Goal-directed Fluid Therapy in Elderly Patients Undergoing Lumbar decompression surgery in the Prone Position: A Randomized Controlled Clinical Trial

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Abstract

Background Major lumber spine surgeries in the prone position have high mortality and morbidity, especially in elderly patients. Intraoperative goal-directed fluid therapy (GDT) has improved outcomes in abdominal and thoracic surgical procedures. However the utility of intraoperative GDT in spine surgery has not been present. In this study, we investigated whether GDT would reduce the postoperative complications in elderly patients undergoing lumbar stenosis decompression in the prone position. Methods In this single-center, randomized controlled clinical trial, we randomly assigned 84 patients aged > 60 undergoing lumbar decompression surgery to either a GDT group or a control group, who received conventional anesthesiologist-directed fluid therapy. Perioperative lactic acid concentrations with 7 different time point, intraoperative fluid balance and postoperative complications from admittance to 30 days after surgery were recorded. Results Lactic acid concentrations were higher in the control group than in the GTD group from the start of operation to 24 h after the operation, reaching maximum concentrations at exit from the post-anesthesia care unit (2.50 ± 1.22 mmol/l compared with 1.32 ± 0.42 mmol/l in controls; p<0.001). More total fluid volume was infused in GDT patients than in control patients (2416 ± 539 ml vs. 2036 ± 424ml, p<0.001). GDT patients had fewer infectious complications that did control patients (4.7% vs. 19.5%, P<0.001) after the surgery. Conclusion GDT during lumbar decompressive surgery under general anesthesia in elderly patients results in significantly better postoperative outcomes, which may be due to optimal fluid management and better perfusion of tissues and organs. Trial registration NCT02470221. Initial registration date was 06/09/2015.

Background

In parallel with the rapid growth of the aged population, the incidence of degenerative spinal disorders is rising[2-4]. The demand for surgical procedure to manage degenerative spinal disease, especially spinal decompression, also has increased in the elderly[1-3]. However, geriatric patients undergoing lumbar spinal decompression may be at risk of adverse postoperative events, such as infection, cardiac and pulmonary complications, which in turn contribute to functional decline, nursing home admission, and even death[4 5].

Intraoperative goal-directed fluid therapy (GDT) is a method to optimize fluids and inotrope use though monitoring hemodynamics during operations[6 7]. GDT has been reported effective in improving the cardiac index and oxygen delivery and consumption in septic patients. In abdominal and thoracic surgery much evidence documents that perioperative GDT lowers lactic acid values, reduces the frequency of cardiac and pulmonary complications, and shortens hospital stay[11-12]. A small sample size cohort study showed that application of a GDT in major spine surgery is feasible and can lead to reduced blood losses and transfusions[13]. However, no randomized controlled trials (RCTs) have been conducted to show the evidence of benefit from GDT in postoperative complications in patients undergoing orthopedic surgery, especially in spine surgery, in prone positions.

In this study, we have conducted a randomized clinical trial to determine if the use of GDT during lumbar decompressive surgery in the prone position improves outcomes and the rate of complications in an

elderly population.

Methods

This was a single-center, parallel-group RCT conducted at Peking Union Medical College Hospital, a class A tertiary comprehensive hospital. Ethical permission was obtained from the Ethical Committee of Peking Union Medical College Hospital (ZS-1290). All patients were instructed about benefits and risks of the study and each participant signed an informed consent form. The trial is registered at www.clinicaltrials.gov (NCT02470221).

Patient Population

Patients admitted to the Department of Orthopedics of Peking Union Medical College Hospital (PUMCH) with the confirmed diagnosis of degenerative spinal stenosis, and who had indication for decompressive surgery under general anesthesia, were enrolled from March 1, 2017 to September 30, 2017. Inclusion criteria were age > 60, American Society of Anesthesiologists score II-III, and expected duration of operation > 2 h. Patients with severe cardiac arrhythmia (which would affect the accuracy of stroke volume variation as an indicator of fluid responsiveness), vascular disease (which would prohibit radial artery cannulation), and mental disorder were excluded.

Randomization

Patients were assigned to one of the two groups (control group and GDT group) using a computer-generated randomization scheme. Allocation concealment was obtained using number labeled opaque envelopes that were opened just before the surgery. Patients were excluded from analysis if any of the following events occurred: vascular access line could not be established; LiDCO cardiac output monitor (LiDCO Ltd, Cambridge, UK) failed to calibrate; or the plan of surgery or anesthesia was changed. Data were collected by persons unaware of treatment allocation.

Intraoperative Management and Monitoring

All patients who received surgical decompression for lumbar spinal stenosis under general anesthesia were managed according to our national guidelines. Thus, after induction, patients were placed in the prone position supported by 4 pads (2 pads under the shoulders and 2 under pelvic sites) to suspend the chest and abdomen from the operation bed. A LiDCO monitor, calibrated according to the manufacturer's instructions, recorded stroke volume, cardiac output and systemic vascular resistance during anesthesia. All patients were monitored intra- and post-operatively according to currently recommended standards to

maintain arterial oxygen saturation of hemoglobin (SaO2) >96%, hemoglobin (>80 g/L), core temperature (>36.5°C) and heart rate (50-100/min). Ringer's lactate was administered at 3 ml/kg/h for maintenance of fluid balance. Additional fluid was administered at the discretion of the attending anesthesiologist, based on patients' pulse, arterial pressure, urine output, core-peripheral temperature gradient, serum lactate, and base excess. A dose of 6 mg ephedrine or 50 µg phenylephrine was given when fluid boluses failed to keep the systolic arterial pressure >90 mm Hg or mean arterial pressure (MAP) >65 mmHg. If such episodes occurred, they were recorded as hypotensive events. Patients in both groups also received a dose of 4 mg ondansetron as a prophylactic antiemetic during induction. Postoperative analgesia was provided with intravenous morphine infusion.

Goal-directed Fluid Therapy

Patients in the GDT group received the fluid management depicted in Figure 1. This protocol was based on the Frank-Starling mechanism of the heart. Fluid maintenance was set at 3-5 ml/kg/h of normal saline. Optimal stroke volume (SV) was maintained with targeted crystalloid boluses given as indicated according to invasive continuous hemodynamics monitoring. If MAP dropped more than 30%, or stroke volume variation (SVV) was more than 13%, boluses of 3 ml/kg (Figure 1) were given and SV response recorded. If a response was recorded (SV increase >10%), another bolus was given. If no response was recorded (SV was not elevated by more than 10%), no further bolus was given unless the SV decreased by 10%. Vasopressor or inotrope was not administered unless the MAP dropped persistently.

Anesthesiologist-directed Fluid Therapy (control group)

Patients in the control group received conventional fluid therapy, decided by the attending anesthesiologists based on the patient's hemodynamic condition and responses, to maintain MAP >65 mm Hg, heart rate 50-100 bpm, and urine output >0.5 ml/kg/h.

Outcomes

The primary outcome of interest was the postoperative complications from admission to the operating theatre to 30 days after the surgery, include nausea and vomiting, infectious complications, delayed wound healing, cardiac events and kidney disorders .

The secondary outcomes of interest was the change of lactic acid concentrations throughout the perioperative period and intraoperative fluid balance. Arterial blood gas (ABG) and lactic acid were measured at 7 predefined times: T0, 24 h before surgery; T1, beginning of the operation; T2, 1h after the

operation began; T3, 2h after the operation began; T4, end of the operation surgery; T5, discharge from the post-anesthesia care unit; and T6, 24 h after surgery.

Statistical Analysis

The primary endpoint of the study was the concentration of lactate acid in the perioperative period. In a previous report, the average lactate concentration during the operative period was 2.015± 0.986 mmol/l[8]. We expected that a difference of 0.50 mmol/l in lactate concentration would be clinically meaningful. Therefore, we estimated that a total of 66 patients (33 in each group) would be needed to detect a difference with a power of 90% (α=0.05). Considering missing data or loss of follow up, we enrolled 40 patients in each arm. Data were analyzed on an intention-to-treat basis. Changes of lactate over time were tested with repeated-measure analysis of variance (ANOVA). The primary outcome data were normally distributed after reciprocal transformation and analyzed with the t-test. Categorical data were tested with Chi-square test and Chi-square test for trend. Data are presented as mean ± standard deviation when normally distributed. A p value of 0.05 was considered significant. All data were analyzed with SPSS (IBM SPSS Statistics v24, IBM, Armonk, NY, USA).

Results

Patient Enrollment

104 patients were screened, and 88 patients were enrolled and randomly assigned to either the control group (43) or the GDT group (45) (Figure 2 consort flow diagram). After excluding patients who did not receive the allocated intervention or were lost to follow-up (radial artery cannulation was failed in 2 patients in GDT group, and one patient was lost to follow up, one patient was found to have atrial fibrillation before the induction in control group) 41 control patient and 43 GDT patients were analyzed. Patients' demographics, comorbidities, duration of anesthesia, length of operation, and other variables were similar between the two groups (Table 1).

Fluid Administration and Balance

Perioperative fluid balance in the control and GDT groups are listed in Table 2. The volumes of crystalloid and total volumes of intravenous fluids administered were significantly more in the GDT group than in the control group. The volumes of intraoperative colloid, number of patients who received blood transfusion, amounts of blood transfused, volume of blood loss, urine output, and total output volumes were not significantly different in the two groups.

Perioperative Lactate

The concentrations of lactic acid during the perioperative period are illustrated in Table 3. Values in the control group and the GDT group were similar at T0 (24 h before operation). Thereafter, values rose in the

control group and were significantly higher than in the GDT group from T2 (1 h after the operations began) until T6 (24 h after the operations concluded). The differences were greatest at T5 (discharge from the post-anesthesia care unit (control, 2.50 ± 1.22 mmol; GDT, 1.32 ± 0.42; p 0.001). Values in the GDT group did not change appreciably through the perioperative period. A lactic acid concentration of >2 mmol/l is defined as hyperlacticaemia. This value was exceeded in 25% of control patients at T5 compared with 7% GDT patients (p<0.001).

Hemodynamic variation

The variation of hemodynamics during the surgery are different in two groups. The monitor parameter CO (caridic output) of G group is higher than that of group C, with statistically significant difference in T4 (the end of the operation surgery, P<0.05 Figure 3.)

Postoperative Outcomes

Postoperative outcomes of the GDT and control group are listed in Table 4. The most common complication is nausea and vomiting without significant difference between the two groups (P>0.05). GDT patients had fewer infectious complications (including fever, pulmonary infection, urinary infection) that did control patients (4.7% vs. 19.5%, P<0.001). Delayed wound healing occurred in 2 patients in the control group, but no patient occurred in the GDT group (P<0.001).

Discussion

In this randomized controlled trial of GDT during lumbar decompressive surgery under general anesthesia the most important finding was a significantly lower concentration of lactic acid in patients who received GDT than in those who received anesthesiologist-directed anesthesia. Total volumes of intravenous fluids administered in the perioperative period also were significantly more in the GDT group. Associated outcomes were a lower incidence of infections and postoperative complications in the GDT group. To our knowledge, this is the first study in which LiDCO-based GDT was used during lumbar surgery with prone position in elderly patients. LiDCO monitoring allowed the administration of fluid in response to changes in SVV measured in real time.

Ideally, a simple, affordable, and reliable method to improve intraoperative fluid management would be available for routine use. Esophageal Doppler has been used to guide fluid management. However, its use is partially limited by the need for experienced staff, and it is not optimal for monitoring patients in the prone position. Hence, we used LiDCO monitoring, which has been extensively evaluated in clinical use for more than 10 years[9].

The prone position can affect heart-lung interaction by decreasing right ventricular pre-load and compliance of the respiratory system. Lumbar decompressive surgery in the prone position is a major

orthopedic operation that may have substantial blood loss, transfusion requirement, and fluid shifts. In patients, especially elderly patients, undergoing these operations, optimized intraoperative fluid management is important for organ perfusion and limiting postoperative complications. Biais et al[10]. found that prone positioning induces a significant increase in SVV (supine position vs. prone position, 10% vs.14%) but does not alter the ability to predict fluid responsiveness. Elderly patients might be more sensitive to prone position and ventricular pre-load change. Thus, we used an SVV of 13% for patients in the prone position as thresholds for hypovolemia to target volume administration.

Blood lactate concentrations and severity of microvascular alterations are strongly correlated, and lactate concentrations can reliably reflect the adequacy of tissue perfusion and oxygenation[11][12]. Lactate values above 2 mmol/L indicate hyperlactatemia. Most instances of excessive accumulation of lactate are due to tissue hypoperfusion caused by problems such as hypovolemia, cardiac failure, sepsis, or cardiopulmonary arrest[13][14]. Tissue hypovolemia or hypoxia during surgery, forcing aerobic metabolism of glucose, leads to production of lactic acid exceeding its removal, with resultant adverse outcomes. Our finding that blood lactate concentrations progressively increased with conventional anesthesia in patients undergoing spinal operation indicates that they developed tissue hypoperfusion. Our study also showed that GDT is a valid method to optimize hemodynamics and oxygen delivery during the high-risk orthopedic surgery for elderly patients.

In 2012, Gao[15] et al. reported that individual GDT could decrease the incidence of hyperlactatemia in elderly patients operated for abdominal cancer. In a retrospectively controlled study, GDT decreased the time for lactate clearance in open- abdominal surgery patients[8], and similar results were found in elderly patients[16]. A recent study had conflicting results, perhaps because of shorter operative times and lower-risk procedures[17]. Several studies have found intimate associations between elevated lactate levels and worse outcomes in major high-risk surgery[18-20], and non-clearers of lactate (below the median level of lactate clearance) have had a higher 30-day mortality rate than have clearers[21]. Early lactate clearance is associated with biomarkers of inflammation, coagulation, apoptosis, organ dysfunction and mortality during operation and intensive care units[22]. In our study, lactic acid concentrations were predictors of outcomes. GDT optimized perfusion during surgery and decreased concentrations of lactic acid, with associated improved outcomes.

Another difference between the GDT and control group in this study was in fluid management; the GDT group received more fluid than did the control group. The control group was given fluid according to local hospital standard practice to maintain desired blood pressure, heart rate and urine output. There are little data for comparison of surgical outcomes based on fluid administration. Srinivasa[23] et al. reported that patients in a GDT protocol group received 2.5 L compared with 1.5 L in a restrictive-fluid group during rectal surgery. Myles et al[30] recently enrolled 2983 patients at high risk for complications undergoing major abdominal surgery to compare restrictive and liberal fluid therapy. There was no difference in the rate of disability-free survival between these two fluid regimen. However, restrictive fluid therapy was associated with a higher rate of acute kidney injury at 30 days after surgery. Variability in fluid volume

may simply reflect the ability of clinicians to adjust fluid administration to individual patient needs; therefore, the local hospital standard protocol may result in suboptimal fluid administration during surgery. We believe that GDT better enables anesthesiologists to give the right amount of fluid at the right time, and thereby improve perfusion.

We also found a lower incidence of postoperative complications, especially for infections, in patients who received GDT[24-26]. In an early study of 100 high-risk surgical patients, GDT was associated with improved outcomes, a finding that was supported by more recent studies with GDT aimed at optimizing intraoperative oxygen delivery in high-risk patients[27]. Recent studies and meta-analyses have reported also that perioperative GDT was associated with a lower incidence of surgical-site infections[28,29], but some studies[30,31] have reported opposing views regarding postoperative complications, meta-analyses have found a decrease in mortality and length of hospital stay in patients receiving GDT after major surgery, but the studies may have been flawed by the inclusion of highly heterogeneous studies. The debate about the benefits of GDT in high-risk patients is unresolved, and additional quality studies are needed, perhaps initially with study of improvement in stroke volume management.

Limitations of the study

Our study has limitations. First, the sample size might have been inadequate to detect significant differences in some complications. Second, in our study we didn't analyze differences in nausea and vomiting with detail, which may lead diverse result in other study. Further studies will be needed to clarify the direct impact of a GDT protocol on complications in a larger prospectively enrolled population.

Conclusions

The use of goal-directed fluid therapy compared with conventional fluid therapy in elderly patients undergoing lumbar stenosis decompression in the prone position was associated with lower concentrations of lactic acid and postoperative complications. It is reasonable that the favorable outcomes of goal-directed therapy were due to optimal fluid management and better perfusion of tissues and organs.

Abbreviations

GDT: goal-directed fluid therapy; RCTs: randomized controlled trials; MAP: mean arterial pressure; SV: stroke volume; SVV: stroke volume variation; ABG: arterial blood gas; CO: caridic output

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Peking Union Medical College Hospital（ZS-1290）, and the protocal was registered at the ClinicalTrials (NCT02470221). Initial registration date was 06/09/2015. All procedures performed in this study involving human participants were in cordance with the Ethical Standards of the Institutional Ethics Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All patients signed writtern informed consent before surgery.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Study conception: L.X.

Study design, study coordination data analysis, manuscript preparation: L.X., D.X., Y.H.

Patient recruitment: D.X., X.L.,

Data collection: L.X., D.X., X.L.

Data analysis: L.X., D.X.

Manuscript review: Y.H.

All authors reviewed the results and approved the final version of the manuscript.

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References

1. Gunzburg R, Szpalski M. The conservative surgical treatment of lumbar spinal stenosis in the elderly. *Eur Spine J* 2003;12 Suppl 2:S176-80. doi: 10.1007/s00586-003-0611-2

2. Imajo Y, Taguchi T, Neo M, et al. Complications of spinal surgery for elderly patients with lumbar spinal stenosis in a super-aging country: An analysis of 8033 patients. *Journal of Orthopaedic Science* 2017;22(1):10-15.

3. Deyo RA, Mirza SK, Martin BI, et al. Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults. *JAMA* 2010;303(13):1259-65. doi: 10.1001/jama.2010.338

4. Machado GC, Ferreira PH, Yoo RI, et al. Surgical options for lumbar spinal stenosis. *Cochrane Database Syst Rev* 2016;11:CD012421. doi: 10.1002/14651858.CD012421

5. O'Lynnger TM, Zuckerman SL, Morone PJ, et al. Trends for Spine Surgery for the Elderly: Implications for Access to Healthcare in North America. *Neurosurgery* 2015;77 Suppl 4:S136-41. doi: 10.1227/NEU.0000000000000945

6. Waldron NH, Miller TE, Gan TJ. Perioperative goal-directed therapy. *J Cardiothorac Vasc Anesth* 2014;28(6):1635-41. doi: 10.1053/j.jvca.2014.07.008

7. Shoemaker WC, Appel PL, Kram HB, et al. Sequence of physiologic patterns in surgical septic shock. *Crit Care Med* 1993;21(12):1876-89.

8. Ghneim MH, Regner JL, Jupiter DC, et al. Goal directed fluid resuscitation decreases time for lactate clearance and facilitates early fascial closure in damage control surgery. *Am J Surg* 2013;206(6):995-9; discussion 99-1000. doi: 10.1016/j.amjsurg.2013.07.021

9. Marquez J, McCurry K, Severyn DA, et al. Ability of pulse power, esophageal Doppler, and arterial pulse pressure to estimate rapid changes in stroke volume in humans. *Crit Care Med* 2008;36(11):3001-7. doi: 10.1097/CCM.0b013e31818b31f0

10. Biais M, Bernard O, Ha JC, et al. Abilities of pulse pressure variations and stroke volume variations to predict fluid responsiveness in prone position during scoliosis surgery. *Br J Anaesth*

2010;104(4):407-13. doi: 10.1093/bja/aeq031

11. De Backer D, Verdant C, Chierego M, et al. Effects of drotrecogin alfa activated on microcirculatory alterations in patients with severe sepsis. *Crit Care Med* 2006;34(7):1918-24. doi: 10.1097/01.CCM.0000220498.48773.3C

12. Okorie ON, Dellinger P. Lactate: biomarker and potential therapeutic target. *Crit Care Clin* 2011;27(2):299-326. doi: 10.1016/j.ccc.2010.12.013

13. Kreisberg RA. Lactate homeostasis and lactic acidosis. *Ann Intern Med* 1980;92(2 Pt 1):227-37.

14. Madias NE. Lactic acidosis. *Kidney Int* 1986;29(3):752-74.

15. Gao T, Li N, Zhang JJ, et al. Restricted intravenous fluid regimen reduces the rate of postoperative complications and alters immunological activity of elderly patients operated for abdominal cancer: a randomized prospective clinical trail. *World J Surg* 2012;36(5):993-1002. doi: 10.1007/s00268-012-1516-1

16. 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 Devel Ther* 2014;8:2113-9. doi: 10.2147/DDDT.S66724

17. 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. *Journal of the American College of Surgeons* 2015;221(2):591-601(1879-1190 (Electronic))

18. Hajjar LA, Almeida JP, Fukushima JT, et al. High lactate levels are predictors of major complications after cardiac surgery. *J Thorac Cardiovasc Surg* 2013;146(2):455-60. doi: 10.1016/j.jtcvs.2013.02.003

19. Munoz R, Laussen PC, Palacio G, et al. Changes in whole blood lactate levels during cardiopulmonary bypass for surgery for congenital cardiac disease: an early indicator of morbidity and mortality. *J Thorac Cardiovasc Surg* 2000;119(1):155-62.

20. Park SJ, Kim SP, Kim JB, et al. Blood lactate level during extracorporeal life support as a surrogate marker for survival. *J Thorac Cardiovasc Surg* 2014;148(2):714-20. doi: 10.1016/j.jtcvs.2014.02.078

21. Chertoff J, Chisum M, Simmons L, et al. Prognostic utility of plasma lactate measured between 24 and 48 h after initiation of early goal-directed therapy in the management of sepsis, severe sepsis, and septic shock. *J Intensive Care* 2016;4:13. doi: 10.1186/s40560-016-0142-7

22. Nguyen HB, Loomba M Fau - Yang JJ, Yang Jj Fau - Jacobsen G, et al. Early lactate clearance is associated with biomarkers of inflammation, coagulation, apoptosis, organ dysfunction and mortality in severe sepsis and septic shock. 2010(1476-9255 (Electronic)) doi: D - NLM: PMC2837000 EDAT- 2010/02/26 06:00 MHDA- 2010/02/26 06:01 CRDT- 2010/02/26 06:00 PHST-2009/09/04 [received] PHST- 2010/01/28 [accepted] PHST- 2010/01/28 [aheadofprint] AID - 1476-9255-7-6 [pii] AID - 10.1186/1476-9255-7-6 [doi] PST - epublish

23. Srinivasa S, Taylor MH, Singh PP, et al. Goal-directed fluid therapy in major elective rectal surgery. *Int J Surg* 2014;12(12):1467-72. doi: 10.1016/j.ijsu.2014.11.010

24. Luo J, Xue J, Liu J, et al. Goal-directed fluid restriction during brain surgery: a prospective randomized controlled trial. *Ann Intensive Care* 2017;7(1):16. doi: 10.1186/s13613-017-0239-8

25. Malbouisson LMS, Silva JM, Jr., Carmona MJC, et al. A pragmatic multi-center trial of goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery. *BMC Anesthesiol* 2017;17(1):70. doi: 10.1186/s12871-017-0356-9

26. Picard J, Bedague D, Bouzat P, et al. Oesophageal Doppler to optimize intraoperative haemodynamics during prone position. A randomized controlled trial. *Anaesth Crit Care Pain Med* 2016;35(4):255-60. doi: 10.1016/j.accpm.2015.12.011

27. Gan TJ, Soppitt A, Maroof M, et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. *Anesthesiology* 2002;97(4):820-6.

28. Jianhu Yuan a, Yanxia Sun b, *, 1, Chuxiong Pan b, Tianzuo Li. Goal-directed fluid therapy for reducing risk of surgical site infections following abdominal surgery A systematic review and meta-analysis of randomized controlled trials. *International Journal of Surgery* 2017;39 (2017) 74-87 doi: 0.1016/j.ijsu.2017.01.081

29. Osawa EA, Rhodes A, Landoni G, et al. Effect of Perioperative Goal-Directed Hemodynamic Resuscitation Therapy on Outcomes Following Cardiac Surgery: A Randomized Clinical Trial and Systematic Review. *Crit Care Med* 2016;44(4):724-33. doi: 10.1097/CCM.0000000000001479

30. Moppett IK, Rowlands M, Mannings A, et al. LiDCO-based fluid management in patients undergoing hip fracture surgery under spinal anaesthesia: a randomized trial and systematic review. *Br J Anaesth* 2015;114(3):444-59. doi: 10.1093/bja/aeu386

31. 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(21):2181-90. doi: 10.1001/jama.2014.5305

Tables

Table 1 Patient characteristics

	Control group (n=41)	GDT group (n=43)	P value
Age (yr)	68.0±6.3	68.7±6.0	0.687
Sex (Male/Female)	15:26	19:24	0.503
BMI (kg/m^2)	25.3±3.9	25.4±3.8	0.614
Comorbidity			
None	7 (17%)	10 (23%)	0.481
CAD	8 (20%)	6 (14%)	0.494
DM	6 (15%)	8 (19%)	0.494
HTN	22 (54)	21 (49%)	0.659
Tumor	0 (0%)	0 (0%)	1
Other	10 (24%)	11 (26%)	0.900
ASA	207.7±56.1	200.7±54.6	0.924
I	3	3	1
II	34	39	0.824
III	4	1	0.325
length of anaesthesia (min)			
Length of surgery (min)	174.8±51.9	165.4±52.0	0.849
Vital sighs baseline			
MAP	97.0±11.2	94.3±10.5	0.439
HR	80.2±11.2	76.3±9.0	0.268
T	36.5±0.3	36.5±0.4	0.365
Lab examination baseline			
WBC(×10^9/L)	6.6±1.9	5.8±1.5	0.429
HGB (g/L)	135.0±15.4	134.4±14.0	0.421
HCT (%)	39.8±4.6	40.8±7.0	0.763
ALT(U/L)	34.2±5.6	32.1±5.4	0.734
Cr(mmol/l)	76±8.7	82±5.6	0.675

Table 2 the fluid management

I.V. fluid (ml)	Control group (n=41)	GDT group (n=43)	P value
Intraoperative (crystalloid)	1500±330	1851±388	0.001
Intraoperative (colloid)	368±276	386±325	0.789
Number of patients transfused	17	17	1
Amount of blood transfusion	167±271	178±303	0.865
Total volume of i.v. fluid	2036±424	2415±539	0.001
Bleeding	344±210	351±171	0.852
Urine	554±367	566±394	0.879
Total volume of output	897±476	910±469	0.905

Table 3 the perioperative lactate level (mmol/l)

	Control group (n=41)	GDT group (n=43)	P value
Before surgery			
T0 24h before surgery	1.49±0.48	1.41±0.47	0.413
Surgery			
T1 at the beginning of the surgery	1.49±0.72	1.35±0.45	0.205
T2 1h after the initial of the surgery	1.52±0.71	1.21±0.47	0.005
T3 2h after initial of the surgery	1.71±0.89	1.25±0.49	0.002
T4 Time ending of surgery	1.92±0.99	1.30±0.59	0.012
T5 Time leaving the PACU	2.50±1.22	1.32±0.42	0.001
After surgery			
T6 24h after surgery	1.90±0.76	1.28±0.49	0.005

Table 4 the result of complications and lab examination

	Control group (n=41)	GDT group (n=43)	P value
Postoperative Nausea and Vomiting(%)	13 (31.7%)	12 (27.9%)	0.703
Infection	8 (19.5%)	2 (4.7%)	0.001
sepsis	1	1	
pulmonary infection	3	0	
urinary infection	2	1	
wound infection	2	0	
Cardiac events	0	0	
Acute kidney injury	0	0	
Number of patients developing one or more complications	21 (51.2%)	12 (27.9%)	0.001

Cardiac events: myocardial infarction; arrhythmia; cardiogenic pulmonary edema; need evidence of clinical findings, cardiac enzymes, ECG changes
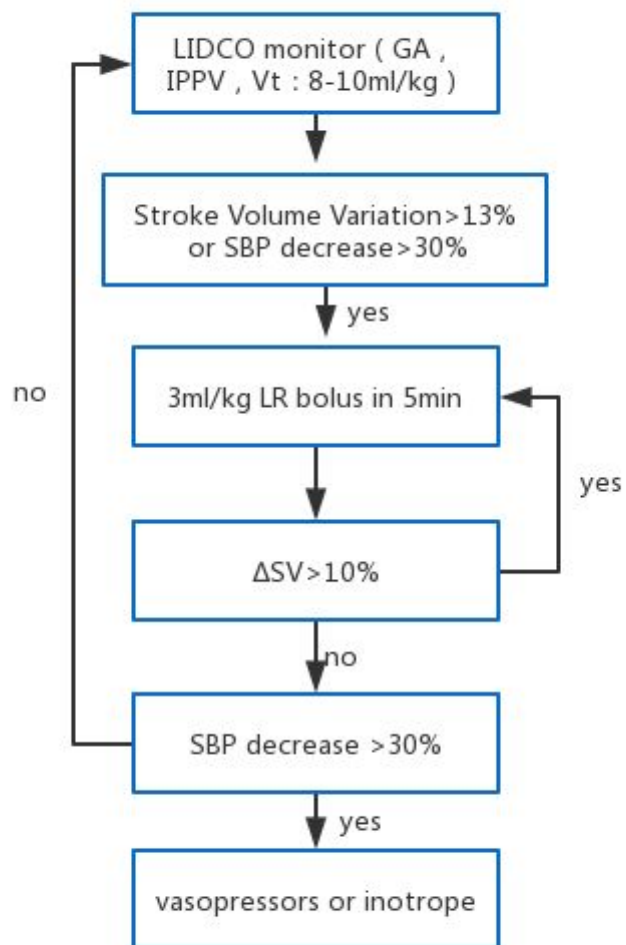
Figures

Figure 1

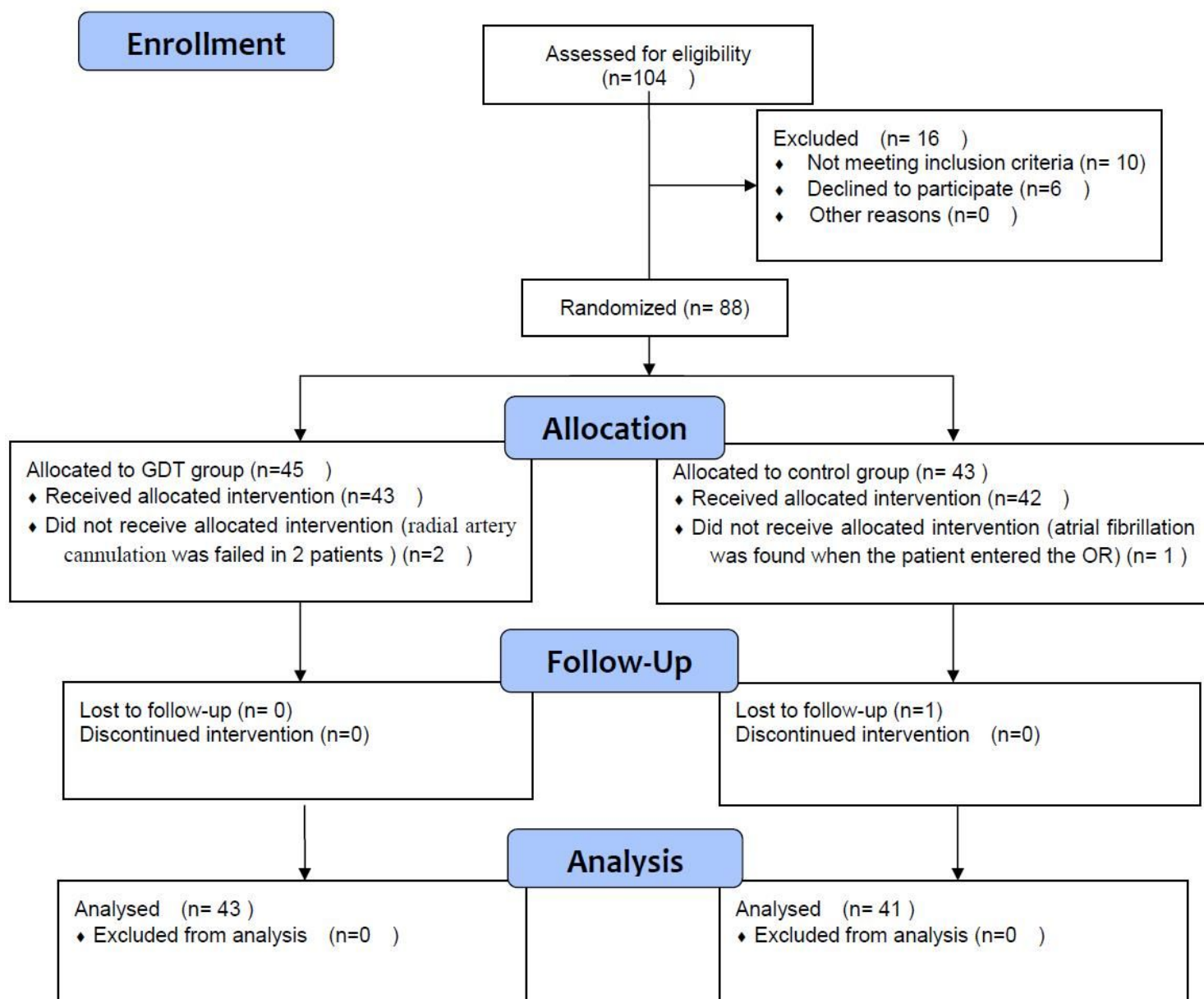Intraoperative fluid optimization protocol applied in the GDT group.

Figure 2

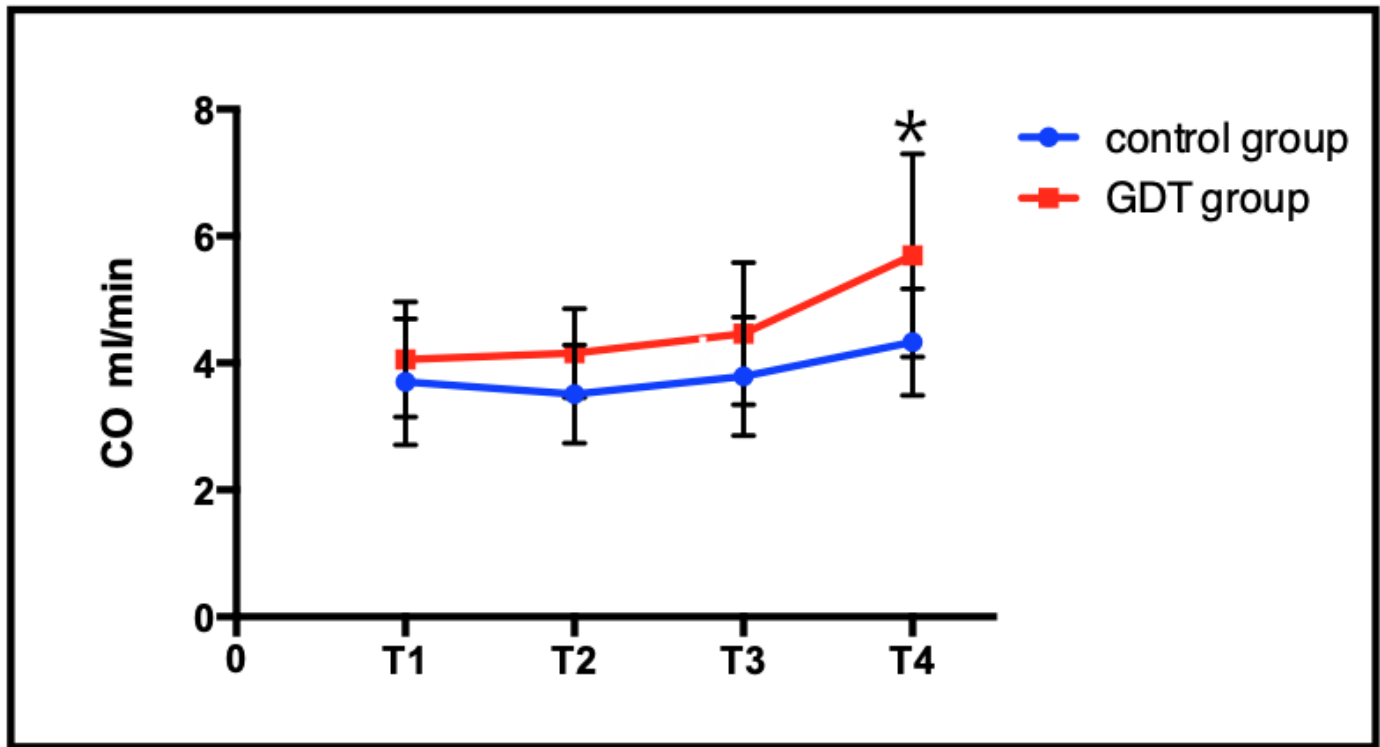CONSORT flow diagram for study.

Figure 3

Cardiac output (CO) of the patients during the surgery: CO of group G is higher than that of group C, with statistically significant difference in T4 (the end of the operation surgery. (*P<0.05).