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Review Article

REVIEW ARTICLE

Perioperative goal-directed therapy with uncalibrated pulse contour methods: impact on fluid management and postoperative outcome

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Abstract

Previous meta-analyses suggest that perioperative goal-directed therapy (GDT) is useful to decrease postoperative morbidity. Most GDT studies analysed were done with pulmonary artery catheters, oesophageal Doppler and calibrated pulse contour methods. Uncalibrated pulse contour (uPC) techniques are an appealing alternative but their accuracy has been questioned. The effects of GDT on fluid management (volumes and volume variability) remain unclear. We performed a meta-analysis of randomized controlled trials investigating the effects of GDT with uPC methods on postoperative outcome. The primary endpoint was postoperative morbidity. Fluid volumes and fluid volume variability (standard deviation/mean) over the GDT period were also studied. Nineteen studies met the inclusion criteria (2159 patients). Postoperative morbidity was reduced with GDT (OR 0.46, 95% CI 0.30–0.70, $P<0.001$). The volume of colloids was higher [weighted mean difference (WMD) +345 ml, 95% CI 148–541 ml, $P<0.001$] and the volume of crystalloids was lower (WMD –429 ml, 95% CI –634 to –224 ml, $P<0.01$) in the GDT group than in the control group. However, the total volume of fluid (WMD –220 ml, 95% CI –590 to 150 ml, $P=0.25$) and the variability of fluid volume (34% *vs* 33%, $P=0.98$) were not affected by GDT. The use of GDT with uPC techniques was associated with a decrease in postoperative morbidity. It was not associated with an increase in total fluid volume nor with a decrease in fluid volume variability.

Key words: cardiac output; general surgery; haemodynamics

Many studies suggest that perioperative goal-directed therapy (GDT) is useful to decrease postoperative morbidity, hospital length of stay and hospital costs.[1–3] As a result, in patients undergoing major surgery, the use of GDT is now recommended by several guidelines and consensus statements from international experts.[4–7] The first perioperative GDT studies were done 20–30 yr ago with the pulmonary artery catheter.[8–10] Then, other studies followed where haemodynamic parameters were derived from the oesophageal Doppler[11 12] or from calibrated pulse contour methods.[13 14] Uncalibrated pulse contour (uPC) methods are relatively new in the GDT arsenal since they became available only a decade ago.[15] They are quick to set up, easy to use, not operator dependent, not affected by electrocautery and are increasingly used for haemodynamic monitoring during major surgery.[16] However, their accuracy and precision have been questioned when compared with clinical

reference methods, such as thermodilution and echocardiography.[17–20] Whether uPC techniques can be useful to guide haemodynamic therapy and improve post-surgical outcome has been investigated by several randomized controlled trials (RCTs) yielding conflicting results.

Both insufficient and excessive fluid administration are associated with an increase in postoperative complications.[21 22] Optimizing haemodynamic parameters such as stroke volume and cardiac output with fluid may result, at least in theory, in excessive fluid administration. In addition, recent studies have reported a very large variability in the volume of fluid administered to surgical patients during the perioperative period.[22 23] By analogy with manufacturing and the Six Sigma concept, it has been suggested that variability of clinical practices is the enemy of quality of care,[24] and that the beneficial effects of GDT may be related to the harmonization of fluid management.[25 26] Therefore, we performed a meta-analysis of RCTs to clarify the impact of GDT with uPC methods on postoperative morbidity, on fluid volume and on fluid volume variability.

Methods

Eligibility criteria

According to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA), studies were searched using the following eligibility criteria.[27] Participants were adult (age 18 yr or over) patients undergoing elective or emergency surgery. Studies involving mixed population of critically ill or non-surgical patients were excluded. The intervention was defined as GDT with uPC methods. RCTs comparing the effects of GDT *vs* standard or usual fluid management were considered for analysis. No language (i.e. article in English), publication date or publication status restrictions were imposed when selecting the studies to be analysed. Primary outcome measure was post-surgical morbidity, defined as the proportion of patients developing one or more post-surgical complications. Post-surgical infectious, cardiac, respiratory, renal and abdominal complications, as well as hospital length of stay and mortality, were assessed as secondary outcome variables. Abdominal complications included both gastro-intestinal and liver complications. The volume of crystalloids and of colloids, as well as the total volume of fluid received during the GDT period were also analysed.

Information sources

Various search strategies were performed to retrieve relevant studies by using MEDLINE, the Cochrane Library and EMBASE databases (last update January, 2016). No date restriction was applied for MEDLINE and The Cochrane Library databases whereas the search was limited to 2006–16 for the EMBASE database. Additional trials were searched in the DARE database and the reference lists of previously published reviews and retrieved articles.

Search

We used the following terms to search for studies: randomized controlled trial, controlled clinical trial, goal directed, goal oriented, goal target, cardiac output, cardiac index, oxygen delivery, oxygen consumption, cardiac volume, stroke volume, fluid therapy, fluid loading, fluid administration, optimization, optimisation, pulse pressure variation, pleth variability index, stroke volume variation, systolic pressure variation (see Supplementary data S1 for details regarding the search strategy).

Study selection

Two investigators (N.B., M.T.G.) first examined each title and abstract to identify potentially relevant articles. The eligibility of the retrieved full-text articles was independently determined by two investigators (N.B., F.M.). The analysis was limited to trials done with uPC methods.

Data collection process

Data were independently collected by two investigators (M.T.G., F.M.) with any discrepancy resolved by re-inspection of the original article. To avoid transcription errors, the data were inputted into statistical software and re-checked by a third investigator (N.B.).

Data items

Data abstraction included type of surgery, number of patients, type of uPC method, GDT protocol end-points, postoperative morbidity, complications, mortality and hospital length of stay. The volume of colloid and crystalloid solutions administered during the GDT period was also collected. When information was not found in original manuscripts, authors were contacted to maximize the number of data available for analysis.

Risk of bias in individual studies

A domain-based evaluation, as proposed by the Cochrane Collaboration,[28] was used to evaluate the methodological quality of RCTs. This is a two-part tool, addressing seven specific domains (sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and 'other issues') that are strongly associated with bias reduction.[29 30] Each domain in the tool includes one or more specific entries in a 'Risk of bias' table. Within each entry, the first part of the tool describes what is reported in the study, in sufficient detail to support a judgment about the risk of bias. The second part of the tool assigns a judgment relating to the risk of bias for that entry. This is achieved by assigning a judgment of 'Low risk', 'High risk' or 'Unclear risk' of bias. After each domain was completed, a 'Risk of bias summary' table was generated. The green symbol plus indicates low risk of bias, the red minus symbol indicates high risk of bias and the white colour indicates unclear risk of bias. For each study, the total number of green plus symbols was calculated: trials with five or six green plus symbols were considered as having an overall low risk of bias. With regard to blinding, studies in which the outcome variables were collected by investigators not aware of the GDT strategy were considered adequately masked.

Summary measures and planned method of analysis

Meta-analytic techniques (analysis software RevMan, version 5.3 Cochrane Collaboration, Oxford, England, UK) were used to combine studies using Odds Ratios (OR) and 95% confidence intervals (CI) for dichotomous variables, and weighted mean difference (WMD) and 95% CI for continuous variables. A statistical difference between groups was considered to occur if the pooled 95% CI did not include 1 for the OR. An OR <1 favoured GDT when compared with standard haemodynamic treatment. Two-sided

P-values were calculated. Statistical heterogeneity and inconsistency were assessed by using the Q and I^2 tests, respectively. When the P-value of the Q test was <0.10 and/or the I^2 was >40%, heterogeneity and inconsistency were considered significant. Both random-effects and fixed-effects models were used for analyses. Random-effects model results are presented in the abstract and figures whereas fixed-effects model are reported and compared in the supplementary data. For the primary outcome (postoperative morbidity), a sensitivity analysis was performed by focusing on studies with a low risk of bias, on studies where cardiac output was used as a target parameter, and on studies where the total fluid volume was <5 litres. A trial sequential analysis was also performed to adjust for random error risk. We calculated information size and monitoring boundary anticipating a 30% relative risk reduction in postoperative morbidity with GDT. We set risk of type I at 5% and power at 80%.

Coefficients of variability of fluid volume were calculated as standard deviation/mean, expressed as a percentage, and compared using a Student's t-test. When mean and standard deviation values were not reported in original manuscripts and not provided when authors were contacted, they were estimated from median and inter-quartile values as previously described.[31]

Results

Study selection

The search strategy identified 3312 (MEDLINE), 9858 (Cochrane Library) and 2212 (EMBASE) articles. Fourteen articles were identified from the reference list of other articles. After initial screening and subsequent selection, a pool of 102 potentially relevant trials was identified. The subsequent eligibility process excluded 83 articles. Overall, 19 articles with a total sample of 2159 patients, were considered for analysis (see Supplementary data Figure S2).

Study characteristics

All studies were published between 2008 and 2015[32–49] (Table 1). The risk of bias assessment revealed that eight out of 19 studies were considered as having a low risk of bias (see Supplementary data Table S3).

Postoperative outcome

The number of patients with one or more postoperative complications was significantly reduced by GDT, when using both a random-effects (Fig. 1) or a fixed-effects model analysis (see Supplementary data Table S4). It also decreased significantly in the GDT group when focusing on studies with a low risk of bias, on studies where cardiac output was used as a target variable, and on studies where the total volume of fluid was <5 litres (see Supplementary data Table S5). In the trial sequential analysis, the cumulative z curve crossed the monitoring boundary before reaching the information size, indicating firm evidence that GDT reduced postoperative morbidity[50 51] (Fig. 2).

A significant reduction in infectious, cardiac and abdominal complications was observed in favour of GDT, when using both the random-effects and the fixed-effects models (see Supplementary data Table S4). Renal and respiratory complications, as well as mortality, were not significantly reduced by GDT (see Supplementary data Table S4). Hospital length of stay tended to decrease (–1.35 days, CI −2.78 to −0.08 days, P=0.06).

Fluid management

Patients in the GDT group received more colloid (Fig. 3) and less crystalloid (Fig. 4) than patients from the control group. The total volume of fluid was not significantly different between the GDT and the control group when using the random-effects model (Fig. 5), and was significantly lower in the GDT group

Table 1 Characteristics of studies analysed. HIPEC, hyperthermic intraperitoneal chemotherapy; AAA, abdominal aortic aneurysm; LiDCOr, LiDCO rapid; SVV, stroke volume variation in %; PPV, pulse pressure variation in %; SVI, stroke volume index in ml m^{-2}; CI, cardiac index in l min^{-1} m^{-2}; SVplateau, stroke volume corresponding to the plateau of the Frank–Starling relationship; DO_2I, oxygen delivery index in ml min^{-1} m^{-2}; $ScvO_2$, central venous oxygen saturation in % SVR, systemic vascular resistance; CO, cardiac output

First author (ref)	Surgery, *n*	uPC method	Haemodynamic goals
Benes[32]	Abdominal and vascular, 120	FloTrac	SVV<10, CI > 2.5
Cecconi[33]	Hip, 40	FloTrac	SVplateau, DO_2I > 600
Colantonio[34]	HIPEC, 80	FloTrac	SVV<15, SVI>35, CI > 2.5
Correa-Gallego[35]	Liver, 135	FloTrac	SVV<15
Funk[36]	AAA, 40	FloTrac	SVV<13, CI > 2.2
Hand[37]	Head and neck, 94	FloTrac	SVV<13, CI > 3, SVR>800
Kapoor[38]	Cardiac, 27	FloTrac	SVV<10, SVI>30, CI > 2.5, $ScvO_2$>70, DO_2I > 450
Lai[39]	Abdominal, 220	LiDCOr	SVV<10
Mayer[40]	Abdominal, 60	FloTrac	SVV<12, SVI>35, CI > 2.5
Pearse[2]	Abdominal, 734	LiDCOr	SVplateau
Peng[41]	Orthopaedic, 80	FloTrac	SVV<10 (supine) or < 14 (prone)
Poso[42]	Bariatric, 50	FloTrac	SVV<12, SV and CO > 70% of baseline
Ramsingh[43]	Abdominal, 38	FloTrac	SVV<12
Salzwedel[44]	Abdominal, 160	ProAQT	PPV<10, CI > 2.5
Scheeren[45]	Abdominal, 64	FloTrac	SVV<10
Van der Linden[46]	Vascular, 37	FloTrac	CI > 2.5
Zeng[47]	Abdominal, 60	FloTrac	8<SVV<13
Zhang[48]	Thoracic, 60	FloTrac	SVV<11, CI > 2.5
Zheng[49]	Abdominal, 60	FloTrac	SVV<12, SVI>35, CI > 2.5

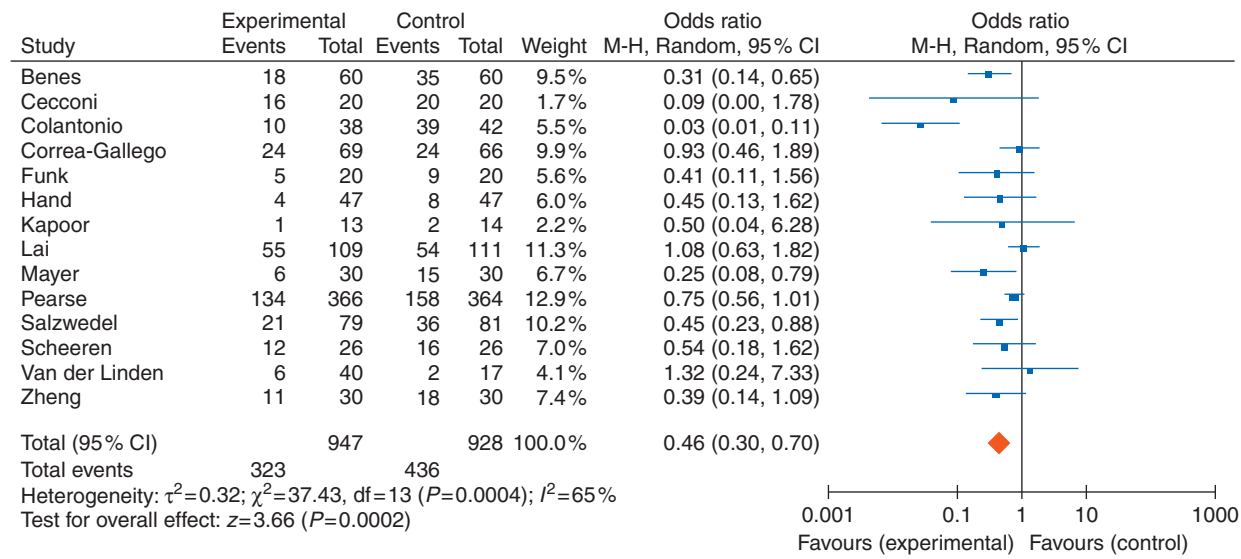

Fig 1 Forest plot for postoperative morbidity (defined as the proportion of patients who developed one or more complications)

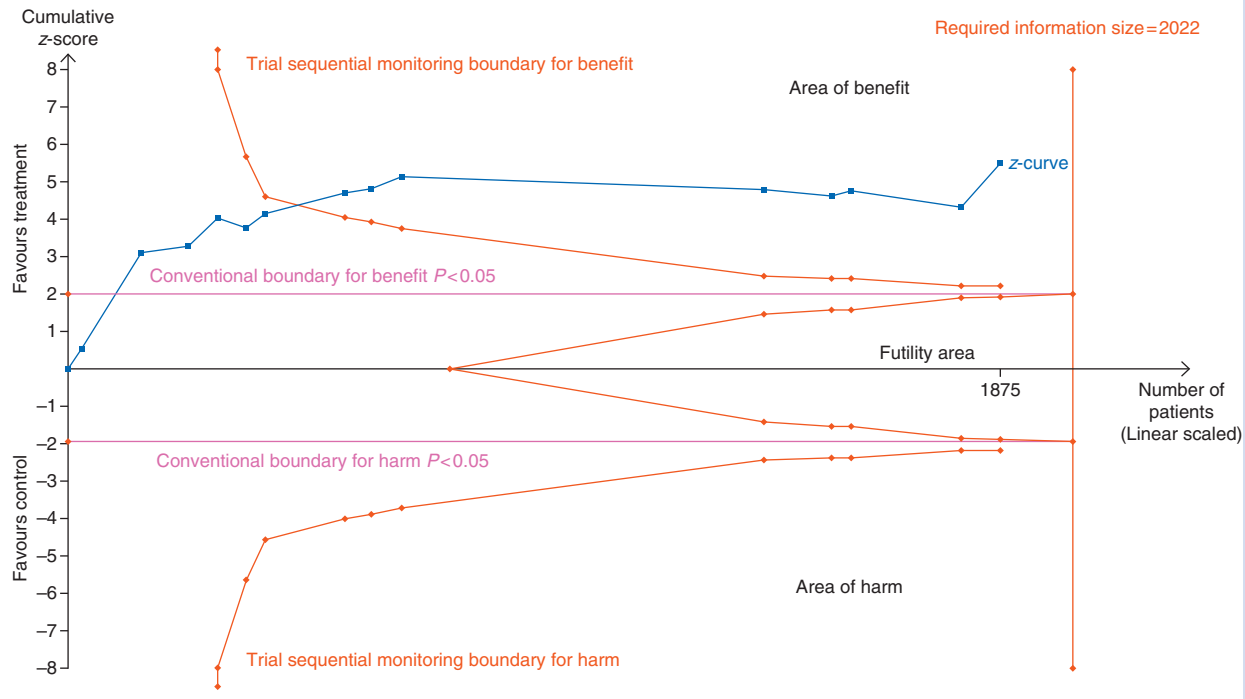

Fig 2 Trial sequential analysis

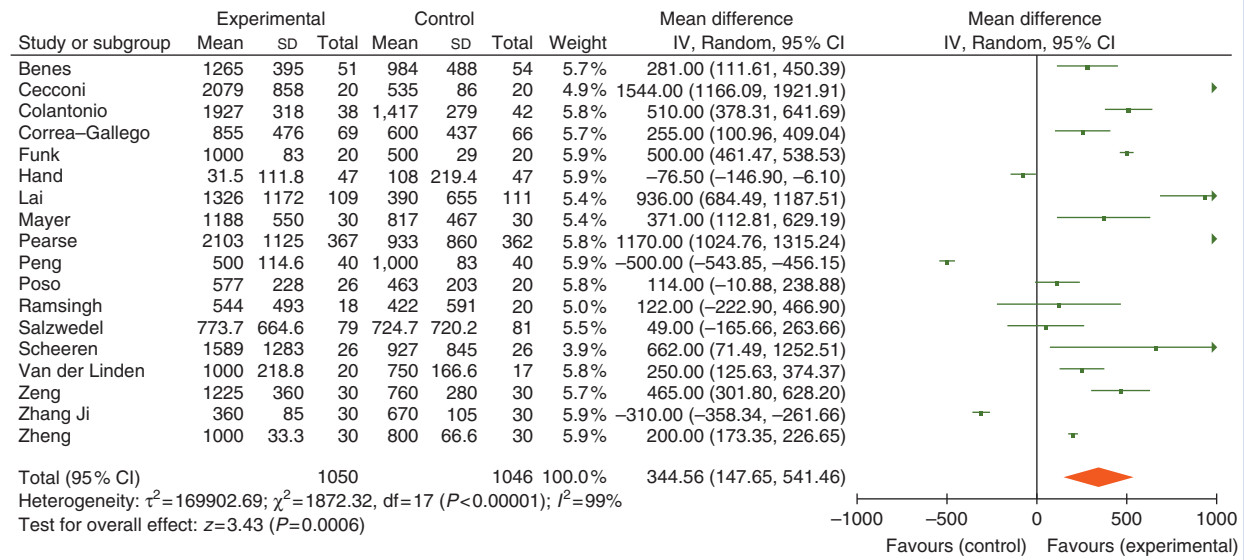

Fig 3 Forest plot for colloid volumes in ml

when using the fixed-effects model (see Supplementary data Table S4). Variability of fluid volume was 34% in the GDT group and 33% in the control group (P=0.98) (Fig. 6).

Discussion

Our meta-analysis shows that the use of GDT with uPC methods is associated with a significant decrease in postoperative morbidity. This effect was mainly related to a decrease in infectious, cardiac and abdominal complications. It was associated with a non-significant reduction in hospital length of stay (–1.35 days, P=0.06) and no change in mortality (2.6% *vs* 2.8%). These findings are consistent with results from previous meta-analyses where more complex and/or more invasive cardiac output monitoring technologies, such as pulmonary or transpulmonary thermodilution, oesophageal Doppler and saline- or lithium-calibrated pulse contour methods,[1–3 52 53] were used for GDT. On one hand, the accuracy and precision of uPC methods has been questioned in patients with high cardiac output and low systemic vascular resistance, such as patients with septic shock receiving vasopressors or patients undergoing liver transplantation.[19 54] On the other hand, uPC methods have been shown to be more reliable in patients undergoing surgery,[55] in particular to track haemodynamic changes during fluid loading.[56] A recent sub-analysis of the large EUSOS study[16] showed that uPC methods became in a few years the preferred choice of European clinicians for haemodynamic monitoring in non-cardiac surgical patients. Our meta-analysis is the first to suggest that, despite their limitations, uPC methods are useful to guide haemodynamic management and improve the postoperative outcome of patients undergoing major surgery.

Another important and new finding of our meta-analysis is that the total volume of fluid administered during the study period did not increase with the use of GDT. Patients received more colloids, but less crystalloids, so that the total volume of fluid was not significantly different between the control and the GDT group when using the random-effects model, and lower with GDT when using the fixed-effects model. This finding goes against the perception or the fear that using haemodynamic optimization protocols may be associated with excessive fluid administration. As a matter of fact, GDT protocols significantly evolved over time from the maximization of oxygen delivery proposed almost 30 years ago by Shoemaker and colleagues[8] to more individualized approaches restricting fluid administration to fluid responders only.[44 45] Because we focused on studies done with uPC methods, which were not available on the market before 2006, our analysis was limited to recent GDT studies (all were published from 2008). This also contributes to the originality of our work, which gives information about the effects of GDT in the era of individualized fluid titration rather than at the time of aggressive haemodynamic strategies.

Recent studies have reported a large intra- and inter-variability of perioperative fluid volumes. In a database study involving 5912 patients undergoing abdominal surgery, Lilot and colleagues[23] showed that a patient weighing 75 kg who had a 4 h procedure with 400 ml blood loss and 1 ml kg^{-1} h^{-1} urine output may have received anything between 700 and 5400 ml of crystalloid depending on the anaesthesiologist in charge. Thacker and colleagues[22] also reported a large variability in fluid volumes in over 650 000 patients undergoing abdominal and orthopaedic surgeries, and suggested that it may be responsible, at least in part, for postoperative adverse events. It has therefore been suggested that reducing variability with GDT protocols may be a way to improve postoperative outcome.[22 26] Our meta-analysis suggests that the use of GDT is not associated with a reduction in the variability of fluid volume. Actually, the easiest way to decrease variability would be to give the exact same volume of fluid with an infusion pump to all surgical patients (e.g. 5 or 10 ml kg^{-1} h^{-1}). However, it is unlikely that one size could fit all patients because they have different fluid needs, depending on what happened during the preoperative

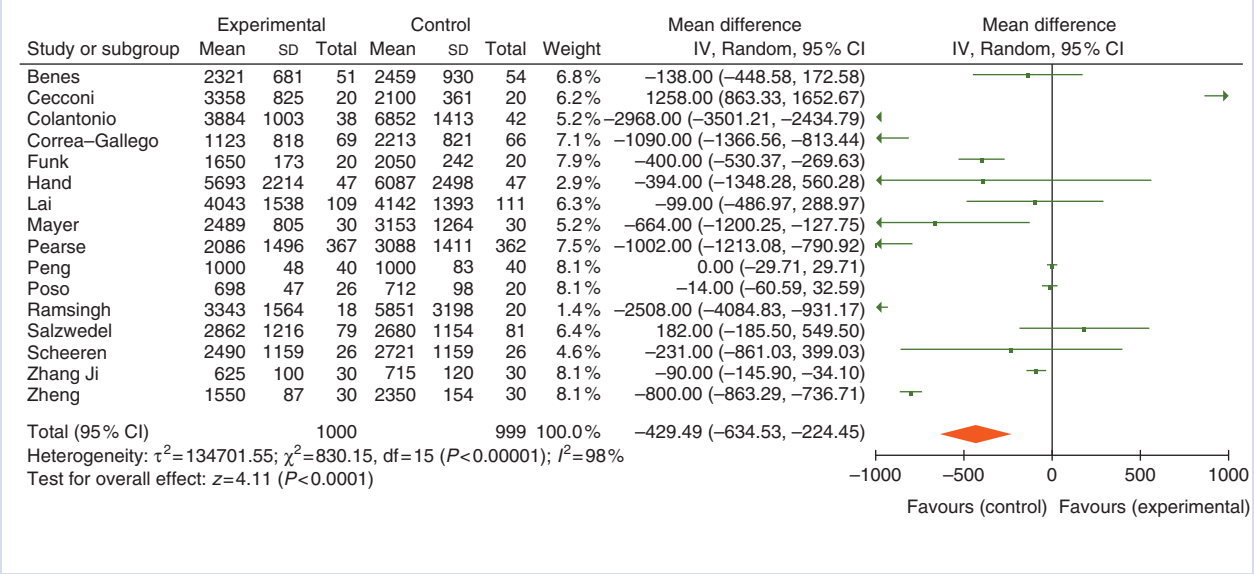

Fig 4 Forest plot for crystalloid volumes in ml

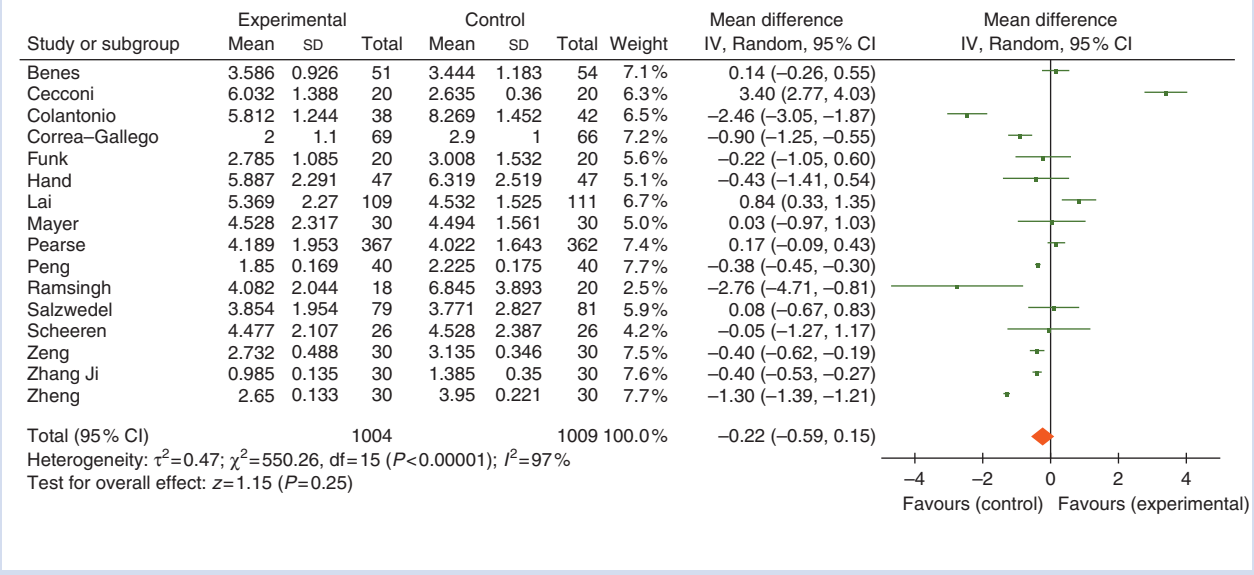

Fig 5 Forest plot for total fluid volumes in l

period (fasting, bowel preparation, carbohydrate drinks, pre-induction fluid load), on the clinical context (dehydration, haemorrhage, congestive heart failure, chronic renal failure) and on surgical blood loss. Therefore, variability in fluid volume may simply reflect the ability of clinicians to adapt fluid administration to individual patient needs. In 6248 patients undergoing high risk surgery, Kim and colleagues[57] recently showed that over 90% of the variability in crystalloid administration can be attributed to patient factors whereas only 10% was due to factors at the level of the care provider. One may then hypothesize that GDT helps clinicians to give the right amount of fluid to the right patients at the right time, without necessarily modifying the average amount of fluid given to a patient population (Fig. 5) nor fluid volume variability (Fig. 6). The importance of timing and individual titration intuitively makes sense, but our study design does not allow us to confirm nor reject this hypothesis. Finally, because crystalloids and colloids have different physiological and side effects, GDT-induced changes in the crystalloid/colloid ratio may have also played a role in the observed reduction in postoperative morbidity.

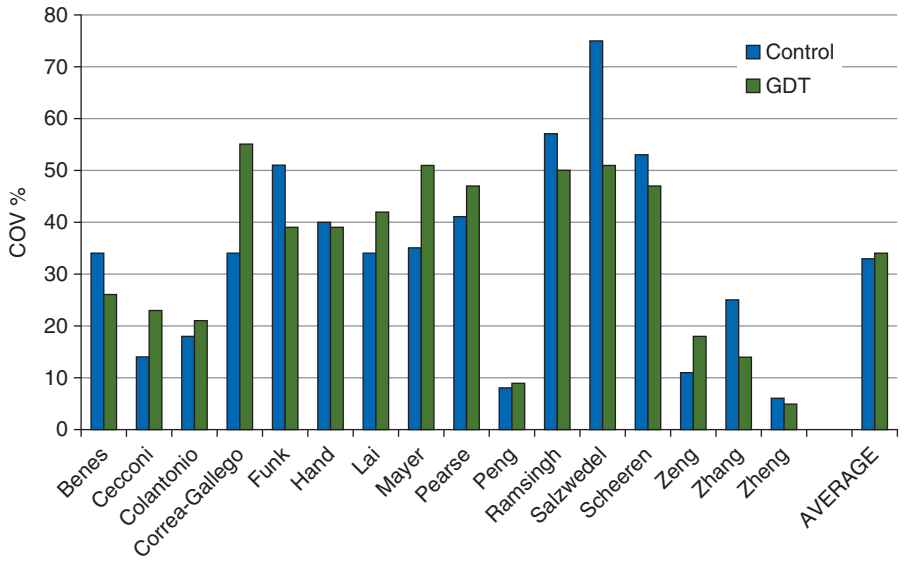

Fig 6 Variability of total fluid volumes. COV, coefficient of variability (standard deviation/mean); GDT, goal-directed therapy

The main limitation of our meta-analysis is the high heterogeneity of studies analysed, which does not allow us to draw definitive conclusions. This limitation is common to most meta-analysis previously published on GDT, and is explained by differences between patient populations, surgical procedures, GDT protocols and definitions of postoperative complications from one RCT to the other. Interestingly, our results were comparable with the random-effects and the fixed-effects models for all but one outcome variables, which reinforced their validity. In addition, the trial sequential analysis, which has been proposed to unmask false-positive results in meta-analysis,[50 51] suggested firm evidence regarding the effects of GDT on postoperative morbidity. The average variability in fluid volume reported in our meta-analysis (around 33%) was lower than variabilities (55% and 70%) reported in recent studies.[23 57] In one of the RCTs we analysed,[44] the variability was very high in the control group (>70%) and decreased (below 50%) with GDT (Fig. 6). Therefore, we cannot exclude an impact of GDT on variability of fluid volume when variability is high (or at least higher than in the present meta-analysis). Another limitation is the fact that our meta-analysis did not take into account the increasing use of enhanced recovery programmes[58] and/or of the zero fluid balance approach.[59] By rationalizing and improving quality of perioperative surgical care, both strategies may diminish the marginal value of GDT.[59 60] As a matter of fact they were not used in most of the trials we analysed. Therefore, a large study would be welcome to assess the effects of GDT with uPC methods in the era of enhanced recovery programmes and zero fluid balance.

Conclusions

Our meta-analysis shows that GDT with uPC methods is associated with a significant decrease in postoperative morbidity. It also shows that GDT with uPC does not increase the volume of fluid administered, and does not decrease the variability of fluid volumes. Therefore, our findings support the notion that uPC methods are useful to guide haemodynamic therapy during the perioperative period, and that studies are needed to clarify by which mechanisms GDT improves postoperative outcome.

Authors' contributions

Contributed equally to the design of the study, interpretation of results and preparation of the manuscript: all authors.
Performed the statistical analysis and created the forest plots: M.T.G.

Supplementary material

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

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Declaration of interest

F.M. has been a consultant for Pulsion Medical Systems and an employee of Edwards Lifesciences. He is the founder and director of MiCo Sarl, a Swiss consulting firm. M.T.G. and N.B. have nothing to declare.

References

1. Grocott MPW, Dushianthan A, Hamilton MA, *et al*. Perioperative increase in global blood flow to explicit defined goals and outcomes after surgery: a Cochrane Systematic Review. *Br J Anaesth* 2013; **111**: 535–48
2. Pearse RM, Harrison DA, MacDonald N, *et al*. Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. *JAMA* 2014; **311**: 2181–90
3. Sadique Z, Harrison DA, Grieve R, *et al*. Cost-effectiveness of a cardiac output-guided haemodynamic algorithm in high-risk patients undergoing major gastrointestinal surgery. *Perioper Med* 2015; **4**: 13
4. Navaro LHC, Bloomstone JA, Auler JOC Jr, *et al*. Perioperative fluid therapy: a statement from the international fluid optimization group. *Perioper Med* 2015; **4**: 3
5. Vincent JL, Pelosi P, Pearse R, *et al*. Perioperative cardiovascular monitoring of high-risk patients: a consensus of 12. *Crit Care* 2015; **19**: 224
6. Mythen MG, Swart M, Acheson N, *et al*. Perioperative fluid management: Consensus statement from the enhanced recovery partnership. *Perioper Med* 2012; **1**: 2
7. Vallet B, Blanloeil Y, Cholley B, *et al*. Guidelines for perioperative haemodynamic optimization. *Ann Fr Anesth Reanim* 2013; **32**: 454–62
8. Shoemaker WC, Appel PL, Kram HB, *et al*. Prospective trial of supranormal values of survivors as therapeutic goals in high-risk surgical patients. *Chest* 1988; **94**: 1176–86
9. Boyd O, Grounds M, Bennett ED. A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients. *JAMA* 1993; **270**: 2699–707
10. Wilson J, Woods I, Fawcett J, *et al*. Reducing the risk of major elective surgery: randomised controlled trial of preoperative optimisation of oxygen delivery. *Br Med J* 1999; **318**: 1099–103
11. Sinclair S, James S, Singer M. Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: a randomised controlled trial. *Br Med J* 1997; **315**: 909–12
12. Gan TJ, Soppitt A, Maroof M, *et al*. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. *Anesthesiology* 2002; **97**: 820–6
13. Pearse R, Dawson D, Fawcett J, *et al*. Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial. *Crit Care* 2005; **9**: R687–93
14. Goepfert MS, Richter HP, Eulenburg CZ, *et al*. Individually optimized hemodynamic therapy reduced complications and length of stay in the intensive care unit. A prospective, randomized controlled trial. *Anesthesiology* 2013; **119**: 824–36
15. Michard F. Pulse contour analysis: fairy tale or new reality? *Crit Care Med* 2007; **35**: 1791–2
16. Ahmad T, Beilstein CM, Aldecoa C, *et al*. Variation in haemodynamic monitoring for major surgery in European nations: secondary analysis of the EuSOS dataset. *Perioper Med* 2015; **4**: 8
17. Camporota L, Beale R. Pitfalls in haemodynamic monitoring based on the arterial pressure waveform. *Crit Care* 2010; **14**: 124
18. Reisner A. Academic assessment of arterial pulse contour analysis: missing the forest for the trees?. *Brit J Anaesth* 2016; **116**: 733–6
19. Monnet X, Vaquer S, Anguel N, *et al*. Comparison of pulse contour analysis by Pulsioflex and Vigileo to measure and track changes of cardiac output in critically ill patients. *Br J Anaesth* 2015; **114**: 235–43
20. Broch O, Renner J, Hocker J, *et al*. Uncalibrated pulse power analysis fails to reliably measure cardiac output in patients undergoing coronary artery bypass surgery. *Crit Care* 2011; **15**: R76
21. Bellamy MC. Wet, dry or something else? *Br J Anaesth* 2006; **97**: 755–7
22. Thacker JKM, Mountford WK, Ernst FR, *et al*. Perioperative fluid utilization variability and association with outcomes. Considerations for enhanced recovery efforts in sample US surgical populations. *Ann Surg* 2016; **263**: 502–10
23. Lilot M, Ehrenfeld JM, Lee C, *et al*. Variability in practice and factors predictive of total crystalloid administration during abdominal surgery: retrospective two-centre analysis. *Br J Anaesth* 2015; **114**: 767–76
24. Dudley N. Tackling practice variation. Threats and opportunities of the NHS reform. *Br Med J* 2011; **342**: d2269
25. Michard F, Biais M. Rational fluid management: dissecting facts from fiction. *Brit J Anaesth* 2012; **108**: 369–71
26. Minto G, Mythen M. Perioperative fluid management: science, art or random chaos? *Brit J Anaesth* 2015; **114**: 717–21
27. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Br Med J* 2009; **339**: b2535
28. Higgins JPT, Altman DG, Sterne JAC. Assessing risk of bias in included studies. In: JPT Higgins, S Green, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 (updated March 2011). The Cochrane collaboration, 2011. Available from www.cochrane-handbook.org
29. Jadad AR, Moore RA, Carroll D, *et al*. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996; **17**: 1–12
30. Jüni P, Witschi A, Bloch R, *et al*. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA* 1999; **282**: 1054–60
31. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Medical Research Methodology* 2005; **5**: 13
32. Benes J, Chytra I, Altmann P, *et al*. Intraoperative fluid optimization using stroke volume variation in high-risk surgical patients: results of a prospective randomized study. *Crit Care* 2010; **14**: R118
33. Cecconi M, Fasano N, Langiano N, *et al*. Goal-directed haemodynamic therapy during elective total hip arthroplasty under regional anaesthesia. *Crit Care* 2011; **15**: R132
34. Colantonio L, Claroni C, Fabrizi L, *et al*. A randomized trial of goal directed vs standard fluid therapy in cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. *J Gastrointest Surg* 2015; **19**: 722–9
35. Correa-Gallego C, Tan KS, Arslan-Carlon V, *et al*. Goal-directed fluid therapy using stroke volume variation for resuscitation after low central venous pressure-assisted liver resection: a randomized clinical trial. *J Am Coll Surg* 2015; **221**: 591–601
36. Funk DJ, Hayglass KT, Koulack J, *et al*. A randomized controlled trial on the effects of goal-directed therapy on the inflammatory response open abdominal aortic aneurysm repair. *Crit Care* 2015; **19**: 247
37. Hand W, Stoll WD, McEvoy MD, *et al*. Intraopertaive goal directed hemodynamic management in free tissue transfer for head and neck cancer. *Head Neck* 2016; **38**: E1974–80

38. Kapoor P, Kakani M, Chowdhury U, *et al*. Early goal-directed therapy in moderate to high-risk cardiac surgery patients. *Ann Card Anaesth* 2008; **11**: 27–34
39. Lai CW, Starkie T, Creanor S, *et al*. Randomized controlled trial of stroke volume optimization during elective major abdominal surgery in patients stratified by aerobic fitness. *Br J Anaesth* 2015; **115**: 578–89
40. Mayer J, Boldt J, Mengistu AM, *et al*. Goal-directed intraoperative therapy based on autocalibrated arterial pressure waveform analysis reduces hospital stay in high-risk surgical patients: a randomized, controlled trial. *Crit Care* 2010; **14**: R18
41. Peng K, Li J, Cheng H, *et al*. Goal-directed fluid therapy based on stroke volume variations improves fluid management and gastrointestinal perfusion in patients undergoing major orthopedic surgery. *Med Princ Pract* 2014; **23**: 413–20
42. Poso T, Winso O, Aroch R, *et al*. Perioperative fluid guidance with transthoracic echocardiography and pulse-contour device in morbidity obese patients. *Obes Surg* 2014; **24**: 2117–25
43. Ramsingh DS, Sanghvi C, Gamboa J, *et al*. Outcome impact of goal directed fluid therapy during high risk abdominal surgery in low to moderate risk patients: a randomized controlled trial. *J Clin Monit Comput* 2013; **27**: 249–57
44. Salzwedel C, Puig J, Carstens A, *et al*. Perioperative goal-directed hemodynamic therapy based on radial arterial pulse pressure variation and continuous cardiac index trending reduces postoperative complications after major abdominal surgery: a multi-center, prospective, randomized study. *Crit Care* 2013; **17**: R191
45. Scheeren TWL, Wiesenack C, Gerlach H, *et al*. Goal-directed intraoperative fluid therapy guided by stroke volume and its variation in high-risk surgical patients: a prospective randomized multicentre study. *J Clin Monit Comput* 2013; **27**: 225–33
46. Van der Linden PL, Dierick A, Wilmin S, *et al*. A randomized controlled trial comparing an intraoperative goal-directed strategy with routine clinical practice in patients undergoing peripheral arterial surgery. *Eur J Anaesthesiol* 2010; **27**: 788–93
47. Zeng K, Li Y, Liang M, *et al*. The influence of goal-directed fluid therapy on the prognosis of elderly patients with hypertension and gastric cancer surgery. *Drug Des Dev Ther* 2014; **8**: 2113–9
48. Zhang J, Chen CQ, Lei XZ, *et al*. Goal-directed fluid optimization based on stroke volume variation and cardiac index during one-lung ventilation in patients undergoing thoracoscopy lobectomy operations: a pilot study. *Clinics* 2013; **68**: 1065–70
49. Zheng H, Guo H, Ye JR, *et al*. Goal-directed fluid therapy in gastrointestinal surgery in older coronary heart disease patients: randomized trial. *World J Surg* 2013; **37**: 2820–9
50. Wetterslev J, Thorlund C, Brok J, Gluud C. Trial sequential analysis may establish when firm evidence is reached in cumulative meta-analysis. *J Clin Epidemiol* 2008; **61**: 64–75
51. Brok J, Thorlund C, Gluud C, Wetterslev J. Trial sequential analysis reveals insufficient information size and potentially false positive results in many meta-analysis. *J Clin Epidemiol* 2008; **61**: 763–9
52. Giglio MT, Marucci M, Testini M, *et al*. Goal-directed haemodynamic therapy and gastrointestinal complications in major surgery: a meta-analysis of randomized controlled trials. *Br J Anaesth* 2009; **103**: 637–46
53. Dalfino L, Giglio MT, Puntillo F, *et al*. Haemodynamic goal-directed therapy and postoperative infections: earlier is better. A systematic review and meta-analysis. *Crit Care* 2011; **15**: R154
54. Biais M, Nouette-Gaulain K, Cottenceau V, *et al*. Cardiac output measurement in patients undergoing liver transplantation: pulmonary artery catheter versus uncalibrated arterial pressure waveform analysis. *Anesth Analg* 2008; **106**: 1480–6
55. Slagt C, Malagon I, Groenevelds ABJ. Systematic review of uncalibrated arterial pressure waveform analysis to determine cardiac output and stroke volume variation. *Br J Anaesth* 2014; **112**: 626–37
56. Biais M, Nouette-Gaulain K, Roullet S, *et al*. A comparison of stroke volume variation measured by Vigileo/FloTrac system and aortic Doppler echocardiography. *Anesth Analg* 2009; **109**: 466–9
57. Kim Y, Gani F, Spoverato G, *et al*. Variation in crystalloid administration: an analysis of 6248 patients undergoing major elective surgery. *J Surg Res* 2016; **203**: 368–77
58. Nicholson A, Lowe MC, Parker J, *et al*. Systematic review and meta-analysis of enhanced recovery programmes in surgical patients. *Br J Surg* 2014; **101**: 172–88
59. Brandstrup B, Svendsen PE, Rasmussen M, *et al*. Which goal for fluid therapy during colorectal surgery is followed by the best outcome: near-maximal stroke volume or zero fluid balance? *Br J Anaesth* 2012; **109**: 191–9
60. Joshi GP, Kehlet H. CON: perioperative goal-directed fluid therapy is an essential element of an enhanced recovery protocol? *Anesth Analg* 2016; **122**: 1261–3

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