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ORIGINAL RESEARCH

Effect of Two-Stage Goal-Directed Crystalloid versus Colloid Fluid Therapy on Postoperative Quality of Recovery in Patients Undergoing Laparoscopic Hepatectomy: A Randomized Controlled Trial

Xiaozhe Zhu[1,2], Yujie Zhu[1,2], Luyao Wang[1,2], Lei Shen[1,2], Xinyang Xiong[1,2], Xiangwen Lu[1,2], Na Zhang[1,2], Chenhui Ye[1,2], Dunyi Qi[1,2], Xiaolu Hu[1,2]

[1]Key Laboratory of Anesthesiology, Xuzhou Medical University, Xuzhou, People's Republic of China; [2]Department of Anaesthesiology, Affiliated Hospital of Xuzhou Medical University, Xuzhou, People's Republic of China

Correspondence: Dunyi Qi; Xiaolu Hu, Key Laboratory of Anesthesiology, Xuzhou Medical University, No. 99 Huaihai West Road, Xuzhou, Jiangsu, 221002, People's Republic of China, Tel +86-18052268338; +86-15852315958, Email qdy6808@163.com; 82496643@qq.com

Objective: This study aimed to investigate the impact of two-stage goal-directed crystalloid versus colloid fluid therapy on postoperative quality of recovery in patients undergoing laparoscopic hepatectomy.

Patients and Methods: A total of 116 patients scheduled for elective laparoscopic hepatectomy were randomly assigned to two groups: the goal-directed fluid therapy (GDFT) crystalloid group and the GDFT colloid group. Both groups were monitored for stroke volume variation (SVV) using the FloTrac/Vigileo system, and GDFT was guided based on SVV values. Primary outcome was the 24 h postoperative Quality of Recovery-15 (QoR-15) score. Secondary outcome included the estimated blood loss, lactate levels, total fluid infusion volume, hemodynamic status, postoperative nausea and vomiting (PONV) scores, pain scores, postoperative liver and kidney function, and the incidence of postoperative complications.

Results: There was no significant difference in the total QoR-15 scores between the two groups at each point in time ($P > 0.05$). Compared with the crystalloid group, the colloid group had lower PONV scores at 24 and 48 h postoperatively, fewer times of rescue fluid infusion, and a lower total fluid infusion volume ($P < 0.05$). Multiple linear regression analysis showed that the estimated blood loss ($\beta = -0.268$, $P = 0.005$) and PONV ($\beta = -0.176$, $P = 0.045$) score were associated with postoperative recovery.

Conclusion: Two-stage goal-directed crystalloid versus colloid fluid therapy had no significant difference in the postoperative quality of recovery in patients undergoing laparoscopic hepatectomy, which is the primary finding of this study. Nevertheless, our data indicated that colloids may reduce postoperative nausea and vomiting (PONV), though this observation requires confirmation in larger-scale trials.

Keywords: crystalloids, colloids, goal-directed fluid therapy, recovery quality, stroke volume variability, laparoscopic hepatectomy

Introduction

Hepatectomy is an effective surgical method for treating various liver diseases.[1] Laparoscopic hepatectomy has become the mainstream surgical approach for hepatectomy due to its minimally invasive nature, rapid postoperative recovery, and low complication rate.[2,3] However, the complex vascular distribution within the liver, rich blood supply, and limited laparoscopic surgical field of view[4] may cause significant hemodynamic fluctuations during liver surgery.[5] Therefore, formulating a reasonable fluid therapy plan to reduce intraoperative bleeding and maintain hemodynamic stability is particularly important.[6]

The low central venous pressure (LCVP) strategy-based fluid therapy plan has been used worldwide for decades. By restricting fluid infusion during liver resection, it aims to lower portal vein pressure and reduce intraoperative bleeding.[7] However, this strategy can lead to insufficient effective circulating blood volume in patients, causing varying degrees of

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hypoperfusion in organs and increasing postoperative complications.[8] Stroke volume variation (SVV) has long been of interest and proposed as a predictor of fluid responsiveness.[9] An increasing number of clinical studies have confirmed its accuracy in goal-directed fluid therapy (GDFT). SVV is continuously analyzed by the FloTrac/Vigileo system from peripheral arterial waveforms and has a good correlation with central venous pressure (CVP).[10] Studies have shown that in different stages of laparoscopic hepatectomy, fluid therapy guided by different SVV values can effectively reduce intraoperative bleeding, improve perfusion, and benefit short-term prognosis.[11] A GDFT strategy with a high SVV value (13% - 20%) during liver resection and a low SVV value (9% - 13%) from the completion of liver resection to the end of the operation can be a safe alternative to the LCVP strategy, effectively reducing intraoperative bleeding and ensuring tissue perfusion.[11,12]

However, in the context of perioperative goal-directed fluid therapy, there remains a paucity of clinical data evaluating how intravenous fluid types influence postoperative outcomes. It also remains unclear which type of fluid holds comparative advantages in GDFT. This directly gives rise to uncertainty in clinical decision-making: when administering goal-directed fluid therapy to patients undergoing laparoscopic hepatectomy, particularly those with cirrhosis or poor renal function reserve, physicians must weigh the trade-offs between the two fluid types. Crystalloids are widely used due to their broad indications, flexible electrolyte modulation, and cost-effectiveness. However, their short half-life limits intravascular volume maintenance, predisposing to interstitial fluid accumulation. Such abnormal fluid distribution may cause tissue edema, weight gain, and prolonged postoperative recovery, thereby exerting potential adverse effects on postoperative outcomes.[13,14] In comparison to crystalloids, colloids can remain in the intravascular space for a longer duration due to their larger molecular weight and higher osmotic pressure. Additionally, a smaller volume of colloids is required to achieve the same hemodynamic goals.[15] Moreover, colloids may also affect coagulant function[16] and increase the risk of acute kidney injury[17] (AKI) and permeability of the microvasculature under conditions of surgery, inflammation, or trauma. Addressing this dilemma, which stems from the absence of robust evidence to guide such choices, is the primary objective of the present study.

Laparoscopic hepatectomy is a major abdominal surgery with significant trauma. Postoperative recovery in these patients requires attention not only to objective indicators but also to subjective experiences, such as pain control, ability to ambulate independently, and nausea/vomiting. These patient-reported outcomes are closely associated with long-term rehabilitation satisfaction and early self-care ability.[18] The Quality of Recovery-15 (QoR-15) scale is a simple, convenient, and commonly used outcome assessment tool.[19] It evaluates patients' physical and mental well-being both preoperatively and postoperatively, and its reliability has been validated in major abdominal surgeries. Compared with single indicators, it enables a more comprehensive assessment of treatment efficacy. Therefore, our study use the QoR-15 scale to explore the impact of two-stage goal-directed crystalloid versus colloid fluid therapy on postoperative quality of recovery in patients undergoing laparoscopic hepatectomy.

Materials and Methods

Participants

This prospective, randomized controlled study has been approved by the Ethics Committee of the Affiliated Hospital of Xuzhou Medical University (XYFY2024-KL250-01), and registered on July 22, 2024 at clini-calTrials.gov with the number (ChiCTR2400087179). This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline for randomized clinical trials and the CONSORT checklist is shown in Appendix 1. Before the patient enrollment, all patients signed the informed consent. This randomised clinical study was designed and conducted according to the guidelines of the Consolidated Standards of Reporting Trials (CONSORT). Inclusion criteria: (1) Patients selected for elective laparoscopic liver resection; (2) Aged 18–65 years; (3) ASA classification I, II or III; (4) BMI 18–24 kg/m²; (5) Child-Pugh grade A or B. Exclusion criteria: (1) Allergy to hydroxyethyl starch; (2) Abnormal coagulation function (partial thromboplastin time greater than 1.5 times the normal value); (3) Previous liver surgery; (4) Arrhythmia; (5) Preoperative failure of important organs such as the heart, lungs, and kidneys. Exclusion criteria during the study: (1) occurrence of serious unexpected situations (such as massive hemorrhage, cardiac arrest, etc).; (2) Patient's request to withdraw from the trial; (3) Conversion to open surgery.

Randomization and Masking

After obtaining informed consent, an anesthesiologist who did not participate in this study divided the participants into two groups according to the random allocation sequence using the random number table method at a ratio of 1:1. Patients were randomly assigned to receive either balanced salt solution containing 6% hydroxyethyl starch (130/0.4) or balanced salt solution alone for hemodynamic optimization. Pharmacy staff placed opaque black packaging paper on the 500 mL bags, leaving the same administration port free to blind the researchers to the trial fluid. Detailed information on each patient's infusion method and intraoperative anesthesia management was kept in an opaque sealed envelope, which could only be opened when the patient entered the operating room. All surgeries were performed by the same surgical team. All participants, preoperative and postoperative follow-up assessors and statisticians were blinded to the group allocation.

Anaesthesia Procedure

All included patients were allowed solid foods up to 6 h before surgery and fluids up to 2 h before surgery. All patients underwent preoperative bowel preparation. After entering the operating room, venous access was opened and the balanced salt solution was infused with 5–7 $mL \cdot kg^{-1} \cdot h^{-1}$. Heart rate (HR), electrocardiogram (ECG), systolic pressure (SBP), diastolic pressure (DBP), pulse oximetry (SpO_2), and bispectral index (BIS) were routinely monitored. Ultrasound-guided transversalis fascia block was performed under local anesthesia. The FloTrac/Vigileo system was connected to monitorarterial blood pressure, SVV, cardiac index (CI), etc. The right internal jugular vein was punctured under local anesthesia and the CVP was monitored. General anesthesia was induced with midazolam 0.05mg/kg, etomidate 0.3mg/kg, sufentanil 0.5ug/kg, propofol 0.5–1.0 mg/kg and cisatracurium 0.2mg/kg. After tracheal intubation, all patients underwent mechanical ventilation with a tidal volume of 8 mL kg^{-1}, inhaling a 60 and 40% mixture of oxygen and air, with an inhalation-expiration ratio of 1:2 with a goal to achieve $PETCO_2$ 35–45 mm Hg and SpO_2> 95%. Anesthesia was maintained with 1%-1.5% sevoflurane, propofol 2–4 mg kg^{-1} h^{-1} and remifentanil 0.1–0.2 ug kg^{-1} min^{-1}. Bispectral index (BIS) was maintained at 40–60. Cisatracurium was intermittently injected to maintain muscle relaxation during operation. Flurbiprofen axetate 100 mg and tropisetron 2mg was given 30min before the end of the operation. The patients were sent to the post-anesthesia care unit (PACU) at the end of the operation. In the PACU, patients were infused with balanced salt solution at a rate of 1.5mL kg^{-1} h^{-1}. Once the patients had resumed spontaneous respiration, Sugammadex Sodium 2 mg/kg was administered to antagonize the residual neuromuscular blockade. The endotracheal tube was extubated after the respiration and circulation were stable Patient-controlled intravenous analgesia (PCIA) was performed after operation, and the parameters were set as follows: Sufentanil 2ug/kg, flurbiprofen axetil 100mg plus normal saline diluted to 100mL, initial dose 2mL, background dose 2mL/h, lockout time 15min. After the patient returns to the ward, the surgeon routinely administers a mixed solution of 150mL crystalloid and flurbiprofen axetil for preventive analgesia. When VAS score > 3, dezocine 5mg was injected intramuscularly as rescue analgesia.

Intraoperative Fluid Management

In this study, rescue fluid infusion is defined as an additional fluid supplementation operation implemented to restore the stroke volume variation (SVV) to the target range when the patient's intraoperative SVV fails to be maintained within the target range. This operation is clearly distinguished from the preset routine fluid infusion in the study protocol.

Regarding the initiation criteria for infusion, it is specifically when the SVV value exceeds the target range of each stage, that is, when SVV > 20% in the Phase 1 or SVV > 13% in the Phase 2, rescue fluid infusion is initiated. In terms of operation specifications, the standard dose for each rescue fluid infusion is a 100mL fluid bolus, and re-evaluation is conducted 5 minutes later. Meanwhile, the type of fluid used for rescue infusion is consistent with that in the main study protocol – hydroxyethyl starch is selected for the colloid group, and balanced salt solution is selected for the crystalloid group, so as to reduce the confounding effects that may be caused by differences in fluid types.

The GDFT protocol is presented in Figure 1. We managed three hemodynamic components: SVV, CI, and MAP. The patients' hemodynamic status was evaluated every 5 minutes during the operation. Urine output was maintained above 0.5 mL/kg/h intraoperatively, and the maximum safe dose of colloid solution was 33 mL/kg. Fluid management was performed in two stages. Stage 1 (From surgery initiation to liver resection completion): high SVV (13%–20%) was

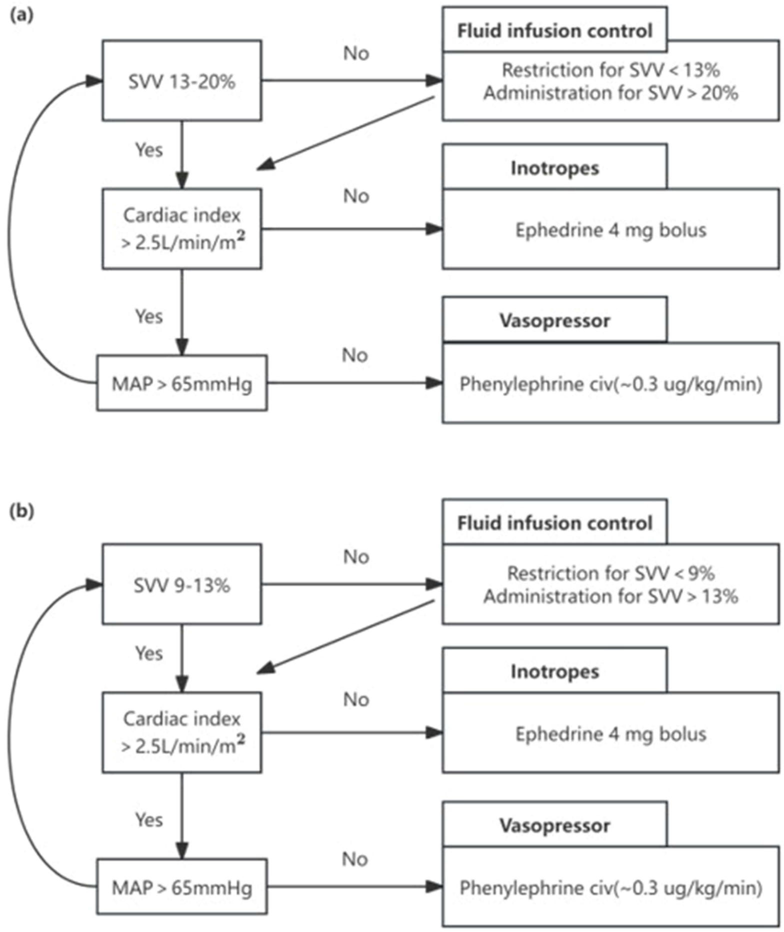

Figure 1 Goal-directed fluid therapy protocol. (**a**) From surgery initiation to liver resection completion; (**b**) From liver resection completion to surgery end.
Abbreviations: SVV, stroke volume variation; MAP, mean arterial pressure.

targeted for fluid management. Specific methods are as follows: When SVV > 20% lasted for 5 minutes, the patient was given 100 mL fluid bolus, the fluid bolus was repeatedly used in patients until SVV reached the target value. If SVV < 13%, the infusion speed was slowed down and nitroglycerin 0.25–0.50 mg was given. Stage 2 (From liver resection completion to surgery end): Fluid administration aimed to maintain SVV between 9% and 13%. The method of fluid administration was the same as described in the phase 1. The cardiac index was maintained at ≥2.5 L/min/m^2 to avoid tissue hypoperfusion, and an ephedrine infusion was administered as needed to maintain this target value. When the cardiac index was ≥2.5 L/min/m^2, the MAP was below 65 mmHg, a continuous phenylephrine infusion (maximum dose 0.3 µg/kg/min) was administered as needed to achieve the target MAP.

Outcomes

The primary outcome of this study was the overall QoR-15 scores at 24 h after surgery. Quality of Recovery-15 (QoR-15) scale[19] was used to evaluate the recovery quality of patients before operation and 24h, 48h, 72h, 7d and 30d after operation. The scale was composed of five parts, which were evaluated from physiological comfort, psychological support, emotion, behavior and pain. Each section is scored from 0 to 10 for a total score of 150, with higher scores indicating better quality of recovery. NRS pain score at rest, nausea and vomiting score were recorded at 1 day before operation and 24h, 48h, 72h, 7 and 30 days after operation. The operative time, the duration of the first and second stages, duration of resection, the time of hepatic portal occlusion, the incidence of hypotension, the use of vasoactive drugs and anesthetic drugs, the estimated blood loss, the total fluid infusion, times of rescue fluid infusion, and the urine output. The HR, MAP and lactic acid (Lac) concentration were recorded at the time of admission (T_0), skin incision (T_1), beginning of liver resection (T_2), completion of liver transection (T_3) and the end of operation (T_4). The extubation time, post-anesthesia care unit (PACU) stay time and sedation observation score (MOAA/S score) were recorded. Creatinine (Cr), blood urea nitrogen (BUN), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL) and direct bilirubin (DBIL) were recorded at 1 day before operation and 1, 2 and 3 days after operation. The time to first exhaust, hospital stay duration, and postoperative complications were recorded.

Statistical Analysis

The sample size was calculated using PASS 15.0 software. The results of pre-experiment showed that the standard deviation of QoR-15 score in group Crystalloid was 10.1 points at 24h after operation, and the average score was 106.8 points. According to the references, the minimal clinically important difference value of QoR-15 scale score was 6 points.[20] Assuming $\alpha = 0.05$, $1\text{-}\beta=0.8$, and considering the dropout rate of about 20%, a minimum of 116 patients were required to be included in this study.

The statistical analysis of this study was conducted based on the Per-Protocol Set. SPSS 27.0 statistical software was used for statistical analysis. Measurement data with normal distribution were expressed as mean±standard deviation ($\bar{x} \pm s$). Independent sample test was used for comparison between groups, and generalized estimating equation was used for comparison within groups. Non-normal distribution measurement data were expressed as median (M) and interquartile range (IQR). Mann–Whitney *U*-test was used for comparison between groups, and generalized estimating equation (GEE) was used for comparison within groups. We performed Bonferroni correction for multiple comparisons within the group. Count data were expressed as examples (%), and comparison between groups was analyzed using X^2 or Fisher exact probability. The QoR-15 score at 24 hours after operation was analyzed by multiple linear regression analysis. Variance inflation factor (VIF) > 10 was considered to indicate statistically significant multicollinearity between variables. Univariate linear regression analysis was performed with groups, age, gender, resection extent, Child-Pugh grade, operative time, hepatic portal occlusion time time, estimated blood loss, total fluid volume, nausea and vomiting score 24 hours after operation as independent variables. Univariate linear regression identified factors with $P < 0.1$, which were subsequently included in the multivariate linear regression analysis. $P < 0.05$ was considered statistically significant.

Results

A total of 130 patients were screened, and 6 were subsequently excluded from further participation. Six patients had their procedures temporarily cancelled. A total of 124 patients were ultimately included in the study. These patients were randomly assigned to two groups. Four cases in each group were excluded due to conversion to laparotomy. Ultimately, 116 patients were included in the statistical analysis.(Figure 2) There was no significant difference in baseline characteristics between the two groups (Table 1).

Comparison of QoR-15 Scores Between the Two Groups

Using generalized estimating equation analysis, there is no interaction between groups and time, so the main effect analysis was conducted (*P* for interaction=0.854). The main effect analysis between groups showed that there was no significant difference in the overall QoR-15 score at each time point between the two groups (*P* for group=0.082). The overall QoR-15 scores of the two groups at 24h, 48h and 72h after operation were significantly lower than preoperative data (*P* for time<0.001) (Figure 3). However, among the 15 QoR-15 scoring items, after Bonferroni correction, 1 individual QoR-15 "items"scores ("enjoy food") in colloid group were significantly higher than those in crystalloid group at 24h after surgery (*P* =0.002) (Table 2). At 48h, 72h, 7 days and 30 days after operation, there was no significant difference in the individual item scores of QoR-15 between the two groups (see Appendix 2).

Comparison of Secondary Outcomes Across the Two Groups

Compared with the crystalloid group, the nausea and vomiting scores of the colloid group were significantly decreased at 24h, 48h after operation (P < 0.05). Compared with preoperative, the nausea and vomiting scores of the two groups were significantly increased at 24h, 48h and 72h after surgery (*P* < 0.05). There were no significant differences in NRS pain

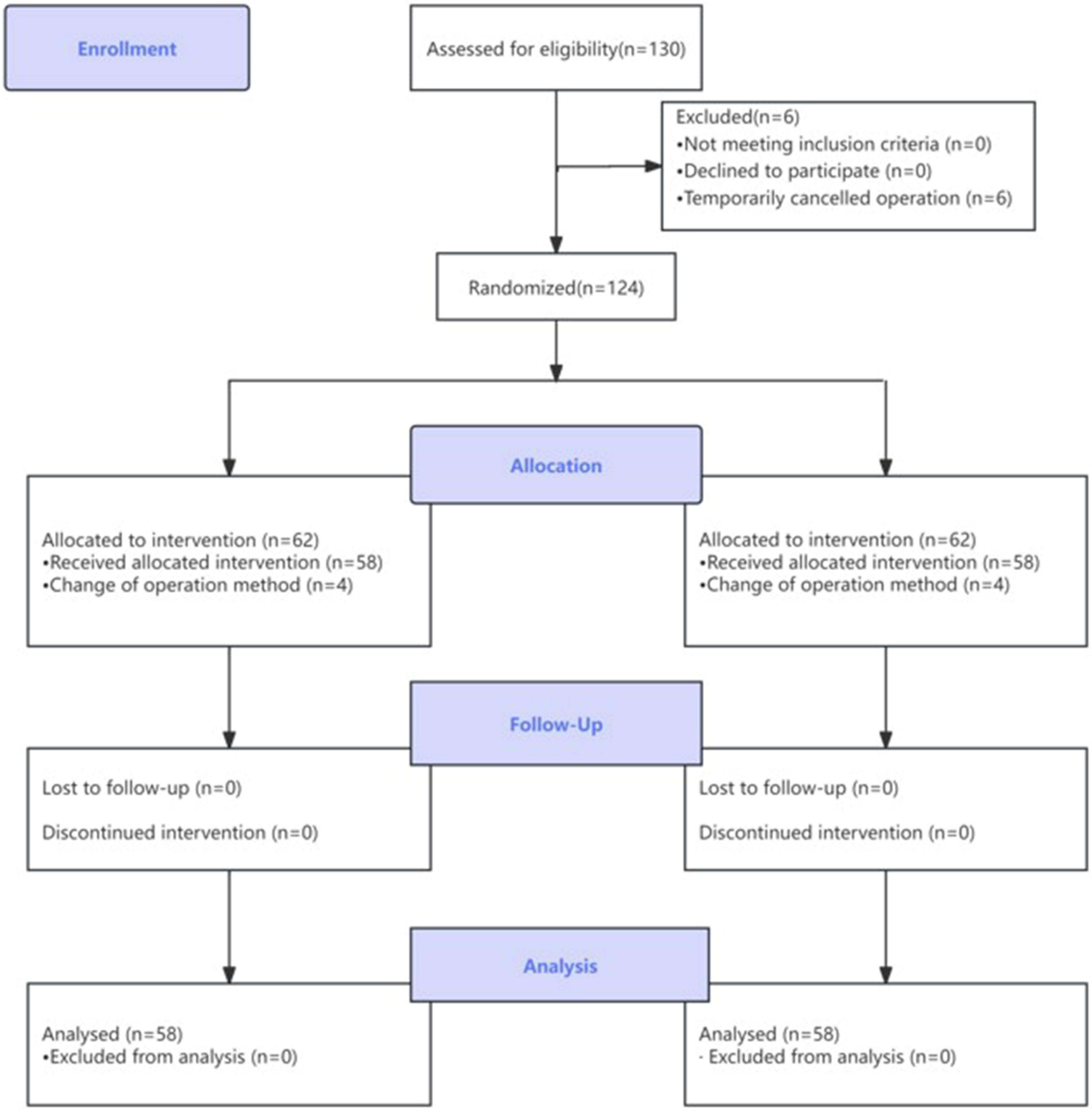

Figure 2 CONSORT flow diagram of the study.

scores between the two groups at each time point. Compared with preoperative, NRS pain scores at 24h, 48h, 72h and 7d after surgery in the two groups were significantly increased ($P < 0.05$) (Table 3).

No statistically significant differences were observed in LAC, MAP, and HR at the each time point ($P > 0.05$) (Figure 4). Compared with the crystalloid group, total fluid volume and times of rescue fluid infusion in the colloid group

Table 1 Demographic Characteristics of the Study Patients

	Crystalloid Group (n=58)	Colloid Group (n=58)	*P*-value
Age (y)	55.0(45.0–60.3)	53.0(42.8–61.3)	0.954[a]
Gender (male/female)	26/32	25/33	0.852[b]
BMI (kg/m^2)	24.0(22.3–25.4)	24.3(21.9–25.3)	0.958[a]
BSA (m^2)	1.8(1.7–1.9)	1.8(1.7–1.9)	0.923[a]
Hypertension	14(24)	13(22)	0.826[b]

(*Continued*)

Table 1 (Continued).

	Crystalloid Group (n=58)	Colloid Group (n=58)	*P*-value
Diabetes mellitus	3(5)	5(9)	0.464[b]
ASA physical status (I/II/III)	7/43/8	6/41/11	0.741[b]
Child-Pugh grade (A/B)	37/21	39/19	0.696[b]
NYHA (I/II/ III)	44/11/3	42/14/2	0.738[b]
Preoperative diagnosis (Hepatolithiasis/Liver cancer/Hemangioma)	2/35/21	2/33/23	0.928[b]
Type of resection (Hemihepatectomy/lobectomy/segmentectomy)	7/12/39	6/14/38	0.885[b]
Resection extent (Major/Minor)	17/41	19/39	0.688[b]

Notes: Value expressed as Mean ± SD, median [IQR] or number (%); [a]Data were analyzed using Mann–Whitney *U*-test. [b]Data were analyzed using Chi-square test.
Abbreviations: BMI, body mass index; BSA, body surface area; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association; Major, The number of liver segments resected was greater than or equal to 3; Minor, The number of liver segments resected was less than 3.

were significantly reduced ($P<0.05$) (Table 4). No significant differences were identified with regard to the operation time, duration of the first and second stages, liver resection time, hepatic portal occlusion time, incidence of hypotension, use of vasoactive and anesthetic drugs, intraoperative blood loss, urine output, maintenance crystalloid volume between the two groups (Table 4). There were no significant differences between the two groups of patients in terms of the extubation time, PACU stay time, MOAA/S score, times of effective PCIA press numbers of rescue analgesia, time to first exhaust, and hospital stay duration (Table 5).

There were no differences in ALT, AST, TBIL, DBIL, Cr and BUN at each time point between the two groups ($P > 0.05$) (see Appendix 3). DBIL, AST, ALT and Cr were elevated at 24h, 48h and 72h postoperation in two groups ($P <0.05$). TBIL were elevated at 24h, 48h and 72h postoperation in colloid group ($P <0.05$). TBIL were elevated at 24h and 48h postoperation in crystalloid group ($P <0.05$). BUN were elevated at 24h and 48h postoperation in crystalloid group ($P <0.05$).

Comparison of Postoperative Complications Between Two Groups

There was no significant difference in the incidence of other postoperative complications and acute kidney injury between the two groups ($P >0.05$) (Table 5).

Regression Analysis of Quality of Recovery Scores at 24h After Surgery

The results of the multiple linear regression analysis comparing the QoR-15 score at 24 h after surgery between the two groups are shown in Appendix 4. Univariate linear regression analysis showed that age, operative time, hepatic portal occlusion time, estimated blood loss, PONV score at 24h after operation were related to the quality of recovery ($P <0.1$). Subsequently, multiple linear regression analysis showed that the estimated blood loss ($\beta = -0.268$, $P = 0.005$) and PONV ($\beta = -0.176$, $P = 0.045$) score were associated with postoperative recovery. (see Appendix 4).

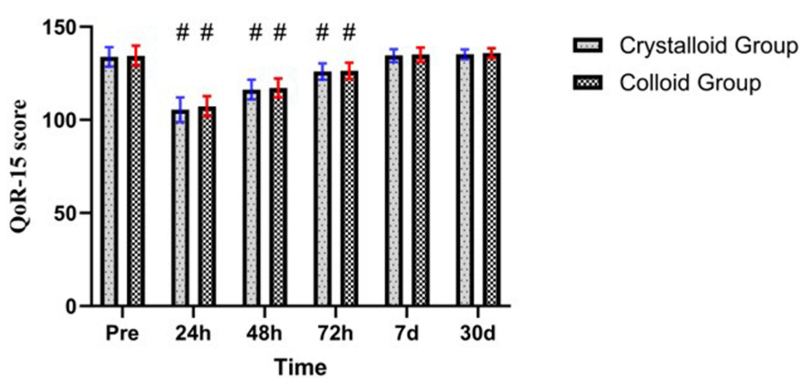

Figure 3 Comparison of overall QoR-15 scores between the two groups. Data are presented as Mean ± SDs. #Compared with baseline, $P < 0.05$.

Table 2 Postoperative 24h QoR-15 Questionnaire Score

	Crystalloid Group (n=58)	Colloid Group (n=58)	Effect Size	*P*-value
Total QoR-15 score	105.45±6.60	107.24±5.43	−0.30 (−0.66 to 0.07)	0.113
Able to breathe	8.10±0.77	8.22±0.99	−0.14 (−0.50 to 0.23)	0.465
Enjoy food	5.17±1.26	5.86±1.03	−0.60 (−0.97 to −0.23)	0.002
Feeling rested	7.16±0.75	7.4±0.92	0.18 (−0.19 to 0.54)	0.349
Good sleep	6.45±1.56	6.84±1.58	−0.25 (−0.62 to 0.11)	0.176
Look after personal hygiene unaided	5.60±1.15	5.52±1.13	0.08 (−0.29 to 0.44)	0.685
Communicate with family and friends	8.38±1.35	8.24±1.14	0.11 (−0.25 to 0.47)	0.554
Support from hospital doctors and nurses	9.02±0.81	9.07±0.77	−0.07 (−0.43 to 0.30)	0.724
Able to return to work or usual home activities	4.40±1.65	4.60±1.76	−0.12 (−0.49 to 0.24)	0.515
Feeling comfortable and in control	6.57±1.23	7.05±1.19	−0.40 (−0.77 to −0.03)	0.034
Feeling of general well-being	6.48±1.27	6.22±1.31	−0.20 (−0.17 to 0.56)	0.284
Moderate pain	6.74±1.12	6.47±1.08	0.25 (−0.12 to 0.62)	0.179
Severe pain	8.00±1.14	8.22±0.92	−0.22 (−0.58 to 0.15)	0.246
Nausea or vomiting	7.10±0.91	7.57±1.39	−0.40 (−0.76 to 0.03)	0.035
Feeling worried or anxious	8.00±0.92	8.03±0.77	−0.04 (−0.41 to 0.32)	0.827
Feeling sad or depressed	8.12±0.77	8.16±0.86	−0.04 (−0.41 to 0.32)	0.823

Notes: Values expressed as mean ± SD; *P* <0.003 significant; Data were analyzed using an unpaired *t*-test, with the effect size presented as the Cohen's d (95% CI).
Abbreviations: QoR-15, Quality of Recovery-15; SD, standard deviation.

Table 3 PONV and NRS Scores Compared at Multiple Points in Time

	Group	Pre	24h	48h	72h	7d	30d
NRS	Crystalloid Group (n=58)	0(0–0)	3(3–4)#	2(1–3)#	1(1–2)#	1(0–1)#	0(0–0)
	Colloid Group (n=58)	0(0–0)	4(2–4)#	2(2–3)#	1(1–2)#	1(0–1)#	0(0–0)
PONV (Likert scale)	Crystalloid Group (n=58)	0(0–0)	1(0–2)#	1(0–1)#	0(0–1)#	0(0–0)	0(0–0)
	Colloid Group (n=58)	0(0–0)	0(0–1)*#	0(0–1)*#	0(0–0)#	0(0–0)	0(0–0)

Notes: Value expressed as median [IQR]; Values expressed as mean ± SD; *P* <0.05 significant; Data were analyzed using GEE. *Compared with group Crystalloid, *P* <0.05; #Compared with baseline, *P* <0.05. Data are presented as medians (interquartile range).
Abbreviations: NRS, Numerical Rating Scale; PONV, postoperative nausea and vomiting; Pre, preoperative baseline; GEE, generalized estimating equation.

Discussion

As assessed systematically by the QoR-15 scale, this prospective, randomized clinical trial found that in patients undergoing laparoscopic hepatectomy, crystalloid or colloid infusion under two-stage goal-directed fluid therapy did not affect the postoperative quality of recovery. Nevertheless, our data indicated that colloids may reduce postoperative nausea and vomiting (PONV), though this observation requires confirmation in larger-scale trials.

Fluid management in laparoscopic hepatectomy remains controversial. Although the technique of controlled central venous hypotension has been widely used for decades to lower portal venous pressure and reduce intraoperative bleeding, this strategy has been increasingly questioned due to the potential risk of tissue hypoperfusion and increased post-operative complications.[21] In recent years, GDFT has attracted attention as an emerging scheme to optimize hemodynamic parameters. However, the optimal type of GDFT infusion for laparoscopic hepatectomy remains inconclusive. Previous studies mostly focused on early recovery indicators and hemodynamic stability, but ignored patient-centered outcome evaluation.[22,23] In this study, the QoR-15 scale was used to systematically evaluate the influence of different infusion regimens on the quality of postoperative recovery through the self-reported results of patients, and comprehensively reflect the recovery level of physiological comfort and psychological state of patients.

In this randomized, controlled trial comparing crystalloids with colloids during the two-stage goal-directed fluid therapy in patients undergoing laparoscopic hepatectomy, there was no statistically significant difference between the two groups in the quality-of-recovery score at 24 hours after surgery (QoR-15). This may be related to the fact that the standardized goal-directed fluid regimen ensured a comparable degree of hemodynamic optimization in the two groups, and the intravascular

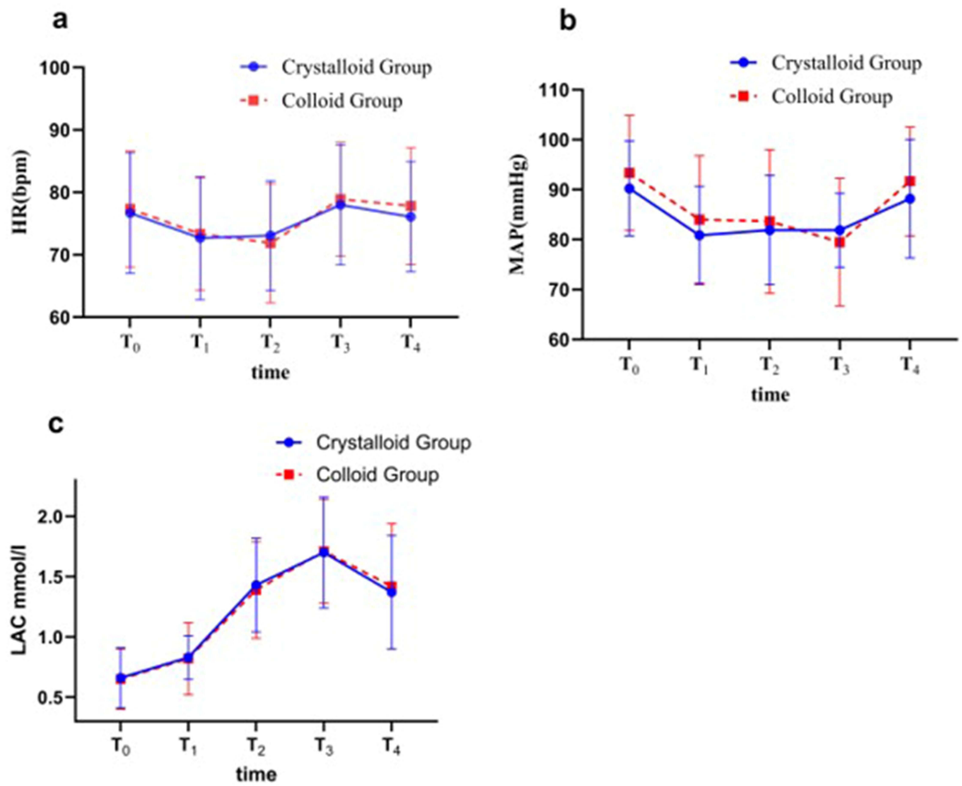

Figure 4 Comparison of intraoperative hemodynamics and LAC between the two groups.
Notes: (**a**) HR at different time points between the two groups; (**b**) MAP at different time points between the two groups; (**c**) LAC at different time points between the two groups; T0: entering the operating room; T1: skin incision; T2: start of liver resection; T3: completion of liver transection; T4: end of surgery. Data are presented as Mean ± SDs.
Abbreviations: HR, heart rate; MAP, mean arterial pressure. LAC, Lactate.

advantage of colloid over crystalloid may be diminished when fluid is administered in a goal-directed manner, counter-balancing the potential effect of fluid type on the quality of early postoperative recovery.[24] In addition, strict perioperative management (standardized anesthesia, analgesia and surgical techniques) also reduces the confounding interference of non-fluid-related factors to a certain extent. Despite the differences in pharmacokinetics and microcirculation effects between crystalloids and colloids,[25] but these differences may not translate into differences in patients' postoperative quality of

Table 4 Intraoperative Data Between the Two Groups

	Crystalloid Group (n=58)	Colloid Group (n=58)	*P*-value
Operative time (min)	220.0(160.0–246.0)	189.0(160.0–220.0)	0.098[a]
Duration of stage 1 (min)	152.0(98.0–180.8)	131.5(103.0–168.0)	0.303[a]
Duration of stage 2 (min)	43.5(37.8–55.0)	47.0(35.0–60.0)	0.486[a]
Duration of resection	62.5(46.0–79.5)	67.5(52.8–95.0)	0.249[a]
Hepatic portal occlusion time (min)	45.0(33.5–55.0)	45.0(35.0–67.5)	0.438[a]
Consumption of remifentanil (mg)	2.6(2.1–3.3)	2.3(1.8–3.0)	0.155[a]
Consumption of sufentanil (ug)	33.5(30.0–36.0)	32.5(29.0–36.4)	0.812[a]
Consumption of propofol (mg)	400.0(326.5–487.3)	360.5(310.8–424.5)	0.190[a]
Use of vasoactive drugs			
Phenylephrine	24(41)	22(38)	0.704[b]
Ephedrine	26(45)	21(36)	0.344[b]
Nitroglycerin	6(10)	10(17)	0.281[b]

(*Continued*)

Table 4 (Continued).

	Crystalloid Group (n=58)	Colloid Group (n=58)	*P*-value
Intraoperative hypotension	18(31)	15(26)	0.537[b]
Blood transfusion	2(3)	4(7)	0.402[b]
Maintenance crystalloid volume(mL)	790.0(588.3–960.0)	650.0(500.0–844.3)	0.142[a]
Times of rescue fluid infusion	11.0(10.0–12.0)	10.0(7.0–10.5)	0.002[a]
Total fluid volume(mL)	1863.0(1612.0–2034.0)	1675.0(1468.3–1900.0)	0.001[a]
Crystalloid volume(mL)	1863.0(1612.0–2034.0)	650.0(500.0–844.3)	<0.001[a]
Colloid volume(mL)	-	1000.0 (700.0–1050.0)	-
Urine output(mL)	250.0 (165.0–300.3)	235.0 (120.0–300.0)	0.337[a]
Estimated blood loss(mL)	290.0 (200.0–350.0)	280.0 (210.0–350.0)	0.797[a]

Notes: Value expressed as Mean ± SD, median [IQR] or number (%); P <0.05 significant; [a]Data were analyzed using Mann–Whitney *U*-test. [b]Data were analyzed using Chi-square test.
Abbreviations: Stage 1, from surgery initiation to liver resection completion; Stage 2, from liver resection completion to surgery end.

Table 5 Postoperative Data and Outcome Variables

	Crystalloid Group (n=58)	Colloid Group (n=58)	*P*-value
Extubation time (min)	23.72±11.30	24.14±10.10	0.836[a]
PACU stay time (min)	38.86±12.39	38.59±17.37	0.922[a]
MOAA/S score	4.0(3.0–4.0)	4.0(3.0–4.0)	0.851[b]
Times of effective PCIA press	6.0(5.0–7.0)	7.0(5.0–8.0)	0.120[b]
Numbers of rescue analgesia	10(17)	11(19)	0.809[c]
Time to first exhaust (h)	46.03±8.35	43.14±10.17	0.096[a]
Hospital stay duration (d)	7.29±3.08	7.19±2.21	0.836[a]
Major complications	15(26)	9(16)	0.169[c]
Minor complications	20(34)	19(33)	0.844[c]
Acute kidney injury	1(2)	2(3)	1.000[c]
KDIGO I	1(2)	2(3)	1.000[c]
KDIGO II	0	0	-
KDIGO III	0	0	-

Notes: Value expressed as Mean ± SD or number (%); P <0.05 significant; [a]Data were analyzed using an unpaired *t*-test; [b]Data were analyzed using Mann–Whitney *U*-test. [c]Data were analyzed using Chi-square test. Major complications: complicated with any of the following diseases: Anastomotic leakage, Peritonitis, Sepsis, Wound dehiscence, Bleeding requiring a redo surgery, Pulmonary embolism, Pulmonary edema, Pneumonia, Acute coronary syndrome, Atrial fibrillation/arrhythmia, Stroke, Reoperation; Minor complications: complicated with any of the following diseases: Superficial wound infection, Urinary and other infection, Paralytic ileus, Need for loop diuretics, Postoperative confusion, Postoperative nausea and vomiting, Pruritus.
Abbreviations: PACU, post-anesthesia care unit; MOAA/S, the Modified Observers Assess-ment of Alertness/Sedation Scale; PCIA, patient controlled intravenous anal-gesia; KDIGO, Kidney Disease: Improving Global Outcomes.

recovery scores in the first 24 hours after surgery, possibly because QoR-15 is more focused on multidimensional functional recovery (eg pain, mobility, psychological status) rather than subclinical physiological interference.[26] These findings are consistent with emerging evidence that fluid type has a limited independent effect on short-term recovery outcomes with goal-directed fluid therapy.[23,27] From the perspective of the core goals of perioperative fluid management, the findings of this study further validate the clinical logic that hemodynamic optimization takes priority over the choice of fluid type. Although laparoscopic hepatectomy is a minimally invasive procedure, patients still face hemodynamic fluctuations caused by hepatic hilar occlusion, intraoperative fluid shifts, and metabolic demands associated with postoperative liver function recovery. Therefore, maintaining stable tissue perfusion and internal environmental homeostasis constitutes the core of fluid therapy. In this study, the standardized two-stage goal-directed fluid protocol ensured that both groups of patients achieved the preset hemodynamic targets at key nodes (such as volume reserve before liver resection and circulatory stability after resection). This implies that regardless of whether crystalloids or colloids are selected, strict adherence to the goal-directed principle can provide a stable physiological basis for critical aspects of postoperative recovery, including hepatic metabolism and intestinal function. This represents the core reason why no difference in recovery quality was observed between the two fluid types, and it holds practical significance for improving perioperative safety and recovery efficiency in minimally invasive procedures such as laparoscopic hepatectomy.

Although there was no significant difference in the total QoR-15 score at 24 hours postoperatively between the two groups in this study, suggesting that the two fluid therapy regimens may not be comparable in terms of early post-operative functional recovery, it is noteworthy that the analysis of secondary outcome indicators revealed that crystalloid and colloid infusion might lead to different perioperative outcomes. The PONV scores in the colloid group were significantly lower at 24 and 48 hours postoperatively. This is consistent with the findings of Jared et al[28,29] that colloid infusion reduces the incidence of PONV, which may be related to the fact that colloid infusion can decrease the serum levels of glycocalyx-degrading enzymes, endothelial glycocalyx shedding products and preserve endothelial glycocalyx thickness, thereby attenuating the increase in vascular permeability during systemic inflammation, protecting the integrity of the endothelial glycocalyx, and resulting in less intestinal interstitial edema.[28,30] The study by Li et al[31] pointed out that the lymphatic system is crucial for maintaining tissue fluid homeostasis, and colloids can indirectly promote lymphatic return by optimizing volume status, thereby reducing the accumulation of intestinal interstitial fluid. Meanwhile, we found that the total infusion volume in the goal-directed colloid therapy group was smaller, which reduced excessive fluid accumulation in the gastrointestinal system. However, it should be specifically noted that the above findings regarding PONV need to be interpreted cautiously in the context of the study design. As a secondary outcome indicator, the analysis of PONV-related indicators in this study did not involve a pre-specified separate sample size calculation. Moreover, the comparison of multiple outcome indicators may increase the risk of Type I error. Therefore, the statistical significance of this difference may not be fully equivalent to a stable effect in clinical practice. In addition, current research on the impact of fluid types (especially crystalloids vs colloids) on the incidence of PONV remains limited. Although this study is the first to observe a potential association between colloid-based goal-directed fluid therapy and improved PONV in patients undergoing laparoscopic hepatectomy, this conclusion is still a preliminary finding, and its reliability needs to be further verified by prospective studies with larger sample sizes.

Even though colloids may alleviate postoperative nausea and vomiting, they are associated with certain adverse effects. Colloids (hydroxyethyl starch) may be linked to an increased risk of acute kidney injury (AKI) and the need for renal replacement therapy,[32] particularly in patients with sepsis or critical illness.[33] Therefore, we measured the concentrations of serum creatinine and blood urea nitrogen before surgery and at 24, 48, and 72 hours postoperatively, which are markers reflecting renal function impairment. The results showed that both markers increased at 24, 48, and 72 hours postoperatively, but there were no statistically significant differences between the two groups. Additionally, there was no significant difference in the incidence of AKI between the two groups. This is consistent with the findings of Yang et al[34] who reported that the use of hydroxyethyl starch in non-cardiac surgery did not increase the incidence of postoperative AKI compared with crystalloids. Furthermore, the dosage of colloids used in this study was much higher than the median dose of 8.5 mL/kg. Thus, we tend to conclude that perioperative use of colloids does not cause renal damage. Kabon et al[35] also reported that in patients undergoing abdominal surgeries with moderate to high risk, the incidence of postoperative complications (including renal dysfunction) was similar between the goal-directed crystalloid therapy group and the colloid therapy group, indicating that colloids do not impair renal function in patients. However, this conclusion still requires verification by more large-scale studies.

Compared with the crystalloid group, the colloid group had significantly fewer fluid bolus administrations and a lower total infusion volume; however, there were no significant differences in hemodynamic parameters or the dosage of vasoactive agents between the two groups. This is consistent with the recent findings by Christian et al,[36] who reported that in patients undergoing major abdominal surgery and receiving goal-directed colloid or crystalloid therapy, although colloids remain in the intravascular space for a longer duration and require a smaller volume to maintain hemodynamic stability, they do not exhibit substantial hemodynamic advantages. Furthermore, a meta-analysis involving 1739 patients[37] also indicated that despite the smaller volume of fluids administered in the colloid group, no clinically significant differences in CVP, MAP, or cardiac output were observed between the two groups among patients undergoing abdominal surgery with goal-directed fluid therapy. On one hand, this may be related to the intrinsic properties of the fluids themselves. Crystalloids begin to leave the vascular compartment within minutes, providing relatively weak hemodynamic support;[38] in contrast, colloids, with their higher molecular weight and osmotic pressure, slow down their passage through the glycocalyx barrier and vascular endothelium, thus remaining in the intravascular space for a longer duration.[23] On the other hand, laparoscopic hepatectomy often involves the Trendelenburg position combined with pneumoperitoneum pressure, which promotes fluid redistribution. Additionally, the infusion strategy in this study adopted a goal-directed fluid therapy protocol guided by SVV, maintaining similar preload levels in both groups. As a result, colloids effectively maintained circulating blood volume, reduced the body's fluid demand, and did not affect hemodynamic changes.

Excessive intraoperative crystalloid administration may induce gastrointestinal edema and delay postoperative recovery, which is associated with the physicochemical properties of crystalloids and the patients' postoperative pathophysiological status. Crystalloids, characterized by small molecular weight and short intravascular retention time, require a larger dose to reach the target volume.[38] Additionally, in patients after hepatectomy, early postoperative albumin levels may decrease,[39] leading to reduced vascular colloid osmotic pressure and increased tendency of fluid extravasation into the interstitial space. When crystalloid infusion accumulates to a certain extent, it is prone to cause intestinal wall edema, impair intestinal peristalsis, and elevate the risk of intestinal bacterial translocation.[40,41] However, in this study, there were no significant differences between the two groups in postoperative fluid-related complications and time to first flatus, possibly due to the strict implementation of the GDFT strategy, which avoided massive crystalloid infusion. Nevertheless, this study did not include direct assessment indicators for gastrointestinal edema, failing to quantify their association. It is recommended that future studies incorporate relevant indicators to improve the evaluation.

Postoperative adverse events can independently affect the quality of postoperative recovery of patients. Each of these events was independently assessed. The multivariate linear regression analysis revealed that only the estimated blood loss and PONV score were negatively associated with the quality of recovery. Intraoperative blood loss can affect post-operative recovery and is also an independent prognostic factor for tumor recurrence and death.[42,43] Reducing intraoperative blood loss requires the cooperation of surgeons and anesthesiologists. There are many methods to control bleeding during hepatectomy, such as Pringle maneuver, portal vein occlusion, controlled low central venous pressure, goal-directed fluid therapy, and so on. In general surgery, postoperative nausea and vomiting can increase the psychological burden, indirectly lead to the decline of rehabilitation compliance, and significantly affect the quality of postoperative recovery.[44] In the future, multidisciplinary and multi-technical cooperation is needed to provide better postoperative recovery for patients undergoing laparoscopic hepatectomy.

However, our study has some limitations. The crystalloids and colloids provide markedly different intravascular volumes. However, the exact ratio of these two liquids remains highly controversial, and as with most studies in this area, we decided to use the same volume of crystalloids and colloids to ensure that our study was properly designed; The sample size calculation is based on a 6-point minimum clinically important difference (MCID) of the 15-item Quality of Recovery Scale (QoR-15). The applicability of this MCID still needs to be further verified in the future for the population undergoing minimally invasive hepatobiliary surgeries. Since the sample size of this study was mainly estimated based on the total score of QoR-15, the primary outcome, and no separate sample size calculation was performed for individual items and secondary outcomes, there may be insufficient statistical power when analyzing differences in scores of individual items and secondary outcomes, making it impossible to fully identify potential true differences. The present study only evaluated the short-term postoperative recovery quality and early complications, without including indicators of long-term functional recovery and long-term prognosis. Therefore, this study cannot address the question of whether different fluid types affect patients' long-term prognosis, and relevant conclusions need to be supplemented by long-term follow-up studies. This study is a single-center research with a small sample size, which may limit the extrapolation of the results. The findings still need to be verified by further multi-center, large-sample clinical trials.

Conclusion

In conclusion, two-stage goal-directed crystalloid versus colloid fluid therapy had no significant difference in the postoperative quality of recovery in patients undergoing laparoscopic hepatectomy, which is the primary finding of this study. Nevertheless, our data indicated that colloids may reduce postoperative nausea and vomiting (PONV), though this observation requires confirmation in larger-scale trials.

Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BIS, bispectral index; BUN, blood urea nitrogen; Cr, creatinine; CI, cardiac index; DBP, diastolic pressure; DBIL, direct bilirubin; ECG, electrocardiogram; GDFT, goal-directed fluid therapy; HR, heart rate; KDIGO, Kidney Disease: Improving Global Outcomes; LAC, Lactate; LCVP, low central venous pressure; MAP, mean arterial pressure; MOAA/S, the Modified Observers Assessment of Alertness/Sedation Scale; NRS, Numerical Rating Scale; PACU, post-anesthesia care unit; PCIA, patient controlled intravenous analgesia; QoR-15, Quality of Recovery-15; SBP, systolic pressure; SpO2, pulse oximetry; SVV, stroke volume variation; TBIL, total bilirubin.

Data Sharing Statement

The data generated during the current study are available from the corresponding author (Dunyi Qi) upon reasonable request. The study protocol, statistical analysis plan, and clinical study report will also be available.

Ethics Approval Statement

This prospective, randomized controlled study has been approved by the Ethics Committee of the Affiliated Hospital of Xuzhou Medical University (XYFY2024-KL250-01), and registered on July 22, 2024 at clini-calTrials.gov with the number (ChiCTR2400087179). The trial is being carried out in compliance with the ethical principles of the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there are no conflicts of interest associated with this work.

References

1. Vitale A, Romano P, Cillo U, et al. Liver resection vs nonsurgical treatments for patients with early multinodular hepatocellular carcinoma. *JAMA Surg*. 2024;159(8):881–889. doi:10.1001/jamasurg.2024.1184
2. Cheung TT, Han H-S, She WH, et al. The Asia pacific consensus statement on laparoscopic liver resection for hepatocellular carcinoma: a report from the 7th Asia-pacific primary liver cancer expert meeting held in Hong Kong. *Liver Cancer*. 2018;7(1):28–39. doi:10.1159/000481834
3. Wei Chieh AK, Chan A, Rotellar F, Kim K-H. Laparoscopic major liver resections: current standards. *Int J Surg*. 2020;82S:169–177. doi:10.1016/j.ijsu.2020.06.051
4. Peng Y, Yang Y, Chen K, et al. Hemihepatic versus total hepatic inflow occlusion for laparoscopic hepatectomy: a randomized controlled trial. *Int J Surg*. 2022;107:106961. doi:10.1016/j.ijsu.2022.106961
5. Wang QB, Li J, Zhang ZJ, et al. The effectiveness and safety of therapies for hepatocellular carcinoma with tumor thrombus in the hepatic vein, inferior vena cave and/or right atrium: a systematic review and single-arm meta-analysis. *Expert Rev Anticancer Ther*. 2025;25(5):561–570. doi:10.1080/14737140.2025.2489651
6. Coeckelenbergh S, Soucy-Proulx M, Van der Linden P, et al. Restrictive versus decision support guided fluid therapy during major hepatic resection surgery: a randomized controlled trial. *Anesthesiology*. 2024;141(5):881–890. doi:10.1097/ALN.0000000000005175
7. Liu T-S, Shen Q-H, Zhou X-Y, et al. Application of controlled low central venous pressure during hepatectomy: a systematic review and meta-analysis. *J Clin Anesth*. 2021;75:110467. doi:10.1016/j.jclinane.2021.110467
8. Myles PS, Bellomo R, Corcoran T, et al. Restrictive versus liberal fluid therapy for major abdominal surgery. *N Engl J Med*. 2018;378(24):2263–2274. doi:10.1056/NEJMoa1801601
9. Perel A. Using dynamic variables to guide perioperative fluid management. *Anesthesiology*. 2020;133(4):929–935. doi:10.1097/ALN.0000000000003408

10. Dunki-Jacobs EM, Philips P, Scoggins CR, McMasters KM, Martin RCG. Stroke volume variation in hepatic resection: a replacement for standard central venous pressure monitoring. *Ann Surg Oncol*. 2014;21(2):473–478. doi:10.1245/s10434-013-3323-9
11. Mizunoya K, Fujii T, Yamamoto M, Tanaka N, Morimoto Y. Two-stage goal-directed therapy protocol for non-donor open hepatectomy: an interventional before-after study. *J Anesth*. 2019;33(6):656–664. doi:10.1007/s00540-019-02688-4
12. Guo Y, Jianling L, Niu Y, et al. Application of high allowable stroke volume variation in laparoscopic hepatectomy in elderly patients. *J Clinical Anesthesiol*. 2021;38(04):351–355.
13. Myburgh JA, Mythen MG. Resuscitation fluids. *N Engl J Med*. 2013;369(13):1243–1251. doi:10.1056/NEJMra1208627
14. Chappell D, Jacob M, Hofmann-Kiefer K, Conzen P, Rehm M. A rational approach to perioperative fluid management. *Anesthesiology*. 2008;109 (4):723–740. doi:10.1097/ALN.0b013e3181863117
15. Joosten A, Coeckelenbergh S, Alexander B, et al. Hydroxyethyl starch for perioperative goal-directed fluid therapy in 2020: a narrative review. *BMC Anesthesiol*. 2020;20(1):209. doi:10.1186/s12871-020-01128-1
16. Kozek-Langenecker SA. Effects of hydroxyethyl starch solutions on hemostasis. *Anesthesiology*. 2005;103(3):654–660. doi:10.1097/00000542-200509000-00031
17. Joosten A, Delaporte A, Mortier J, et al. Long-term impact of crystalloid versus colloid solutions on renal function and disability-free survival after major abdominal surgery. *Anesthesiology*. 2019;130(2):227–236. doi:10.1097/ALN.0000000000002501
18. Tao J, Zheng Y, Huang Q, Pu F, Shen Q, Hu Y. Patient-reported outcomes measurement information system in patients with gastrointestinal cancer: a scoping review. *Support Care Cancer*. 2023;31(10):567. doi:10.1007/s00520-023-08010-z
19. Myles PS, Shulman MA, Reilly J, Kasza J, Romero L. Measurement of quality of recovery after surgery using the 15-item quality of recovery scale: a systematic review and meta-analysis. *Br J Anaesth*. 2022;128(6):1029–1039. doi:10.1016/j.bja.2022.03.009
20. Myles PS, Myles DB. An updated minimal clinically important difference for the QoR-15 scale. *Anesthesiology*. 2021;135(5):934–935. doi:10.1097/ALN.0000000000003977
21. Chirnoaga D, Coeckelenbergh S, Ickx B, et al. Impact of conventional vs. goal-directed fluid therapy on urethral tissue perfusion in patients undergoing liver surgery: a pilot randomised controlled trial. *Eur J Anaesthesiol*. 2022;39(4):324–332. doi:10.1097/EJA.0000000000001615
22. Feldheiser A, Pavlova V, Bonomo T, et al. Balanced crystalloid compared with balanced colloid solution using a goal-directed haemodynamic algorithm. *Br J Anaesth*. 2013;110(2):231–240. doi:10.1093/bja/aes377
23. Yates DRA, Davies SJ, Milner HE, Wilson RJT. Crystalloid or colloid for goal-directed fluid therapy in colorectal surgery. *Br J Anaesth*. 2014;112 (2):281–289. doi:10.1093/bja/aet307
24. Reiterer C, Kabon B, Zotti O, Obradovic M, Kurz A, Fleischmann E. Effect of goal-directed crystalloid- versus colloid-based fluid strategy on tissue oxygen tension: a randomised controlled trial. *Br J Anaesth*. 2019;123(6):768–776. doi:10.1016/j.bja.2019.08.027
25. Kimberger O, Arnberger M, Brandt S, et al. Goal-directed colloid administration improves the microcirculation of healthy and perianastomotic colon. *Anesthesiology*. 2009;110(3):496–504. doi:10.1097/ALN.0b013e31819841f6
26. Stark PA, Myles PS, Burke JA. Development and psychometric evaluation of a postoperative quality of recovery score: the QoR-15. *Anesthesiology*. 2013;118(6):1332–1340. doi:10.1097/ALN.0b013e318289b84b
27. Niu W, Li J, Wang S. The effect of colloids versus crystalloids for goal-directed fluid therapy on prognosis in patients undergoing noncardiac surgery: a meta-analysis of randomized controlled trials. *Anesthesiol Res Pract*. 2024;2024(1):4386447. doi:10.1155/2024/4386447
28. Lee MJ, Lee C, Kang H, Kim H. The impact of crystalloid versus colloid fluids on postoperative nausea and vomiting: a systematic review and meta-analysis of randomized controlled trials. *J Clin Anesth*. 2020;62:109695. doi:10.1016/j.jclinane.2019.109695
29. Herman JA, Urits I, Kaye AD, Urman RD, Viswanath O. Perioperative crystalloid versus colloid fluids: impact on postoperative nausea and vomiting reduction. *J Clin Anesth*. 2022;79:110025. doi:10.1016/j.jclinane.2020.110025
30. Margraf A, Herter JM, Kühne K, et al. 6% Hydroxyethyl starch (HES 130/0.4) diminishes glycocalyx degradation and decreases vascular permeability during systemic and pulmonary inflammation in mice. *Crit Care*. 2018;22(1):111. doi:10.1186/s13054-017-1846-3
31. Li J, Liang YB, Wang QB, et al. Tumor-associated lymphatic vessel density is a postoperative prognostic biomarker of hepatobiliary cancers: a systematic review and meta-analysis. *Front Immunol*. 2025;15:1519999. doi:10.3389/fimmu.2024.1519999
32. Raiman M, Mitchell CG, Biccard BM, Rodseth RN. Comparison of hydroxyethyl starch colloids with crystalloids for surgical patients: a systematic review and meta-analysis. *Eur J Anaesthesiol*. 2016;33(1):42–48. doi:10.1097/EJA.0000000000000328
33. Opperer M, Poeran J, Rasul R, Mazumdar M, Memtsoudis SG. Use of perioperative hydroxyethyl starch 6% and albumin 5% in elective joint arthroplasty and association with adverse outcomes: a retrospective population based analysis. *BMJ*. 2015;350(mar27 5):h1567. doi:10.1136/bmj.h1567
34. Yang M-J, Chen N, Ye C-Y, et al. Association between hydroxyethyl starch 130/0.4 administration during noncardiac surgery and postoperative acute kidney injury: a propensity score-matched analysis of a large cohort in China. *J Clin Anesth*. 2024;96:111493. doi:10.1016/j.jclinane.2024.111493
35. Kabon B, Sessler DI, Kurz A; Crystalloid–Colloid Study Team. Effect of intraoperative goal-directed balanced crystalloid versus colloid administration on major postoperative morbidity: a randomized trial. *Anesthesiology*. 2019;130(5):728–744. doi:10.1097/ALN.0000000000002601
36. Reiterer C, Kabon B, Halvorson S, Sessler D, Mascha EJ, Kurz A. Hemodynamic responses to crystalloid and colloid fluid boluses during noncardiac surgery: erratum. *Anesthesiology*. 2022;136(1):253. doi:10.1097/ALN.0000000000004091
37. Lu R, Kacha S, Phothikun N, Supphapipat A, Chittawatanarat K. Comparative balanced salt solution and 6 % hydroxyethyl starch in goal-directed therapy for major abdominal surgery: a systematic review and meta-analysis. *Am J Surg*. 2025;245:116355. doi:10.1016/j.amjsurg.2025.116355
38. Hahn RG, Drobin D, Ståhle L. Volume kinetics of Ringer's solution in female volunteers. *Br J Anaesth*. 1997;78(2):144–148. doi:10.1093/bja/78.2.144
39. Norberg Å, Rooyackers O, Segersvärd R, Wernerman J. Leakage of albumin in major abdominal surgery. *Crit Care*. 2016;20(1):113. doi:10.1186/s13054-016-1283-8
40. Lundsgaard-Hansen P, Blauhut B. Die beziehung von hypoxie und odem in darmwand und haut zum kolloidosmotischen druck [Relation of hypoxia and edema of the intestinal wall and skin to colloid osmotic pressure]. *Anaesthesist*. 1988;37(2):112–119.
41. Marjanovic G, Villain C, Juettner E, et al. Impact of different crystalloid volume regimes on intestinal anastomotic stability. *Ann Surg*. 2009;249 (2):181–185. doi:10.1097/SLA.0b013e31818b73dc
42. Katz SC, Shia J, Liau KH, et al. Operative blood loss independently predicts recurrence and survival after resection of hepatocellular carcinoma. *Ann Surg*. 2009;249(4):617–623. doi:10.1097/SLA.0b013e31819ed22f

43. Yang P, Gao S, Chen X, Xiong W, Hai B, Huang X. Milrinone is better choice for controlled low central venous pressure during hepatectomy: a randomized, controlled trial comparing with nitroglycerin. *Int J Surg*. 2021;94:106080. doi:10.1016/j.ijsu.2021.106080
44. Myles PS, Wengritzky R. Simplified postoperative nausea and vomiting impact scale for audit and post-discharge review. *Br J Anaesth*. 2012;108 (3):423–429. doi:10.1093/bja/aer505