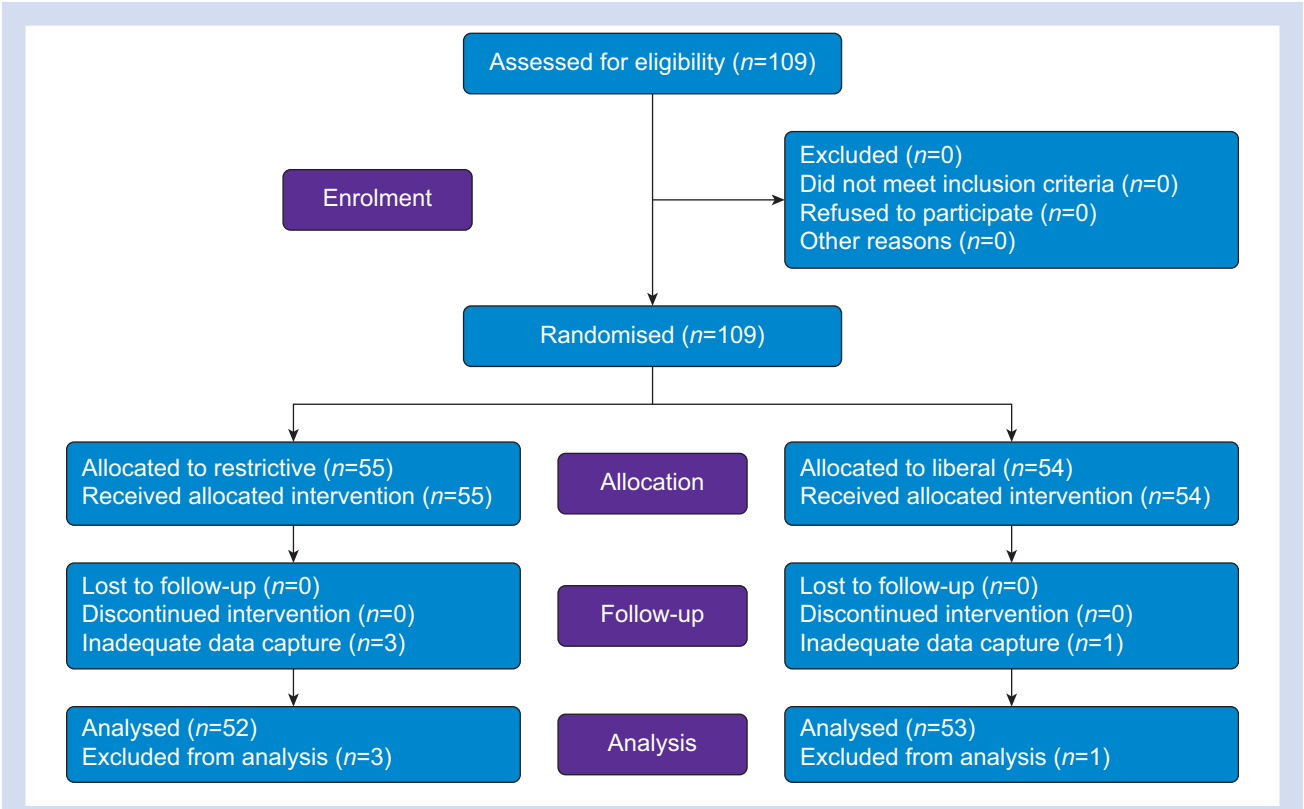

Fig 2. Consolidated Standards of Reporting Trials (CONSORT) diagram for the study of the effect of fluid strategy on stroke volume, cardiac output, and fluid responsiveness in adult patients undergoing major abdominal surgery.

directed fluid therapy in colorectal resection surgery.[15] This represents a clinically relevant increase in stroke volume that is sufficiently high to observe changes over the inherent variance associated with cardiac output monitoring. We planned to recruit 108 patients to allow for dropouts and exclusions, such as technical difficulties with data collection or other sources of data attrition.

As most of our continuous variables were not normally distributed (Shapiro–Wilk normality test), we present results as medians (inter-quartile ranges [IQRs]) with analysis using the Mann–Whitney test for comparisons between groups and Wilcoxon matched-pairs test for within-group comparisons between the start and end of surgery. Fisher's exact test was used to compare proportions of patients who were fluid responsive. Statistical analysis was performed using Stata™ v14 (Stata Corp. LP, College Station, TX, USA).

Results

Of 109 patients consented prospectively for the haemodynamic study across three centres (Fig. 2), the haemodynamic protocol was performed and adequate data were available in 105 patients for analysis. Baseline patient characteristics and data are presented in Table 1. Haemodynamic results are presented in Table 2.

The intraoperative fluid protocol resulted in lower mean intraoperative fluid volume in the restrictive group (7.06 [5.60–8.60] ml kg^{-1} h^{-1}) compared with the liberal group (10.7 [9.56–13.0] ml kg^{-1} h^{-1}; $P<0.001$). There were similar rates of vasoactive medication use intraoperatively for the restrictive (92%) and liberal (86%) groups ($P=0.322$).

Primary outcome SVI_D

Doppler-monitor-derived SVI (SVI_D) values were comparable between groups at the start of surgery (Table 2; Fig. 3a). At the end of surgery and the completion of the intraoperative fluid protocol, SVI_D was significantly lower in the restrictive group (38.5 [28.6–48.8] ml m^{-2}) (median [IQR]) compared with the liberal group (44.0 [34.9–61.9] ml m^{-2}; $P=0.043$).

Within the restrictive group, no difference was found between SVI_D at the start and end of surgery (35.2 [28.9–44.9] ml m^{-2} *vs* 38.5 [28.6–48.8] ml m^{-2}; $P=0.139$). In the liberal group, there was an increase in SVI_D at the end of surgery (39.6 [29.8–47.1] *vs* 44.0 [34.9–61.9] ml m^{-2}; $P<0.001$).

Secondary outcomes

The Doppler CI (CI_D) was higher at the end of the intraoperative fluid protocol in the liberal group (2.42 [1.94–3.26] *vs* 2.96 [2.32–4.05] L min^{-1} m^{-2}; $P=0.015$). There was no significant difference between groups at the beginning of surgery (Table 2; Fig. 3b).

Liljestrand and Zander's algorithm for arterial-pressure-based stroke index (SVI_p) and CI (CI_p) did not differ significantly between the two groups at the end of surgery. Respiratory-induced parameter variations were only analysed for patients with tidal volumes ≥8 ml kg^{-1} ideal body weight.

Table 1 Baseline patient characteristics and data. IQR, interquartile range; PMCC, Peter MacCallum Cancer Centre; SVH, St Vincent's Hospital

	Restrictive, median (IQR), N=53	Liberal, median (IQR), N=52
Age (yr)	67.5 (59–74)	66 (57–73)
Male sex (%)	50	58.5
Height (cm)	167.5 (161–174.5)	168 (161–176)
Preoperative weight (kg)	85 (78.5–100)	85 (70–105)
Tidal volume per weight (ml kg^{-1})	6.52 (5.30–7.66)	6.67 (5.58–7.71)
Tidal volume per ideal weight (ml kg^{-1})	9.26 (7.41–10.31)	9.10 (7.56–10.51)
Blood loss (ml)	200 (100–400)	250 (150–500)
Urine output (ml)	300 (150–500)	450 (300–700)
Surgical duration (h)	3.10 (2.73–4.36)	3.98 (2.92–4.57)
Total intraoperative fluid volume (ml kg^{-1} h^{-1})	7.06 (5.60–8.60)	10.7 (9.56–13.0)
ASA physical status 1/2/3/4	1/13/36/2	0/9/43/1
Hospital: Austin, SVH, PMCC	14/87/4	
Disability-free survival at 12 months, *n* (%)	47 (89)	48 (94)
Mortality 12 months	3	3
Sepsis all cause, *n* (%)	6 (11)	1 (2)
Anastomotic leak	1	0
Renal replacement therapy	1	0
Creatinine highest at Day 3 (mM)	65 (53–91)	72 (51–79)
Lactate highest at Day 1 (mM)	1.25 (0.8–2.55)	1.75 (1.25–2.18)

Stroke volume (SVV_P), PPV, and PVI were not significantly different between groups at the start or end of surgery.

A threshold of change in SVI_D >10% after a PLR manoeuvre was deemed an indicator of fluid responsiveness. At the end of surgery, 40% of patients in the restrictive group and 30% of patients in the liberal group showed fluid responsiveness without a significant difference between groups: mean difference 10% (95% confidence interval: 28% to −8.0%); P=0.31.

Discussion

We found haemodynamic differences between the restrictive and liberal fluid therapy groups at the end of surgery in this sub-study of the RELIEF trial. The primary outcome, Doppler monitor-derived SVI, was 14% higher in the liberal group compared with the restrictive group at the end of surgery. A comparable increase (22%) also occurred in Doppler monitor-derived CI. Whilst modest, the increased SVI and CI in the liberal group may offer an explanation for the observed decreased rate of acute renal injury, 8.6% in the restrictive fluid group and 5.0% in the liberal fluid group (P<0.001), and possible decreased rate of surgical-site infection (16.5% *vs* 13.6%; P=0.02 unadjusted).[1] These complications have been reduced in studies targeting an optimised haemodynamic state or macrocirculation using cardiac output monitoring.[7] Although stroke volume and CI are important, a complete picture of hypoperfusion should also include measures of the microcirculation, such as lactate.[16,17]

The SVI and CI observed in the liberal group were similar to an optimised haemodynamic profile reported previously with goal-directed fluid therapy. The CI at the end of the liberal fluid therapy protocol of 2.96 L min^{-1} m^{-2} is similar to that of optimised patients undergoing goal-directed fluid therapy with the oesophageal Doppler in a previous study of 3.1 L min^{-1} m^{-2}.[7] This study of 450 adult patients undergoing major abdominal surgery found a reduced risk of complications with goal-directed fluid therapy compared with controls. The observed increases in SVI and CI in the liberal group lead to increased perfusion in regional circulations sensitive to hypovolaemia, such as the splanchnic system. In patients undergoing cardiac surgery, a modest but significantly higher cardiac output with Doppler-monitor-guided goal-directed fluid therapy compared with controls (5.6 *vs* 6.6 L min^{-1}) was associated with reduced gut mucosal hypoperfusion and reduced risk of complications.[18]

Nevertheless, the differences between treatment groups in final stroke volume and cardiac output were modest in our study. This is arguably consistent with a pragmatic trial design for the RELIEF trial, where there was a similarly modest, but significant additional volume of fluid in the liberal group compared with the restrictive group. Disability-free survival was not different between the liberal and restrictive groups in RELIEF, and any improvement in cardiac output in the liberal group did not therefore confer an overall survival benefit. Recent studies specifically targeting an increased cardiac output using goal-directed fluid therapy have been unable to replicate improvements in morbidity convincingly despite an optimised haemodynamic state either with the Doppler cardiac monitor or an arterial-pressure-derived monitor.[6,15,19]

Stroke volume and cardiac output measured by the arterial pressure algorithm of Liljestrand and Zander, incorporated within the ODM+ monitor, showed no significant difference between the restrictive and liberal groups. Whilst the performance of this algorithm is better than MAP at quantifying cardiac output and detecting direction of changes in cardiac output (78% concordance), it nevertheless has wide limits of agreement in comparison with a thermodilution standard and may not have the ability to track smaller changes in cardiac output.[20] It should be noted that the arterial pressure algorithm (Liljestrand and Zander) may not be comparable directly with commercially available technologies, for example Vigileo FloTrac™ (Edwards Lifesciences, Irvine, CA, USA) or LiDCOrapid™ (LiDCO Pty Ltd, Cambridge, UK) that use their own proprietary algorithms. However, concordance of the aforementioned commercial arterial-pressure-derived cardiac output monitors with the ODM-measured cardiac output has been shown to be limited, at around 61–70%.[21] We observed that the arterial-pressure-based SVI did not reflect a difference between the SVI of the two fluid regimens that was demonstrated with the oesophageal Doppler SVI at the end of surgery.

Positive-pressure-ventilation-induced variations in stroke volume and pulse pressure are used in anaesthesia and critical care as predictors of fluid responsiveness, with a grouped cohort threshold to predict fluid responsiveness of ~12.5% and 11.6%, respectively, and are considered superior to conventional and static measures, such as central venous

Table 2 Haemodynamic data (n=73–105). CI_D, cardiac index Doppler; CI_P, cardiac index arterial pressure; IQR, inter-quartile range; PPV, pulse pressure variation; PVI, plethysmographic variability index; SVI_D, stroke volume index Doppler; SVI_P, stroke volume index arterial pressure; SVV_P, stroke volume variation. *Wilcoxon matched-pairs test. †Mann–Whitney test

	Restrictive median	IQR	Within group*	Liberal median	IQR	Within group*	Between group†
SVI_D start (ml m^{-2})	35.2	28.9 –44.9	0.139	39.6	29.8 –47.1	<0.001	0.352
SVI_D end	38.5	28.6 –48.8		44.0	34.9 –61.9		0.043
CI_D start (L min^{-1} m^{-2})	2.26	1.86 –2.78	0.114	2.30	1.80 –3.27	<0.001	0.780
CI_D end	2.42	1.94 –3.26		2.96	2.32 –4.05		0.015
SVI_P start (ml m^{-2})	36.9	26.4 –43.6	0.706	35.7	29.4 –46.3	0.878	0.532
SVI_P end	35.9	26.6 –50.6		43.5	28.1 –52.5		0.226
CI_P start (L min^{-1} m^{-2})	2.27	1.83 –2.93	0.789	2.46	2.00 –3.18	0.823	0.277
CI_P end	2.28	1.70 –3.61		2.79	1.83 –3.66		0.104
	Haemodynamic values only with tidal volume ≥8 ml kg^{-1} ideal body weight (n=48–68)						
SVV_P start (%)	10.33	7.22 –12.9	0.144	8.05	4.95 –11.9	0.50	0.522
SVV_P end	10.43	10.1 –14.3		8.20	6.17 –10.6		0.144
PPV start (%)	10.7	8.75 –13.4	0.225	11.3	6.6–16.6	0.173	0.935
PPV end	11.9	10.3 –18.1		8.08	3.93 –16.1		0.150
PVI start (%)	13.3	10.7 –17.8	0.273	8.83	3.83 –14.2	0.735	0.174
PVI end	17.2	14.5 –20.7		9.83	5.83 –15.8		0.074

pressure.[16,22] Landsdorp and collegues[23] demonstrated very good predictive value of PPV for fluid responsiveness only when tidal volumes were >7 ml kg^{-1} after analysing 47 fluid bolus events in 29 patients with a reduction in predictive ability at lower tidal volumes.[23] After limiting the analysis of PPV and SVV to patients ventilated at a tidal volume ≥8 ml kg^{-1} ideal body weight, our study had a similar number of events and did not reveal significant differences between the liberal and restrictive groups. At the start and end of surgery, PPV for both liberal and restrictive groups in our study ranged between 8% and 11%. Larger numbers would be required to draw any conclusions about differences between the two groups.

The least invasive fluid responsive parameter, PVI, did not differ between the liberal and restrictive groups either at the start or at the end of surgery. With an average value of 8–10% across the two fluid groups, this is below most thresholds demonstrated for fluid responsiveness, although there are now a wide range of published cut-off values of between 9.5% and 17%.[24] The respiratory variations in pulse pressure, stroke volume, and plethysmographic waveform show that mean values of both groups are within the range of fluid responsive thresholds, as published in earlier studies. However, interpretation of fluid responsiveness based on a single threshold is not recommended, as there can be diagnostic uncertainty within a diagnostic grey zone, where either sensitivity or specificity can be too low in up to 25% of patients.[25] Secondly, the optimal diagnostic predictive ability of dynamic parameters may not be replicated in clinical settings as demonstrated in an analysis of SVV and PPV in 100 patients receiving goal-directed fluid therapy as part of the Optimisation of Perioperative Cardiovascular Management to Improve Surgical Outcome (OPTIMISE) study. That study found that PPV and SVV had a poor ability to predict fluid responsiveness (SVV 0.69 [0.63–0.77]; PPV 0.70 [0.62–0.77]) and cautioned against using these parameters primarily as the endpoint of fluid resuscitation.[26]

A PLR manoeuvre has been recommended to have a high diagnostic performance in the prediction of fluid responsiveness, and as a result, it was incorporated as a key part of this study.[10,27] It can also be utilised in the presence of spontaneously ventilating patients and in the presence of arrhythmias. Although there are many studies in critical care patients and after cardiac surgery, intraoperative general surgery is largely unexplored. At the end of surgery, the percentage of patients who were fluid responsive, based on a change in Doppler-derived SVI of >10% after a PLR, was not significantly different (40% in the restrictive group and 30% in the liberal group). Although it is certain that a larger study would have more power to detect such a difference, this study of 108 patients is one of the largest cohorts of patients with cardiac output monitoring during a PLR. This study used a PLR from a supine position that would mobilise a smaller blood volume

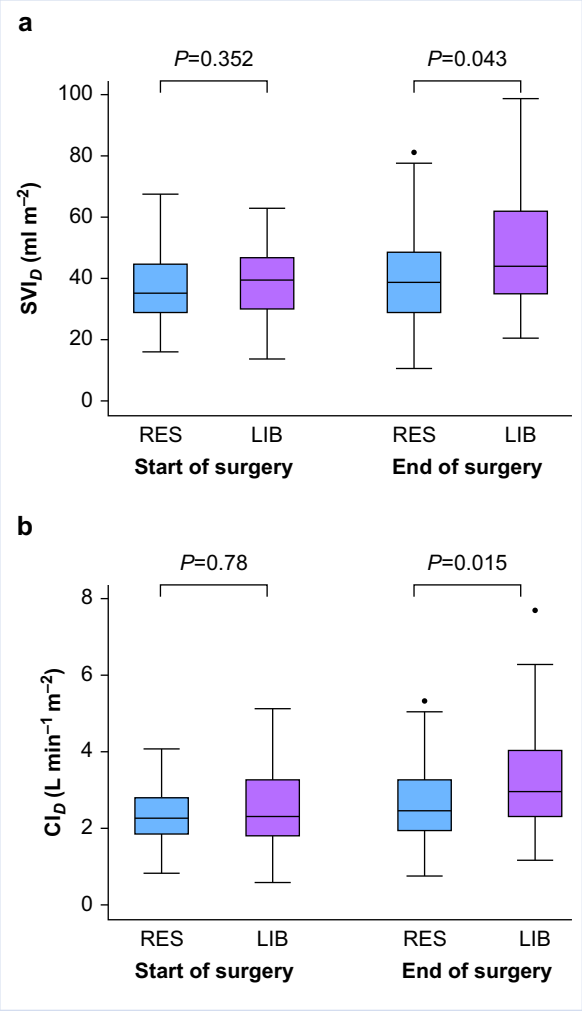

Fig 3. Doppler-derived stroke volume index and cardiac index. (a) SVI was compared between restrictive (n=52) and liberal (n=51) fluid groups at the start and end of surgery. The baseline reading, representing three time points over 2 min and before the passive leg raise, was used for analysis. Data are presented as a box plot and analysed for difference between groups, Mann–Whitney test. (b) Cardiac index was compared between restrictive (n=52) and liberal (n=52) fluid groups at the start and end of surgery. The baseline reading, representing three time points over 2 min and before the passive leg raise, was used for analysis. Data are presented as a box plot and analysed for difference between groups, Mann–Whitney test. CI_D, cardiac index Doppler; LIB, grey box; RES, white box; SVI_D, stroke volume index Doppler.

shift than a semi-recumbent position, which unfortunately is impractical in an intraoperative setting.

There are some points of caution in extrapolating this haemodynamic study to the larger RELIEF cohort. This substudy represents a smaller cohort of 109 patients enrolled in the RELIEF study of 3000 patients, and the findings are limited to exploring the haemodynamic mechanisms related to the outcomes of the whole group. Secondly, only the intraoperative component of the RELIEF trial was studied, excluding the postoperative component of the fluid protocol that continued for 24 h postoperatively. The logistics and cost of studying patients using a number of different cardiac output technologies limited the number of patients that could be enrolled. It was also not feasible to deploy the oesophageal-Doppler- or arterial-pressure-based algorithms postoperatively, as it would have required general anaesthesia and an arterial line, respectively, when most patients are on the ward.[28] Nevertheless, the intraoperative fluid protocol gave rise to a significant difference in fluid volumes between groups, leading to a significant change in the stroke volume.

Conclusions

A more liberal i.v. fluid strategy for adult patients undergoing major abdominal surgery resulted in a higher stroke volume and CI, as measured by oesophageal Doppler, at the end of surgery. However, pulse pressure, stroke volume, plethysmographic waveform respiratory variations, and a passive leg raise manoeuvre did not reveal significant differences in fluid responsiveness between the two groups at the end of surgery.

Authors' contributions

Study design: TDP, PJP
Patient recruitment: TDP, YU, PJP
Data collection: TDP, YU, PJP
Data analysis: TDP, RK, PJP, PSM
Preparation of paper: all authors.

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Declarations of interest

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