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ORIGINAL ARTICLE

Goal-directed fluid therapy during post-resection phase in low central venous pressure assisted laparoscopic hepatectomy: a randomized controlled superiority trial

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Abstract

Purpose The purpose of this prospective single blinded randomized controlled trial was to find out whether goal-directed fluid therapy (GDFT) strategy in post-transection period in low central venous pressure (CVP) assisted laparoscopic hepatectomy (LH) has more benefit than traditional fluid strategy.

Methods Between April 2020 and Dec 2021, patients who were scheduled for laparoscopic liver resection surgery were eligible to participate in the study. Patients were randomly divided into two groups: control group that received traditional fluid strategy in post-transection period in low CVP assisted laparoscopic hepatectomy and GDFT strategy group that received GDFT strategy in post-transection period. The primary outcome parameter is the incidence of postoperative complications. Secondary outcome parameters include perioperative clinical outcomes, postoperative clinical outcomes, length of hospital stay after surgery, postoperative lactic acid, fluids and vasoactive medications during the operation.

Results A total of 159 patients in the control group and 160 patients in the GDFT were included. Two groups had no significant difference in the incidence of postoperative complications including pneumonia ($P=0.34$), acute kidney injury ($P=0.72$), hepatic insufficiency ($P=0.25$), pleural effusion ($P=0.08$) and seroperitoneum ($P=1.00$), respectively. The amount of perioperative urine output is fewer in GDFT group than in the control group ($P=0.0354$), while other perioperative variables and postoperative variables were comparable between two groups.

Conclusions The results show the implementation of GDFT strategy is not associated with fewer postoperative complications. GDFT strategy did not result in improved outcomes in low CVP-assisted laparoscopic hepatectomy.

Keywords Goal-directed fluid therapy (GDFT) strategy · Laparoscopic hepatectomy · Low central venous pressure

Introduction

Hepatectomy is an effective and widely used surgical method for the treatment of various liver diseases [1]. Laparoscopic hepatectomy (LH), as a minimally invasive approach for hepatectomy, is used increasingly worldwide [2]. However, LH is incredibly challenging because of the indirect vision and narrow operative space [3]. Low central venous pressure (CVP) is an option to reduce operative blood loss. Previous studies reported that controlling CVP < 5 cmH_2O or 3 mmHg can significantly reduce hepatic venous bleeding in LH [4]. A worldwide survey has shown that 85% of centers utilized a strategy of limiting intraoperative infusion volume to decrease CVP and reduce intraoperative blood loss during hepatectomy [5].

Although low CVP has been shown to be effective in reducing operative blood loss in several studies, concerns have been raised about the potential for morbidity that may derive from the hypoperfusion of abdominal organs during the low CVP phase of liver resection. A retrospective analysis showed postoperative biochemical acute kidney injury (bAKI) was seen in 17% ($n=350$) of patients in low CVP assisted liver resection [6].

To alleviate the hypoperfusion during liver resection, large amounts of fluid are often required post-transection

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in LH to compensate for blood loss and fluid shifts. The fluid management during this period is still controversial. A goal-directed fluid therapy (GDFT) strategy has been advocated recently [7]. This approach, based on optimizing flow variables and dynamic indices of fluid responsiveness has been associated with fewer postoperative complications in patients undergoing high-risk surgery [8]. The studies on GDFT strategy in liver resection are mainly about open surgery, not the LH especially low CVP assisted LH [9]. While hemodynamic management during low CVP-assisted LH is not the same as that during open hepatectomy, the intra-abdominal pressure induced by the pneumoperitoneum may deteriorate the perfusion of kidney and liver. Another concern discussed in LH is carbon dioxide embolism and hypercapnia which will have great influence on hemodynamic management. Therefore, it is time to evaluate the safety and effectiveness of GDFT in low CVP assisted LH.

The purpose of this prospective single-blinded randomized controlled trial was to find out whether GDFT strategy in post-transection period in low CVP assisted LH has more benefit than traditional fluid strategy. We hypothesized that for patients undergoing low CVP assisted LH, the addition of GDFT fluid optimization algorithm will improve perioperative fluid-related complications.

Methods

Study design

This is a superiority, randomized, single-blinded, controlled study. This study has been approved by the Ethics Committee of Zhongshan Hospital Fudan University (Approval No.: B2018-303R). The study has been registered in Chinese Clinical Trial Registry (www.chictr.org.cn) and the registration number is ChiCTR1900027017.

Patients

Between April 2020 and Dec 2021, patients who were scheduled for laparoscopic liver resection surgery were eligible to participate in the study. The included criteria were: (1) preoperative diagnosis of liver tumor patients, aged above 18 years and BMI < 30 kg/m^2; (2) American Society of Anesthesiologists (ASA) physical statuses 1–3; (3) with normal coagulation function who can accept transversalis fascia plane block; (4) no history of coronary heart disease, cerebral infarction, cerebral hemorrhage and renal insufficiency. Renal insufficiency is defined as glomerular filtration rate (GFR) < 60 ml/(min × 1.73 m^2). The patients were interviewed for background information about age, height, weight, previous operations, medical conditions and medications. We excluded the patients who had a history of aortic stenosis and aortic regurgitation and we excluded the patients with cardiac arrhythmia such as atrial fibrillation. Withdrawal criteria included withdrawal of informed consent by participants and conversion to open surgery.

Randomization and blinding

Eligible patients were identified by an anesthetist the day before the surgery. The same anesthetist informed the patients of the study protocol and got written informed consent from them. Once eligibility was confirmed, the patients were randomly assigned in a 1:1 ratio to either Goal-Directed Fluid Therapy (GDFT) group or the control group with a sealed envelope according to a computer-generated random sequence by another anesthetist. Anesthesia nurses who were not involved in the evaluation of the patient opened the patient's envelope before the surgery and prepared the equipment needed. An anesthesiologist and an anesthesia assistant were responsible for the intraoperative anesthesia management. The team performed the anesthesia was not the same anesthesiologist and was unblinded on the allocation group. None of the researchers who were involved in the assessment of the patients or the data collection was aware of the patient assignment.

Procedures

After entering the operating room, patients were performed deep venipuncture. All patients had standard monitoring with electrocardiogram (ECG), invasive blood pressure (ABP), pulse oximetry (SpO_2), and central venous pressure (CVP).

Anesthesia was induced with propofol (AstraZeneca Company, Italy) and remifentanil (Yichang Renfu Pharmaceutical Industry, Hubei, China) via target-controlled infusion (TCI, effect site Marsh model for propofol and plasma TCI Minto model for remifentanil) using a TCI pump (8913030, B.Braun Melsungen AG, Germany). The initial target plasma concentration (*Cp*) of propofol was set at 3–4 μg/ml and *Cp* of remifentanil was set at 3–4 ng/ml. Sufentanil 0.2 μg/kg (Yichang Renfu Pharmaceutical Industry, Hubei, China) was also used during induction. After loss of consciousness, 0.6 mg/kg rocuronium (Merck Sharp & Dohme Corp, New Jersey, USA) was given to patients. Once intubation was completed, propofol and remifentanil were stopped.

After induction, a bilateral transversalis fascia plane block with 0.375% ropivacaine (AstraZeneca, Sweden) under ultrasound guidance (30 ml each side) was performed. Anesthesia was maintained with inhaled halogenated gas (sevoflurane or desflurane) during the surgery with MAC between 0.8 and 1.2. Sufentanil and rocuronium would be given if necessary. The ventilator was set up as follows: tidal

volume 6–8 ml/kg, respiratory rate 12–14/min and peak airway pressure below 30 mmHg. Permissive hypercapnia was allowed during the surgery. The pneumoperitoneum pressure during LH is 12 mmHg. Ketorolac tromethamine (Chengdu Beite Pharmaceutical Co., Ltd.) in 15 mg and ramosetron in 0.3 mg (Chongqing Changhui Pharmaceutical Co., Ltd.) were given before the end of the operation.

After anesthesia induction, in GDFT group, radial artery line was connected to a FloTrac™ sensor (Edwards Lifesciences, Irvine, CA, USA) to continuously measure the SVV, cardiac output and cardiac index. The FloTrac™ sensor continuously determined the arterial pressure-based cardiac output. The stroke volume was calculated based on the patient's arterial pressure in conjunction with some demographic data, such as age, sex, height, and weight. The FloTrac data were masked to the anesthesiologist during the resection phase. Before removal of the tumor, the control group and GDFT group had the same restrictive fluid strategy. The fluid management was 2 ml/kg/h Ringer's solution to maintain MAP > 60 mmHg and CVP < 5 mmHg. When MAP < 60 mmHg vasoactive agents, such as norepinephrine, phenylephrine and ephedrine were used. When CVP > 5 mmHg, dobutamine was used. After removal of the tumor, dobutamine was stopped. Then, the fluid management was guided by anesthesiologist's experience and GDFT algorithm in control group and GDFT group, respectively. The GDFT algorithm is shown in Fig. 1. SVV target of greater than 12% was used as a fluid intervention target for restoration of euvolemia. When SVV<8%, vasoactive agents were used according to the blood pressure and CI.

Outcome parameters

The primary outcome parameter is the incidence of postoperative complications including acute myocardial infarction, cerebrovascular accident, prolonged mechanical ventilation, pneumonia, acute kidney injury, hepatic insufficiency, pleural effusion, seroperitoneum, wound infection, arrhythmia and large volume of drainage. The definition of acute myocardial infarction is according to Universal Definition of Myocardial Infarction [10]. The definition of cerebrovascular accident is focal brain injury that persists for > 24 h, combined with an increase in disability of at least one grade on the modified Rankin scale, confirmed by cerebral CT scan. The definition of prolonged mechanical ventilation is postoperative mechanical ventilation for more than 24 h (any cause), including noninvasive pressure support ventilation through a face mask. The definition of acute kidney injury is RIFLE criterion. The definition of hepatic insufficiency is PHLF criterion. PHLF was classified as grade A if it required routine postoperative care, grade B if it required non-routine management without invasive treatment, or grade C if it required non-routine management that was invasive. Grade B and C are regarded as hepatic insufficiency. The criterion of pneumonia, pleural effusion and seroperitoneum is confirmed by X-ray and ultrasound. Wound infection and large volume of drainage are diagnosed and confirmed by surgeon. The criterion of arrhythmia is dysrhythmia requiring extra medical treatment. Secondary outcome parameters include perioperative clinical outcomes, postoperative clinical outcomes (time of Foley discontinuation, getting out-of-bed, return of bowel function, and postoperative feeding time), length of hospital stay after surgery, postoperative lactic acid, fluids and vasoactive medications during the operation.

Statistical analysis

The study was designed as a superiority trial. A review of data in our hospital revealed the incidence of the postoperative complication after low CVP assisted LH was about 26%. Assuming a 26% rate of postoperative complications after low CVP assisted LH for the primary outcome, we calculated that 145 patients/group would be needed to have 80% power at a two-sided α level of 0.05 to show a relative between-group difference of 50% in the primary outcome measure (26–13%). To allow for the potential unevaluable patients, the number of patients to be enrolled was increased to 320 patients.

Descriptive statistics were summarized using either the mean (SD) or median (interquartile range). Categorical outcomes were summarized using percentage frequency distributions. The primary endpoint was compared between the two groups with the chi-square or Fisher exact test. For the analysis of the other endpoints, continuous outcomes were compared between the groups with the Mann–Whitney U test or t-tests. The chi-test or Fisher exact test was used for categorical comparisons. *P* values of 0.05 were considered statistically significant. The analysis was performed using SPSS V23 (IBM, USA) and GraphPad Prism 6.0 (GraphPad Software, USA).

Results

Of the 1361 screened patients from Apr 2020 to Dec 2021, 320 patients underwent randomization, and 319 patients (159 patients in the control group, 160 patients in the GDFT group) were included in the analysis (Fig. 2). Data on primary outcome were finally available for 319 patients. The demographic and clinical characteristics of the two groups were similar at baseline (Table 1).

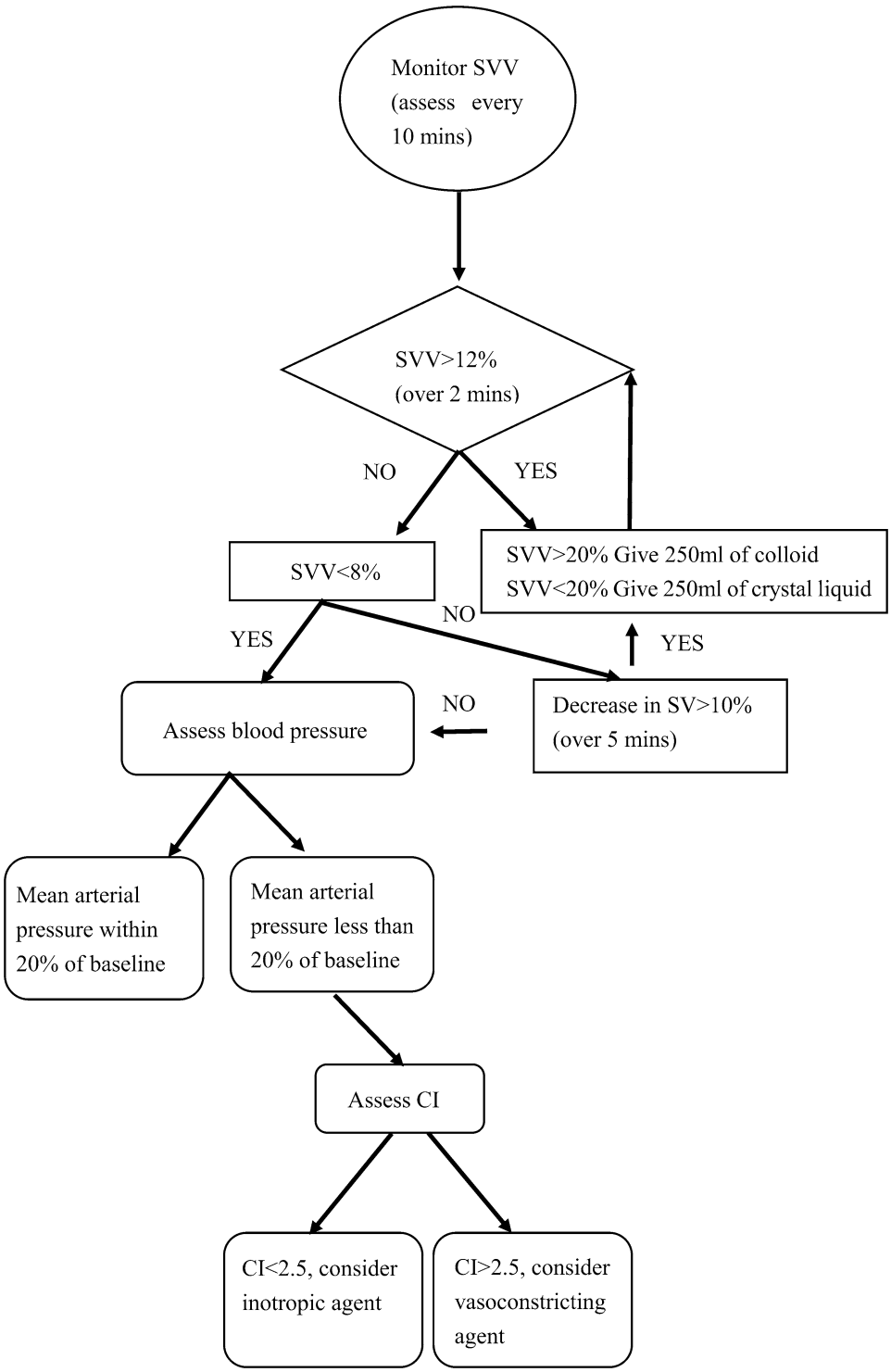

Fig. 1 GDFT algorithm for patients undergoing low central venous pressure assisted laparoscopic hepatectomy. *SVV* stroke volume variation, *SV* stroke volume, *CI* cardiac index

Primary outcome

We use Chi-square and Fisher exact test to analyze the postoperative complications. 36 patients (22.7%) in the control group and 47 patients (29.4%) in the GDFT group had postoperative complications including major and minor complications ($P=0.17$). No patient occurred acute myocardial infarction, cerebrovascular accident and prolonged mechanical ventilation. 6 patients (3.8%) in the control group and 3 patients (1.9%) in the GDFT group had pneumonia ($P=0.34$). 3 patients (1.9%) in the control group and 5 patients (3.1%) in the GDFT group had acute kidney injury ($P=0.72$). 2 patients (1.3%) in the control group and no patient in the GDFT group had hepatic insufficiency

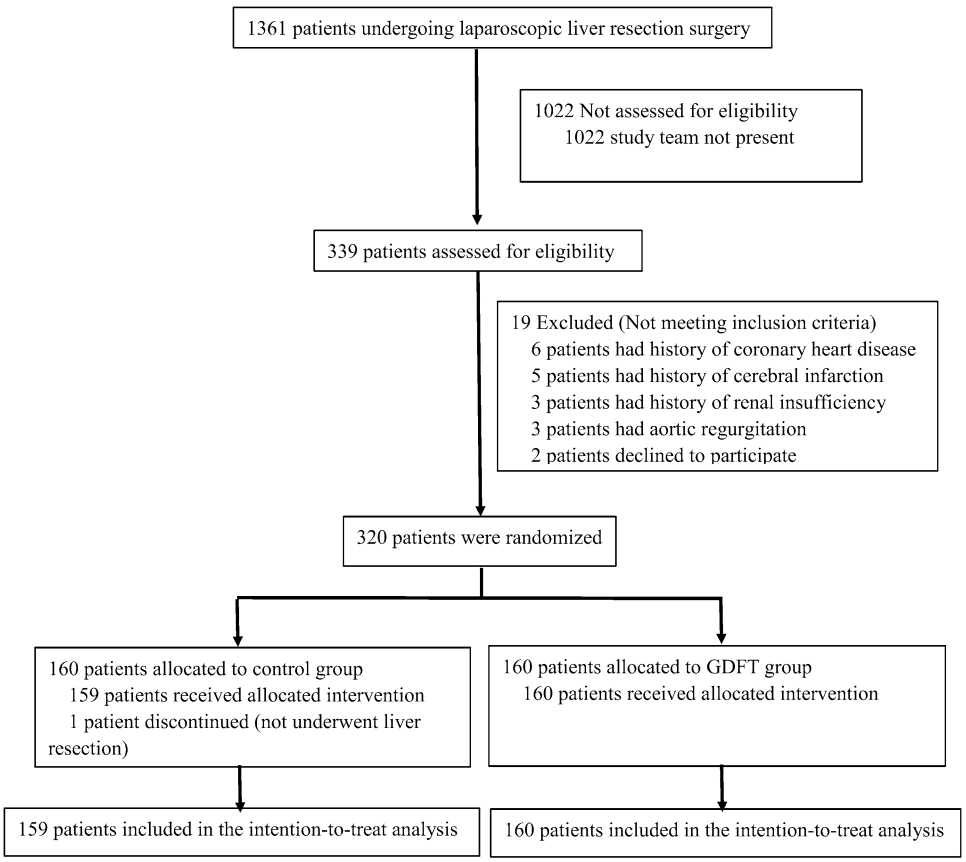

Fig. 2 Consort diagram

($P=0.25$). 21 patients (13.2%) and 2 patients (1.3%) in the control group and 33 patients (20.6%) and 3 patients (1.9%) in the GDFT group had pleural effusion ($P=0.08$) and seroperitoneum ($P=1.00$), respectively (Table 2).

Secondary outcomes

The CVP of baseline, after intubation, during the liver resection and before the extubation are similar between the control group and GDFT group ($P=0.66$, 0.71, 0.43 and 0.23, respectively). The incidence of air embolism had no difference between two groups ($P=0.77$) (Table 3).

Many perioperative variables were compared between the two groups (Table 4). The duration of surgery and anesthesia are similar between the two groups ($P=0.76$ and 0.94, respectively). Time for post-resection phase and time for low CVP application are similar between two groups ($P=0.77$ and 0.84, respectively). Blood loss between two groups had no significant difference ($P=0.68$). The amount of perioperative urine output is fewer in GDFT group than the control group ($P=0.0354$), while the amount of urine output adjusting for weight and operation time has no significant difference ($P=0.08$).

Many postoperative variables indicating postoperative recovery were compared between two groups (Table 4). Time of Foley discontinuation, getting out-of-bed, return of bowel function and postoperative feeding time had no significant difference between two groups. With Mann–Whitney test, the length of hospital stay after surgery was 5 days in control group and 6 days in GDFT group (5 [5, 6] vs 6 [5–7], $P=0.11$) (Table 4). There is also no difference in postoperative lactic acid ($P=0.70$).

The amount of crystal liquid infusion is similar between the two groups (Table 4), while the amount of colloid infusion is much more in the GDFT group (118.6 ± 162.5 vs 268.8 ± 196.3, $P=0.0001$). The number of patients received transfusion is similar between two groups.

The amount of ephedrine is more in the control group than in the GDFT group (13.25 ± 9.08 vs 10.97 ± 9.09, $P=0.0259$), while there is no difference in the amount of phenylephrine ($P=0.57$), dobutamine ($P=0.38$) and norepinephrine ($P=0.99$) (Table 4).

Discussion

This prospective randomized controlled trial compared the postoperative complication of low-CVP assisted LH patients receiving traditional fluid strategy or GDFT strategy. The results show that the implementation of GDFT strategy

Table 1 Characteristics of the patients at baselines

	Control group ($n=159$)	GDT group ($n=160$)	*P* value
Age, year (mean, SD)	50.5 ± 13.4	50.0 ± 12.1	0.70
Female sex	69 (43.4%)	73 (45.6%)	0.69
Weight, kg (mean, SD)	64.9 ± 11.2	64.8 ± 10.9	0.98
Height, cm (mean, SD)	166.0 ± 7.8	165.5 ± 7.7	0.58
Body mass index, kg/m^2 (mean, SD)	23.4 ± 2.9	23.6 ± 3.2	0.57
ASA			0.83
I	44	46	
II	115	114	
Pathological results			0.24
Primary liver cancer	101	92	
Metastatic tumor	14	9	
Hemangioma	25	26	
Focal nodular hyperplasia	14	22	
Others	5	11	
Tumor size, cm^3 (mean, SD)	137.0 ± 241.2	176.4 ± 563.8	0.42
Performed procedure			0.98
Partial hepatectomy	99	103	
Segmentectomy	15	14	
Hepatolobectomy	36	34	
Hemihepatectomy	9	9	
Hypertension	33 (20.8%)	29 (18.1%)	0.55
Diabetes	18 (11.3%)	14 (8.8%)	0.44
Preoperative Scr, μmol/l (mean, SD)	70.1 ± 15.1	71.4 ± 13.5	0.43
Preoperative AST, U/l (mean, SD)	22.8 ± 13.9	22.7 ± 12.4	0.95

Values are presented as mean ± SD, counts and percentage (%)

ASA American Society of Anesthesiologists physiological status, *Scr* serum creatinine, *AST* aspartate aminotransferase

Table 2 Major and minor postoperative complications

	Control group ($n=159$)	GDT group ($n=160$)	*P* value
Overall postoperative complications	36 (22.7%)	47 (29.4%)	0.17
Major complications			
Acute myocardial infarction	0	0	1.00
Cerebrovascular accident	0	0	1.00
Prolonged mechanical ventilation	0	0	1.00
Pneumonia	6 (3.8%)	3 (1.9%)	0.34
Acute kidney injury	3 (1.9%)	5 (3.1%)	0.72
Hepatic insufficiency	2 (1.3%)	0	0.25
Pleural effusion	21 (13.2%)	33 (20.6%)	0.08
Seroperitoneum	2 (1.3%)	3 (1.9%)	1.00
Wound infection	1 (0.6%)	0	0.50
Minor complication			
Arrhythmia	0	0	1.00
Large volume of drainage	1 (0.6%)	3 (1.9%)	0.62

Values are presented as counts and percentage (%)

Table 3 Perioperative CVP and air embolism

	Control group ($n=159$)	GDT group ($n=160$)	*P* value
Baseline CVP, mmHg (mean, SD)	2.7 ± 2.5	2.8 ± 2.7	0.66
CVP after intubation, mmHg (mean, SD)	5.3 ± 2.8	5.4 ± 2.7	0.71
CVP during the liver resection, mmHg (mean, SD)	4.9 ± 2.4	5.2 ± 2.8	0.43
CVP before the extubation, mmHg (mean, SD)	7.9 ± 3.0	8.3 ± 3.0	0.23
Air embolism	5 (3.1%)	7 (4.4%)	0.77

Values are presented as mean ± SD, counts and percentage (%)

CVP central venous pressure

Table 4 Clinical outcomes and the amount of fluids and vasoactive medications during the operation

	Control group ($n=159$)	GDT group ($n=160$)	*P* value
Perioperative outcomes			
Surgical time, min (mean, SD)	142.4 ± 61.6	140.1 ± 72.5	0.76
Anesthesia time, min (mean, SD)	182.4 ± 65.7	181.7 ± 81.2	0.94
Time for post-resection phase, min (mean, SD)	56.4 ± 24.0	55.5 ± 29.0	0.77
Time for low CVP application, min (mean, SD)	124.8 ± 53.1	126.2 ± 65.1	0.84
Blood loss, ml (mean, SD)	103.7 ± 87.6	109.4 ± 144.8	0.68
Perioperative urine output, ml (mean, SD)	190.7 ± 159.2	157.2 ± 121.5	0.0354
Perioperative urine output, ml/kg/h (mean, SD)	1.1 ± 1.0	0.9 ± 0.7	0.08
Postoperative outcomes			
Foley discontinuation, h (median, IQR)	64 (46,70)	66 (45,70)	0.50
Get out-of-bed time, h (median, IQR)	44 (28,48)	44 (31.5,48)	0.68
Return of bowel function, h (median, IQR)	48 (35,57)	48 (42.25,60.75)	0.17
Postoperative feeding time, h (median, IQR)	28 (22,45)	24.5 (21,44.75)	0.34
Length of hospital stay after surgery, day (median, IQR)	5 (5,6)	6 (5,7)	0.11
Postoperative lactic acid, mol/l (mean, SD)	1.9 ± 0.9	1.8 ± 1.0	0.70
Fluids			
Crystalloid, ml (mean, SD)	842.8 ± 240.1	836.3 ± 269.6	0.82
Colloid, ml (mean, SD)	118.6 ± 162.5	268.8 ± 196.3	0.0001
Transfusion			
Red blood cells	2 (1.3%)	4 (2.5%)	0.68
Blood plasma	0	1 (0.6%)	1.00
Vasoactive medications			
Dobutamine, mg (mean, SD)	5.6 ± 3.4	5.2 ± 3.2	0.38
Phenylephrine, μg (mean, SD)	771.7 ± 1100.9	841.9 ± 1077.6	0.57
Ephedrine, mg (mean, SD)	13.3 ± 9.1	11.0 ± 9.1	0.0259
Norepinephrine, μg (mean, SD)	6.1 ± 33.4	6.1 ± 42.1	0.99

Values are presented as mean ± SD, median (IQR) and counts and percentage (%)

is not associated with fewer postoperative complications. Moreover, perioperative and postoperative clinical outcomes between two groups had no significant difference. On the other hand, patients in GDFT group received more colloid infusion and less ephedrine than patients in control group.

The incidence of postoperative complications in our study was higher in both groups compared to other studies [11, 12]. Kevin Tri Nguyen reported the overall morbidity is about 10.5% in a worldwide review of laparoscopic liver resection of 2804 patients [12]. The main difference in the incidence of postoperative complications between our study and previous studies is about the incidence of pleural effusion which in our study the incidence of pleural effusion is much higher. It can be explained by the criterion and severity of pleural effusion. The criterion of pleural effusion is confirmed by X-ray and ultrasound in our study and many cases of pleural effusion in our study are minor and did not need pleural drainage.

Our data demonstrated that the incidence of complications and perioperative/postoperative clinical outcomes were similar between two groups. Effects of GDFT on other relevant outcome measures such as lactic acid and length of hospital stay after surgery were also not observed. It can be explained by several reasons. First of all, it is affected by the relatively low complication rate due to laparoscopic liver resection itself and the nature of the patients included. Complication rate is lower in laparoscopic liver resection compared to the open procedure in many studies [13, 14]. Moreover, although the trial was implemented in high-risk surgery, the patient population represented in our study is not high risk. The strict exclusion criteria in our study restricted our study subjects to a relatively healthy pool. We excluded the patients who had a history of aortic stenosis, aortic regurgitation, previous coronary heart disease, cardiac arrhythmia such as atrial fibrillation, cerebral infarction, cerebral hemorrhage and renal insufficiency. These patients had more chance to have postoperative complications such as acute myocardial infarction, cerebrovascular accident and AKI and gain benefit from GDFT therapy. Secondly, the fluid strategy was different only after the liver resection, which lasted a relatively short period. The duration of GDFT strategy is too short to make significant difference in organ perfusion and function. The duration of GDFT strategy lasted to the PACU or the first 24 h after surgery may have difference. Thirdly, the cutoff of SVV and CI in our study is according to the study of Kazuyuki Mizunoya [15], while the threshold at which SVV should trigger fluid administration during major liver resection remains a matter of debate. The SVV target cut-off used in our study (12%) is lower than that reported by other research groups, who used cut-offs of 15–20% [16, 17]. The threshold at CI in our study is 2.5. Optimal cardiac index and related cardiovascular variables may differ according to age [18] and an age-specific target value for CI cut-off may be more accurate. Last but not least, improved knowledge of hemodynamic management and its consequences might have had effects on hemodynamic treatment in the control group.

In our study, we found the CVP before the extubation are similar between the control group and GDFT group. It indicated two groups achieved similar fluid resuscitation at the end of the surgery and organ perfusion has improved. It may explain why the incidence of postoperative complications had no difference between two groups.

Moreover, our data showed the amount of colloid infusion during the surgery was much more than the control group. It can be explained by the GDFT algorithm. When SVV is beyond 20%, the choice of fluid intervention target for restoration of euvolemia is colloid, thus increasing the whole usage of colloid infusion. In our study, patients in GDFT group received more fluids during the surgery but had similar incidence of postoperative complications. On the contrary, Camilo Correa-Gallego [19] found patients in the GDFT received less intraoperative fluid (mean 2.0 L GDFT vs 2.9 L standard perioperative resuscitation) and he found higher intraoperative fluid volume was associated with higher 30-day morbidity which is not observed in our study. It can be explained that in our study intraoperative fluid in both groups is about 1 L, which is much less than the amount of fluid resuscitation in Camilo Correa–Gallego's study. Therefore, both groups in our study had lower incidence of postoperative complications and there was no difference between two groups. Furthermore, the outcomes of fluids and postoperative complications between two groups in our study are similar to Eric's study [20], Eric's found a CI and SVV driven algorithm did not result in improved outcomes after high-risk abdominal surgery in a large randomized multicenter trial. While we chose different surgeries, the conclusions of two studies were similar.

In our study, the larger amount of colloid infusion and total fluid infusion may lead to less ephedrine usage during the operation. Contrary to the colloid infusion, the amount of perioperative urine output is fewer in GDFT group than the control group. Furthermore, we adjusted amount of urine output for weight and surgery time and found it had no significant difference between two groups. Collectively, these data suggest whether GDFT strategy led to less urine output still needs to be explored.

Our study had some limitations. First, the patients in the control group had no data of CI and SVV in order not to provoke therapeutic decisions based on these measurements. A major drawback of this approach is that we do not know whether CI differences between the GDFT and the control group were absent, although CVP between two groups at the end of the surgery was similar. Secondly, we enrolled relatively healthy patients in the study which may restrain the conclusion expand to high-risk patients.

In summary, we evaluated the performance of goal-directed fluid strategy in low CVP assisted LH and found it had no advantage over control group in postoperative complications and peri/postoperative clinical outcomes. Whether the high-risk patients can benefit from goal-directed fluid strategy in low CVP assisted LH is next to explore.

Conclusions

The implementation of GDFT strategy is not associated with fewer postoperative complications. GDFT strategy based on SVV and CI did not result in improved outcomes in low CVP assisted LH.

Author contributions Conception and design: JC, HY, SL; administrative support: JC; provision of study materials or patients: HY, SL,

YY; collection and assembly of data: YY, PW, LJ; data analysis and interpretation: SL, HY; manuscript writing: all authors; final approval of manuscript: all authors.

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Data availability The data that support the fndings of this study are available on request from the corresponding author, YH.

Declarations

Conflict of interest Jing Cang received research support from Edward (Shanghai) Medical Supplies Co., Ltd. Shichao Li, Yue Yin, Pei Wang, Long Jiang and Huan Yan declare that they have no competing interests.

Ethical statement This study has been approved by the Ethics Committee of Zhongshan Hospital Fudan University (Approval No.: B2018-303R). The study has been registered in Chinese Clinical Trial Registry (www.chictr.org.cn) and the registration number is ChiCTR1900027017. Written informed consent was obtained from all participants. The research is conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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