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Original Article

Comparison of combined intravenous-inhalation anesthesia and total intravenous anesthesia in perioperative stress and outcomes of elderly patients undergoing hepatectomy

Chen Zhang, Juan Liu

Department of Anesthesiology, Beijing Chaoyang Hospital, Capital Medical University, Beijing 100020, China

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Abstract: Objective: To compare the effects of combined intravenous-inhalation anesthesia (CIVIA) and total intravenous anesthesia (TIVA) in elderly patients undergoing hepatectomy, and to evaluate their impact on perioperative stress response and postoperative outcomes. Methods: A retrospective analysis was performed on 208 elderly patients who had undergone hepatectomy. The patients were divided into the CIVIA group (n=106) and the TIVA group (n=102) according to their anesthesia protocol. The CIVIA group received sevoflurane inhalation combined with propofol intravenous-inhalation anesthesia, while the TIVA group received only propofol and remifentanil intravenous infusion anesthesia. Baseline clinical indicators were compared between the groups. Stress response markers, hemodynamic parameters, and inflammatory indices were assessed at four timepoints: before anesthesia induction, immediately after surgery, and 12 h and 24 h postoperatively. In addition, the Observer's Assessment of Alertness/Sedation (OAA/S) score, Aldrete score, Mini-Mental State Examination (MMSE) score, perioperative pain score, Ramsay score, and the incidence of complications were compared between the two groups. Results: Intraoperative blood loss (OR=0.868, 95% CI=0.818-0.921), anesthesia maintenance time (OR=0.695, 95% CI=0.592-815), and intraoperative complications (OR=0.0.159, 95% CI=0.030-0.853) were significantly associated with anesthesia techniques (all $P < 0.05$). The CIVIA group showed significantly shorter postoperative recovery, time to regain consciousness, and extubation time compared with the TIVA group ($P < 0.05$). Moreover, the CIVIA group exhibited more favorable results in stress response, hemodynamic stability, inflammatory indices, OAA/S score, Aldrete score, MMSE score, perioperative pain score, and postoperative complication rates at the immediate, 12 h, and 24 h postoperative assessments. Conclusion: CIVIA shows significant clinical advantages in elderly patients with liver disease undergoing hepatectomy. This regimen provides effective anesthetic depth, maintains intraoperative hemodynamic stability, attenuates perioperative stress response, and reduces the risk of postoperative complications, making it a preferred anesthesia strategy in this population.

Keywords: Sevoflurane, propofol, remifentanil, elderly hepatic lobectomy, perioperative stress response, prognosis

Introduction

Hepatectomy is an effective treatment for localized liver lesions, including liver cancer, benign liver tumors, and liver abscesses. The surgical outcome largely depends on the nature and extent of the lesion as well as the patient's overall condition [1]. Although hepatectomy is technically challenging due to the complex hepatic anatomy, advances in surgical techniques in recent years have substantially improved patient prognosis. However, in elderly patients, age-related physiological decline, multiple comorbidities, and impaired stress responses pose significant challenges for perioperative management [2]. In addition, elderly patients are more susceptible to exaggerated perioperative stress responses, which may increase postoperative complications, delay recovery, and adversely affect the prognosis [3]. Hepatectomy is a major abdominal operation that requires adequate physical reserve and physiological stability. Therefore, comprehensive assessment of the perioperative stress response and postoperative outcomes in elderly surgical patients is critical.

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As with other upper abdominal procedures, an appropriate anesthesia regimen is essential to ensure the smooth implementation of hepatobiliary surgery. Currently, commonly used techniques include combined intravenous-inhalation anesthesia (CIVIA) and total intravenous anesthesia (TIVA) [4]. However, increasing evidence suggests that general anesthesia alone has inherent limitations [5]. The large perioperative opioid doses may increase the risk of respiratory depression and adverse effects such as nausea and vomiting, thereby impairing postoperative gastrointestinal recovery, prolonging convalescence, and reducing quality of life [6]. Although studies have compared the effects of CIVIA and TIVA in surgical populations [7, 8], evidence in elderly patients remains scarce, especially among those undergoing hepatectomy. Elderly patients typically exhibit age-related physiological decline, reduced tolerance to anesthesia and surgery, and delayed postoperative recovery. CIVIA is widely used in hepatectomy, as it ensures adequate oxygenation, allows for precise anesthesia depth control, and provides effective postoperative analgesia [9].

Therefore, this study aimed to compare the effects of CIVIA and TIVA in elderly patients undergoing hepatectomy, with particular emphasis on perioperative stress response and postoperative outcomes. The novelty of this study lies in its focus on this special population, using multi-dimensional evaluation to assess the impact of both anesthetic techniques on inflammatory and oxidative stress markers, recovery quality, and postoperative complications. The findings are expected to provide a scientific basis for anesthetic choice and offer comprehensive guidance for the perioperative management of elderly patients undergoing hepatectomy.

Materials and methods

Study population

A retrospective analysis was performed on 208 elderly patients who underwent elective hepatectomy at Beijing Chaoyang Hospital, Capital Medical University between January 2020 and December 2024. Patients were divided into the CIVIA group (n=106) and the TIVA group (n=102) according their anesthesia regime.

Inclusion criteria: (1) Patients met the established indications for hepatectomy [10]; (2) Age ≥ 60 years; (3) American Society of Anesthesiologists (ASA) grade I-II [11] (ASA grade I: healthy, well-developed, and well-nourished patients with normal organ function and extremely low perioperative mortality; ASA grade II: patients with mild systemic diseases in addition to the surgical condition, with preserved functional compensation and relatively low perioperative mortality); (4) Anesthetic regimen: CIVIA with sevoflurane inhalation plus propofol, or TIVA with propofol and remifentanil infusion.

Exclusion criteria: (1) patients with psychiatric disorders, coagulopathy, or audiovisual/cognitive impairment; (2) known allergy to anesthetic agents used in this study; (3) contraindications to hepatectomy; (4) receipt of immunosuppressants, opioids, and related treatments within three months prior to surgery; (5) presence of other malignant tumors, active infections, disorders, and autoimmune diseases; (6) severe impairment of major organs (heart, kidney or lung). This study was approved by the Ethics Committee of Beijing Chaoyang Hospital, Capital Medical University.

Surgery and anesthesia methods

Both groups underwent radical hepatectomy. Preoperatively, fasting and water deprivation were required for 6 h. Thirty minutes before operation, patients in both groups received intramuscular injections of atropine sulfate 0.5 mg (Huazhong Pharmaceutical Co., Ltd., China; Approval No.: H42021498, Specification: 1 ml:1 mg) and phenobarbital sodium 0.1 g (Tianjin Jinyao Amino Acid Co., Ltd., China; Approval No.: H12020381, Specification: 1 ml:1 mg).

Anesthesia induction: Both groups received intravenous propofol 3-5 μg/mL (Xi'an Libang Pharmaceutical Co., Ltd., China; Approval No.: H20040300, specification: 50 ml:500 mg), remifentanil 3-5 ng/mL (Yichang Renfu Pharmaceutical Co., Ltd., China; Approval No.: H42022076, specification: 2 ml:0.1 mg), and rocuronium bromide 0.6 mg/kg (Fuan Pharmaceutical Group Qingyutang Pharmaceutical Co., Ltd., Chian; Approval No.: H20183105, specification: 2.5 ml:25 mg) for rapid anesthesia induction. After tracheal intubation patients were connected to an anesthesia machine.

CIVIA group: After induction, anesthesia was maintained with sevoflurane inhalation at 1.0%-1.5% (Jiangsu Hengrui Pharmaceutical Co., Ltd., China; Approval No.: H20070172, Specification: 120 mL), combined with intermittent intravenous remifentanil (0.05-0.1 mg) and propofol infusion (50-100 mg/h).

TIVA group: After induction, anesthesia was maintained with propofol (50-100 mg/h) and remifentanil infusion (0.1-0.3 μg/kg/min).

During the operation, infusion rates of propofol and remifentanil were adjusted as needed to maintain appropriate anesthetic depth and hemodynamic stability. Arterial blood gas analysis was performed intermittently. If hypotension or bradycardia occurred, interventions such as fluid resuscitation, blood transfusion, or vasoactive agents were administered as needed. All anesthetics were discontinued at the end of surgery.

Observed indexes

(1) Baseline and intraoperative indicators: Basic clinical characteristics were collected for both groups. Variables included age, sex, body mass index (BMI), ASA classification, history of diabetes and history of hypertension. Intraoperative parameters included operation time, intraoperative blood loss, anesthesia maintenance time, and intraoperative complications. Multivariate logistic regression analysis was performed to identify independent influencing factors.

(2) Anesthesia-related indicators: Postoperative recovery time, time to regain consciousness, and extubation time were recorded.

(3) Perioperative stress response: At four timepoints-before anesthesia induction, immediately after surgery, and 12 h and 24 h postoperatively-5 mL of fasting venous blood was collected. After centrifugation at 3,500 r/min for 5 min, serum was obtained. Serum epinephrine (E) and norepinephrine (NE) levels were measured by radioimmunoassay, and cortisol (Cor) levels were determined by enzyme-linked immunosorbent assay (ELISA).

(4) Hemodynamic parameters: Peripheral oxygen saturation (SpO_2), mean arterial pressure (MAP), and heart rate (HR) were measured at four timepoints. SpO_2 was assessed using an IL-1620 blood gas analyzer (Instrumentation Laboratory, USA), and HR and MAP were monitored with a Dash 300 multifunction monitor (Shenzhen Maoye Medical Equipment Co., Ltd., China).

(5) Inflammatory response indicators: Serum levels of C-reactive protein (CRP) and tumor necrosis factor-α (TNF-α) were measured before anesthesia induction, immediately after surgery, and at 12 h and 24 h postoperatively using ELISA.

(6) Awakening quality: At extubation, and 15 min and 30 min after extubation, the quality of awakening was assessed using the modified Observer's Assessment of Alertness/Sedation (OAA/S) scale [12] and the Aldrete score [13]. The OAA/S scale ranges from 1 to 5 points, with higher scores indicating lighter sedation. The Aldrete score ranges from 0 to 10 points, with higher scores reflecting better recovery status and readiness for safe discharge from the recovery room.

(7) Cognitive function: The Mini-Mental State Examination (MMSE) was used to evaluate the cognitive function [14]. The total score of MMSE ranges from 0 to 30: 0-9 indicates severe impairment, 10-20 moderate impairment, 21-26 mild impairment, and ≥ 27 normal cognitive function.

(8) Perioperative pain: Visual Analogue Scale (VAS) was used to evaluate pain intensity at the four timepoints. The scale ranges from 0 to 10 points, with higher score indicating greater pain intensity.

(9) Sedation level: The Ramsay sedation score was evaluated immediately after operation and at 12 h and 24 h postoperatively. Score of 1 indicates insufficient sedation, 5-6 excessive sedation, and 2-4 moderate sedation.

(10) Postoperative complications: Complications were recorded, including agitation, nausea and vomiting, dizziness, headache, hypotension, and tachycardia.

Statistical methods

SPSS 27.0 statistical software was used for data analysis. Continuous variables were expressed as mean ± standard deviation (SD),

Table 1. Comparison of baseline characteristics between the two groups [(mean ± SD), n (%)]

Group	CIVIA group (n=106)	TIVA group (n=102)	χ^2/t	*P*
Age/years	66.82±3.62	66.12±3.45	1.433	0.153
Sexuality			1.848	0.174
Male	67 (63.21)	55 (53.92)		
Female	39 (36.79)	47 (46.08)		
BMI (kg/m^2)	23.19±1.25	23.04±1.35	0.824	0.411
ASA grade			0.630	0.427
I grade	66 (62.26)	58 (56.86)		
II grade	40 (37.74)	44 (43.14)		
Diabetes mellitus history			0.195	0.659
Yes	50 (47.17)	45 (44.12)		
No	56 (52.83)	57 (55.88)		
Hypertension history			1.552	0.213
Yes	58 (54.72)	47 (46.08)		
No	48 (45.28)	55 (53.92)		
Operation time (min)	154.232±31.28	149.68±32.65	1.025	0.307
Intraoperative blood loss (mL)	300.60±18.24	345.54±21.47	16.288	< 0.001
Anesthesia maintenance time (min)	172.58±8.35	193.37±10.58	15.690	< 0.001
Intraoperative complications			8.408	0.004
Yes	38 (35.85)	57 (55.88)		
No	68 (64.15)	45 (44.12)		

Notes: CIVIA, combined intravenous-inhalation anesthesia; TIVA, total intravenous anesthesia; BMI, body mass index. Intraoperative complications include hypotension, arrhythmia, respiratory depression.

and between-group comparisons were performed using the independent-samples *t* test. Factors showing significant differences were further confirmed using Multivariate logistic regression. Repeated measures analysis of variance (ANOVA) was applied for within-group comparisons across different timepoints, and results were expressed as *F* values. Categorical variables were expressed as frequencies and percentages (n, %) and compared using the chi-square (χ^2) test. A two-sided *P* value < 0.05 was considered statistically significant.

Results

Comparison of basic clinical indicators between the two groups

(1) Intraoperative blood loss in the CIVIA group was significantly lower than that in the TIVA group (t=16.288, P < 0.001). The duration of anesthesia maintenance was shorter in the CIVIA group (t=15.690, P < 0.001), and the incidence of intraoperative complications was lower (χ^2=8.408, P=0.004). No significant differences were observed in other baseline clinical indicators (P > 0.05) (**Table 1**). The screening flowchart of patient selection is shown in **Figure 1**.

(2) Multivariate logistic regression analysis further confirmed that intraoperative blood loss (OR=0.868, 95% CI=0.818-0.921), anesthesia maintenance time (OR=0.695, 95% CI=0.592-0.815), and intraoperative complications (OR=0.0.159, 95% CI=0.030-0.853) (all P < 0.05) remained significantly associated with anesthesia technique (**Table 2**).

Anesthesia-related indicators

The CIVIA group demonstrated significantly shorter postoperative awakening time (6.28±1.42 min), time to regain consciousness (14.35±1.82 min), and extubation time (16.55±1.78 min) compared with the TIVA group (9.33±1.56 min, 18.28±1.95 min, 19.64±2.12 min, respectively) (all P < 0.05) (**Figure 2**). These results suggest that CIVIA facilitated faster recovery during anesthesia emergence.

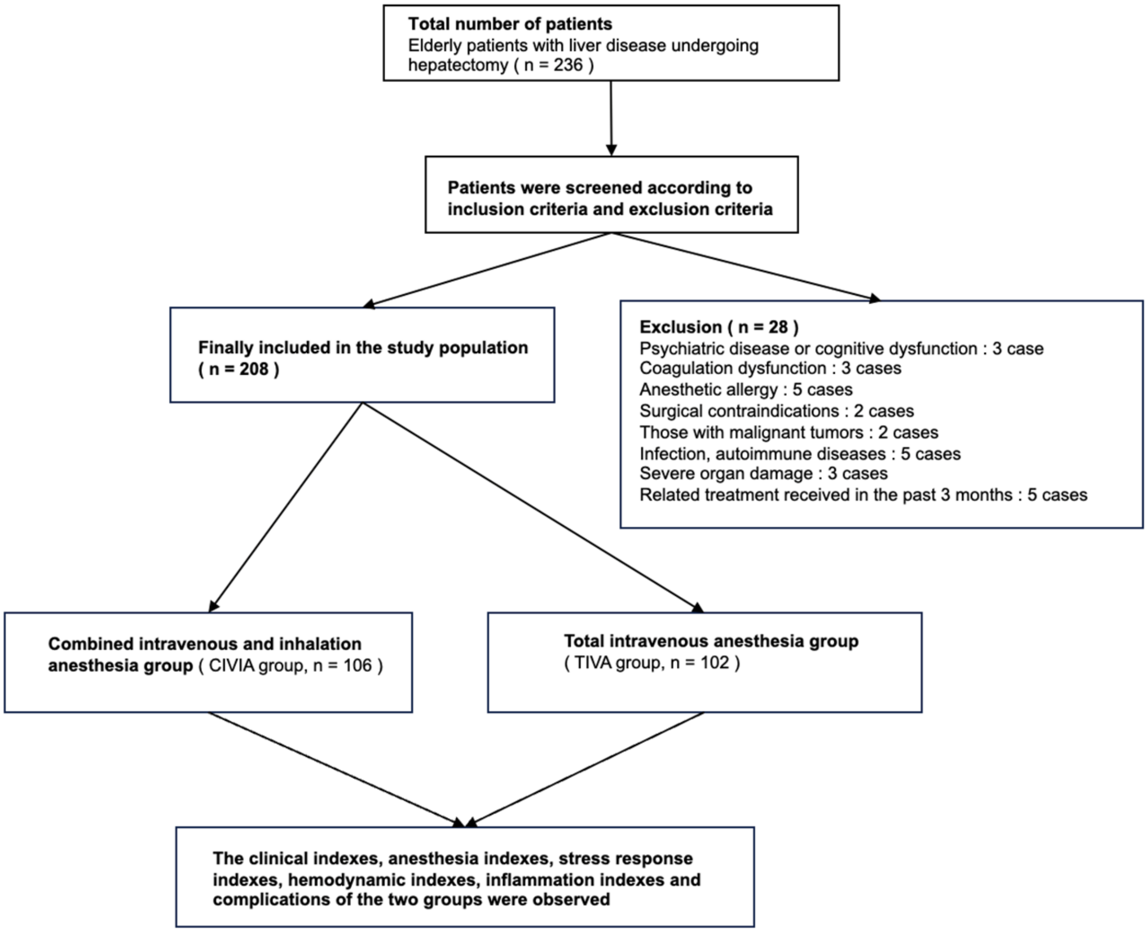

Figure 1. Flow chart of patient screening. Notes: CIVIA, combined intravenous and inhalation anesthesia; TIVA, total intravenous anesthesia.

Table 2. Multivariate logistic regression analysis

Index	*β*	*SE*	*Wald* χ^2	*P*	*OR (95% CI)*
Intraoperative blood loss	-0.142	0.030	21.773	< 0.001	0.868 (0.818-0.921)
Anesthesia maintenance time	-0.365	0.082	19.982	< 0.001	0.695 (0.592-815)
Intraoperative complications	-1.838	0.857	4.601	0.032	0.159 (030-0.853)

Perioperative stress response

Before anesthesia induction, there were no significant differences in serum levels of E, NE, or Cor between the two groups (P > 0.05). Immediately after surgery, levels of E, NE, and Cor were significantly lower in the CIVIA group compared with the TIVA group [(30.66±3.85) pg/mL vs. (69.43±5.48) pg/mL, (154.32±12.45) pg/mL vs. (188.87±17.52) pg/mL, (25.69±3.73) μg/mL vs. (42.51±5.82) μg/mL; all *P* < 0.05]. At 12 hours postoperatively, these levels remained lower in the CIVIA group [(33.24±3.46) pg/mL vs. (77.21±6.93) pg/mL, (169.59±13.77) pg/mL vs. (217.91±19.46) pg/mL, (29.45±4.28) μg/mL vs. (57.62±6.14) μg/mL; all *P* < 0.05]. At 24 hours postoperatively, the CIVIA group continued to show significantly lower levels of E, NE, and Cor [(27.42±2.85) pg/mL vs. (54.40±4.72) pg/mL, (139.32±10.43) pg/mL vs. (162.85±13.45) pg/mL, (20.72±2.86) μg/mL vs. (34.53±4.27) μg/mL; all *P* < 0.05]. The details are shown in **Table 3**. These findings indicate that CIVIA attenuated the perioperative stress response more effectively than TIVA, which may contribute to reduced complications and improved postoperative recovery.

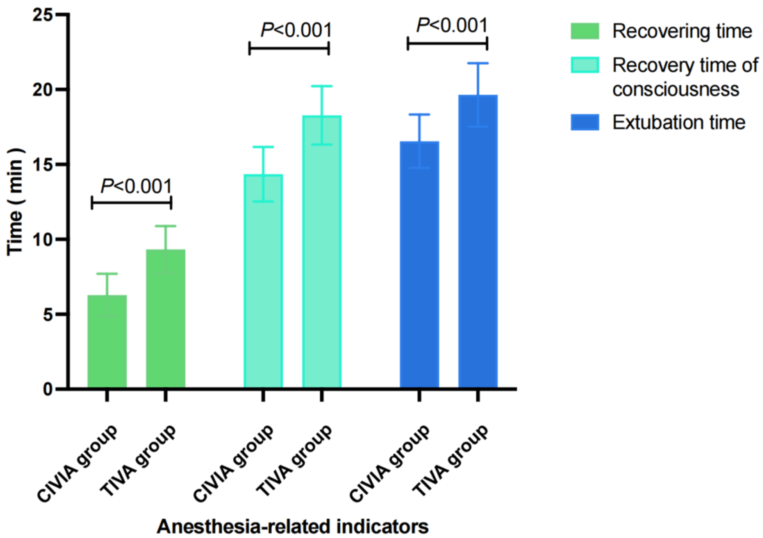

Figure 2. Comparison of anesthesia-related indicators between the two groups. Notes: CIVIA, combined intravenous and inhalation anesthesia; TIVA, total intravenous anesthesia.

Perioperative hemodynamics

No significant differences in SpO_2, MAP or HR were observed between the two groups before anesthesia induction (P > 0.05). Immediately after surgery, the CIVIA group showed significantly higher SpO_2 but lower MAP and HR compared with the TIVA group [(82.61±4.67)% vs. (80.60±4.75)%, (77.58±7.23) mmHg vs. (87.96±7.29) mmHg, (75.34±6.55) beats/min vs. (89.32±6.27) beats/min; all P < 0.05]. At 12 hours postoperatively, SpO_2 remained significantly higher while MAP and HR remained significantly lower in the CIVIA group [(85.13±4.25)% vs. (82.51±4.82)%, (82.17±7.23) mmHg vs. (94.95±3.26) mmHg, (83.40±7.35) beats/min vs (93.50±3.57) beats/min; all P < 0.05]. At 24 hours postoperatively, these levels maintained similar disparity patterns [(91.16±5.47)% vs. (88.56±5.38)%, (85.76±6.78) mmHg vs. (91.50±3.12) mmHg, (73.67±6.92) beats/min vs. (81.38±6.64) beats/min; all P < 0.05]. The details are shown in **Table 4**. These results suggest that CIVIA provides superior perioperative hemodynamic stability compared with TIVA.

Inflammatory response

Before anesthesia induction, there was no significant difference in CRP and TNF-α levels between the two groups (P > 0.05). Immediately after surgery, CRP and TNF-α levels were lower in the CIVIA group compared with the TIVA group [(14.34±2.74) mg/L vs. (19.61±3.18) mg/L, (28.38±3.86) μg/L vs. (30.50±4.24) μg/L; all P < 0.001]. At 12 hours postoperatively, these levels remained significantly lower in the CIVIA group [(21.65±3.85) mg/L vs. (25.43±3.73) mg/L, (31.48±4.13) μg/L vs. (34.76±4.85) μg/L; all P < 0.001]. At 24 hours postoperatively, CRP and TNF-α levels were still reduced in the CIVIA group compared with the TIVA group [(34.31±4.16) mg/L vs. (38.32±4.85) mg/L, (33.89±4.75) μg/L vs. (39.50±5.27) μg/L; all P < 0.001]. The details are shown in **Table 5**. These findings indicate that TIVA was associated with a stronger perioperative inflammatory response compared with CIVIA.

Awakening quality

Immediately after extubation, both the OAA/S score and Aldrete score were significantly higher in CIVIA group than in the TIVA group [(4.15±0.51) vs. (3.56±0.49), P < 0.001; (8.20±0.83) vs. (8.00±0.56), P=0.045]. At 15 min after extubation, the CIVIA group continued to show higher scores compared with the TIVA group [(4.48±0.50) vs. (4.02±0.54), P < 0.001; (8.56±0.72) vs. (8.28±0.60), P=0.003]. However, by 30 minutes after extubation, there were no significant differences between the two groups in terms of OAA/S score or Aldrete score (P > 0.05) (**Table 6**).

Cognitive function

Postoperative cognitive dysfunction (POCD) occurred in 8 patients in the CIVIA group and 17 cases in TIVA group (χ^2=4.088, P=0.043). The MMSE scores were significantly higher in the CIVIA group compared with the TIVA group at 12 h postoperatively [(25.92±1.35) vs. (23.26±2.46); P < 0.05], and at 24 h postoperatively [(27.62±1.54) vs. (25.34±1.87); P < 0.05] (**Figure 3**).

Perioperative pain

Before anesthesia induction, there was no significant difference in VAS score between the

Table 3. Comparison of perioperative stress response indicators between the two groups at various timepoints (mean ± SD)

Group	Time	CIVIA group (n=106)	TIVA group (n=102)	χ^2/t	*P*
E (pg/mL)	Before induction	26.21±2.57	25.62±2.71	1.605	0.110
	Immediately after surgery	30.66±3.85	69.43±5.48	58.689	< 0.001
	12 h after surgery	33.24±3.46	77.21±6.93	57.579	< 0.001
	24 h after surgery	27.42±2.85	54.40±4.72	49.673	< 0.001
F		103.597	1960.136		
P		< 0.001	< 0.001		
NE (pg/mL)	Before induction	132.58±11.35	130.50±10.42	1.372	0.172
	Immediately after surgery	154.32±12.45	188.87±17.52	16.339	< 0.001
	12 h after surgery	169.59±13.77	217.91±19.46	20.597	< 0.001
	24 h after surgery	139.32±10.43	162.85±13.45	14.063	< 0.001
F		197.992	580.530		
P		< 0.001	< 0.001		
Cor (μg/mL)	Before induction	16.58±2.54	15.99±2.56	1.646	0.101
	Immediately after surgery	25.69±3.73	42.51±5.82	24.723	< 0.001
	12 h after surgery	29.45±4.28	57.62±6.14	38.268	< 0.001
	24 h after surgery	20.72±2.86	34.53±4.27	27.274	< 0.001
F		286.876	1272.777		
P		< 0.001	< 0.001		

Notes: CIVIA, combined intravenous-inhalation anesthesia; TIVA, total intravenous anesthesia; E, epinephrine; NE, noradrenaline; Cor, cortisol.

Table 4. Hemodynamic comparison (mean ± SD)

Group	Time	CIVIA group (n=106)	TIVA group (n=102)	χ^2/t	*P*
SpO_2 (%)	Before induction	93.60±2.98	93.20±3.26	0.918	0.360
	Immediately after surgery	82.61±4.67	80.60±4.75	3.065	0.002
	12 h after surgery	85.13±4.25	82.51±4.82	4.158	< 0.001
	24 h after surgery	91.16±5.47	88.56±5.38	3.460	< 0.001
F		141.205	158.666		
P		< 0.001	< 0.001		
MAP (mmHg)	Before induction	88.06±6.03	88.61±6.41	0.635	0.526
	Immediately after surgery	77.58±7.23	87.96±7.29	10.307	< 0.001
	12 h after surgery	82.17±7.23	94.95±3.26	15.231	< 0.001
	24 h after surgery	85.76±6.78	91.50±3.12	7.890	< 0.001
F		47.418	27.156		
P		< 0.001	< 0.001		
HR (times/min)	Before induction	70.19±5.86	69.41±6.24	0.931	0.353
	Immediately after surgery	75.34±6.55	89.32±6.27	15.717	< 0.001
	12 h after surgery	83.40±7.35	93.50±3.57	12.675	< 0.001
	24 h after surgery	73.67±6.92	81.38±6.64	8.202	< 0.001
F		74.139	339.174		
P		< 0.001	< 0.001		

Notes: CIVIA, combined intravenous-inhalation anesthesia; TIVA, total intravenous anesthesia; SpO_2, Speripheral oxygen saturation; MAP, mean arterial pressure; HR, heart rate.

two groups (P > 0.05). However, VAS scores were significantly lower in the CIVIA group than in the TIVA group immediately after surgery [(3.26±0.25) vs. (3.92±0.23), P < 0.05], at 12

Table 5. Perioperative inflammatory response indicators (mean ± SD)

Group	Time	CIVIA group (n=106)	TIVA group (n=102)	χ^2/t	*P*
CRP (mg/L)	Before induction	5.23±1.36	5.18±1.42	0.278	0.781
	Immediately after surgery	14.34±2.74	19.61±3.18	12.815	< 0.001
	12 h after surgery	21.65±3.85	25.43±3.73	7.178	< 0.001
	24 h after surgery	34.31±4.16	38.32±4.85	6.412	< 0.001
F		1542.302	1544.277		
P		< 0.001	< 0.001		
TNF-α (μg/L)	Before induction	26.93±3.52	27.13±3.46	0.420	0.675
	Immediately after surgery	28.38±3.86	30.50±4.24	3.776	< 0.001
	12 h after surgery	31.48±4.13	34.76±4.85	5.265	< 0.001
	24 h after surgery	33.89±4.75	39.50±5.27	8.063	< 0.001
F		61.677	143.808		
P		< 0.001	< 0.001		

Notes: CIVIA, combined intravenous-inhalation anesthesia; TIVA, total intravenous anesthesia; CRP, C reactive protein; TNF-α, tumor necrosis factor-α.

Table 6. Comparison of recovery quality between the two groups (mean ± SD)

Group	Time	CIVIA group (n=106)	TIVA group (n=102)	*t*	*P*
OAA/S score	Immediately after extubation	4.15±0.51	3.56±0.49	8.442	< 0.001
	15 min after extubation	4.48±0.50	4.02±0.54	6.348	< 0.001
	15 min after extubation	4.84±0.39	4.77±0.46	1.088	0.278
F		56.331	151.346		
P		< 0.001	< 0.001		
Aldrete score	Immediately after extubation	8.20±0.83	8.00±0.56	2.017	0.045
	15 min after extubation	8.56±0.72	8.28±0.60	2.955	0.003
	15 min after extubation	8.88±0.74	8.77±0.68	1.144	0.254
F		20.907	40.113		
P		< 0.001	< 0.001		

Notes: CIVIA, combined intravenous-inhalation anesthesia; TIVA, total intravenous anesthesia; OAA/S: alertness-sedation scale score; Aldrete: Wake-up room standard score.

hours postoperatively [(2.52±0.18) vs. (3.14±0.22), P < 0.05], and at 24 hours postoperatively [(1.37±0.15) vs. (2.23±0.17), P < 0.05] (**Figure 4**).

Ramsay sedation

There was no significant difference in Ramsay score between the two groups immediately after operation, or at 12 h and 24 h after operation (P > 0.05). Both groups remained within the range considered appropriate for sedation and comfort (**Table 7**).

Postoperative complications of the two groups

The overall incidence of postoperative complications was significantly lower in the CIVIA group compared with the TIVA group (16.03% [17/106] vs. 31.37% [32/102], P < 0.05) (**Table 8**).

Discussion

Hepatectomy is a common surgical procedure for liver diseases, aiming to maximize preservation of the structural and functional integrity of the remnant liver. This operation typically utilizes anatomical planes to resect the liver, thereby avoiding injury to major vessels, bile ducts, and their branches, which helps minimize intraoperative bleeding, maintain a clear operative vision, and reduces postoperative complications [15, 16]. Therefore, hepatectomy plays an important role in the treatment of liver diseases. However, during hepatectomy, hepatic

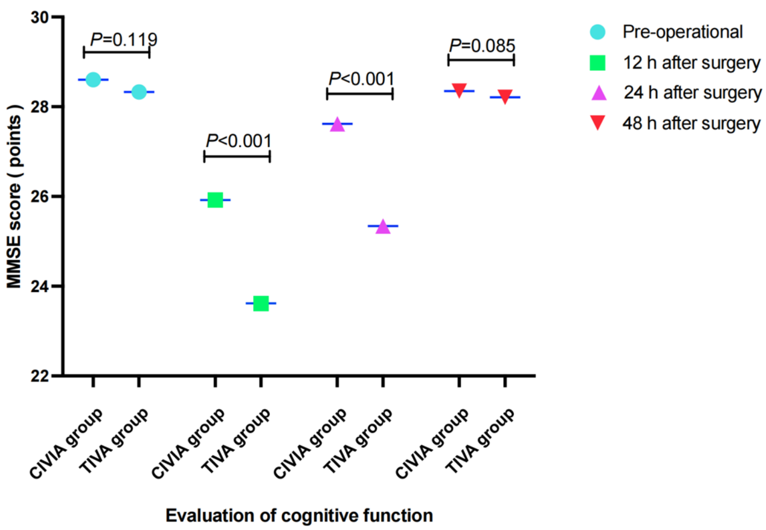

Figure 3. Comparison of cognitive function between the two groups. Notes: CIVIA, combined intravenous and inhalation anesthesia; TIVA, total intravenous anesthesia; MMSE, Mini-Mental State Examination.

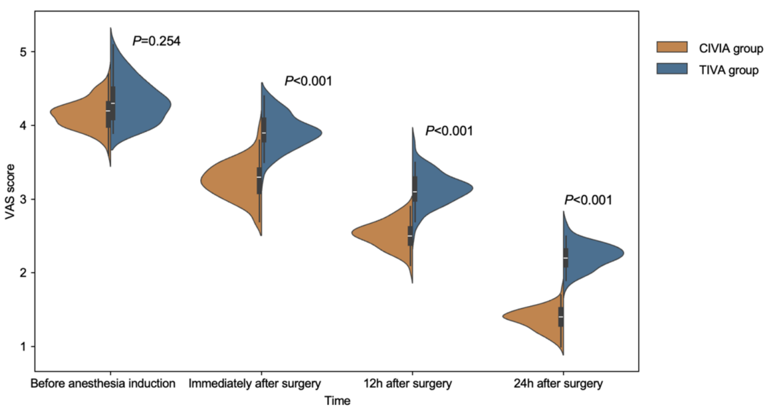

Figure 4. Comparison of VAS scores between the two groups. Notes: CIVIA, combined intravenous and inhalation anesthesia; TIVA, total intravenous anesthesia; VAS, Visual Analogue Scale.

blood flow must be interrupted. When blood supply is restored, ischemia-reperfusion may cause hepatocellular damage and systemic stress response that compromise hemodynamic stability. These pathophysiological changes can exacerbate surgical trauma, increase the risk of postoperative complications, and prolong patient recovery [17]. Therefore, the scientific design and anesthesia regimens are of critical importance in liver surgery.

General anesthesia is an essential prerequisite for major and prolonged surgical procedures. In patients undergoing hepatectomy, impaired liver function may unpredictably alter the metabolism and pharmacodynamics of anesthetic drugs. Therefore, controlling anesthetic depth in liver surgery is challenging: insufficient dosing may lead to intraoperative awakening and surgical interference, while overdosing may cause drug accumulation, resulting in delayed postoperative recovery [18, 19]. In elderly patients, hepatic functional reserve is further diminished, with age-related declines in synthesis, metabolism, and detoxification capacity. In addition, multiple comorbidities increase surgical risk and complexity, making the choice of anesthetic technique particularly critical. In recent years, CIVIA has gained attention as a potentially superior approach [20]. However, evidence regarding its effects on perioperative stress response and prognosis in elderly patients with liver disease remains limited. Therefore, this study focused on this unique population, in contrast to previous studies that focused primarily on younger or middle-aged patients. By addressing the unique physiological and pathological challenges of elderly individuals, such as heightened stress response, more complex inflammatory reactions, and a greater risk of postoperative complications, our findings provide novel insights into optimizing anesthetic strategies for this vulnerable group.

In this study, postoperative awakening, time to regain consciousness, and extubation time were significantly shorter in the CIVIA group. Multivariate logistic regression analysis further demonstrated significant differences in intraoperative blood loss (OR=0.868, 95% CI=0.818-0.921), anesthesia maintenance time (OR=0.695, 95% CI=0.592-0.815), and intraoperative complications (OR=0.159, 95% CI=0.030-0.853) between the two groups. One

Table 7. Comparison of Ramsay scores between the two groups (mean ± SD)

Group	N	Immediately after surgery	12 h after surgery	24 h after surgery	*F*	*P*
CIVIA group	106	2.34±0.22	2.78±0.26	3.15±0.28	122.361	< 0.001
TIVA group	102	2.28±0.25	2.74±0.26	3.10±0.28	154.196	< 0.001
t		1.788	1.103	1.276		
P		0.075	0.271	0.204		

Notes: CIVIA, combined intravenous-inhalation anesthesia; TIVA, total intravenous anesthesia.

Table 8. Comparison of postoperative complications between the two groups [n (%)]

Group	Agitation	Nausea and vomiting	Dizziness and headache	Hypotension	Tachycardia	Total
CIVIA group (n=106)	4 (3.77)	3 (2.83)	4 (3.77)	3 (2.83)	3 (2.83)	17 (16.03)
TIVA group (n=102)	7 (6.86)	6 (5.88)	5 (4.91)	7 (6.86)	7 (6.86)	32 (31.37)
χ^2						6.788
P						0.009

Notes: CIVIA, combined intravenous-inhalation anesthesia; TIVA, total intravenous anesthesia.

possible explanation is that TIVA relies primarily on intravenous anesthetics such as propofol and remifentanil, which enter the blood circulation quickly to produce anesthetic effect [21]. However, these drugs are mainly metabolized in the liver, and variations in metabolic rate can influence their distribution and duration of action. This may limit the ability to promptly adjust anesthetic depth, resulting in delayed recovery. In contrast, CIVIA combines inhalational agents (e.g., sevoflurane, metabolized via pulmonary exhalation and minimally by the liver) with intravenous anesthetics (propofol and remifentanil, metabolized by the liver) [22, 23]. This multimodal approach provides more stable anesthetic depth, reduces intraoperative stress responses, and suppresses the release of stress hormones, thereby improving anesthetic quality [24]. For elderly patients with reduced hepatic reserve and impaired cardiovascular function, CIVIA offers additional benefits. By decreasing the required dose of intravenous anesthetics, CIVIA lessens hepatic metabolic burden and supports hemodynamic stability, providing a more balanced anesthetic effect. Studies have shown that CIVIA not only attenuates endocrine fluctuations but also reduces the overall anesthetic requirement, minimizes perioperative changes in T lymphocyte subsets, and partially blocks nociceptive transmission in the central nervous system [25]. This can lower the sedative-hypnotic threshold, enhance anesthetic sensitivity, and ultimately optimize perioperative management.

The stress response is a systemic physiological reaction mediated through humoral, central nervous, and endocrine pathways. The intraoperative stress response can stimulate the neuroendocrine system and aggravate tissue and organ damage [26, 27]. As a major stressor, the operation stimulates the sympathetic-adrenal medullary axis. Increased sympathetic activity enhances acetylcholine release, which in turn promotes adrenal secretion of a large amount of E and NE. Elevated circulating E and NE accelerate HR, increase myocardial contractility, and disturb hemodynamic stability [28]. In this study, serum levels of E, NE, and Cor in the CIVIA group were significantly lower than those in TIVA group immediately after surgery, and at 12 h and 24 h postoperatively. Perioperative SpO_2 was significant higher, while MAP and HR were significant lower immediately after surgery, and at 12 h and 24 h postoperatively in the CIVIA group. These findings suggest that sevoflurane inhalation combined with propofol anesthesia attenuates sympathetic conduction and nociceptive transduction during surgery. Sevoflurane exerts less airway irritation and effectively suppresses catecholamine and cortisol release, thereby providing analgesia, reducing stress responses, maintaining intraoperative hemodynamic stability, and lowering complication risk [29]. For elderly patients with diminished physiological reserves and reduced tolerance to surgical and anesthetic stress, these advantages are particularly relevant. CIVIA not only mitigates perioperative stress responses and stabilizes hemodynamics but also helps reduce immunosuppression, accelerates postoperative recovery, and improves overall quality of life.

Our study also demonstrated that serum levels of CRP and TNF-α increased significantly in both groups immediately after surgery and at 12 h and 24 h after surgery, with the TIVA group showing consistently higher levels than the CIVIA group. These findings indicate that while hepatectomy inevitably triggers an acute inflammatory response, CIVIA attenuates this effect more effectively than TIVA. A possible reason is that the anti-inflammatory effects of propofol and remifentanil in the TIVA group are relatively weak, and the slower metabolic clearance of intravenous anesthetics may prolong drug exposure and exacerbate inflammatory responses. In contrast, inhaled anesthetics possess inherent anti-inflammatory effect. Sevoflurane, in particular, can suppress the release of inflammatory mediators and is rapidly eliminated through pulmonary exhalation, thereby reducing the inflammatory burden [30]. The anti-inflammatory properties of sevoflurane is thought to involve modulation of intracellular signaling pathways, especially inhibition of NF-κB activation, which downregulates cytokine production. Moreover, the pharmacokinetic properties of propofol may complement the anti-inflammatory actions of sevoflurane, potentially enhancing its regulatory effect on perioperative inflammation [31, 32]. Therefore, the use of sevoflurane combined with propofol anesthesia in CIVIA appears to mitigate perioperative inflammation and oxidative stress, providing additional benefits for elderly patients undergoing hepatectomy.

In this study, we compared the effects of CIVIA and TIVA on recovery quality, postoperative cognitive function, and complications in elderly patients undergoing hepatectomy. The OAA/S and Aldrete scores were significantly higher in the CIVIA group at extubation and 15 min after extubation, indicating that sevoflurane combined with propofol improves recovery quality and facilitates early postoperative awakening [33]. In addition, POCD occurred less frequently in the CIVIA group than in the TIVA group (8 vs. 17). At both 12 h and 24 h after operation, the MMSE scores were higher in the CIVIA group than in the TIVA group, indicating that sevoflurane combined with propofol target controlled infusion which may promote earlier recovery of cognitive function in elderly patients, which is conducive to consciousness recovery [34]. Pain assessment showed that although VAS scores declined over time in both groups, CIVIA patients consistently reported lower pain scores immediately, 12 h, and 24 h after surgery. However, no significant differences in Ramsay score were observed between groups at any postoperative timepoint, indicating that both anesthesia methods provided adequate and appropriate sedation during recovery. In addition, the incidence of postoperative complications was significantly lower in the CIVIA group compared with the TIVA group (16.03% [17/106] vs. 31.37% [32/102]). These findings suggest that sevoflurane combined with propofol not only improves recovery quality and cognitive outcomes but also reduces adverse events, thereby enhancing surgical safety and facilitating postoperative recovery in elderly patients with liver disease [35].

The innovation of this study lies in the systematic comparison of CIVIA and TIVA in elderly patients with liver disease undergoing hepatectomy. For the first time, we comprehensively evaluated not only traditional anesthesia-related indicators such as postoperative recovery time, return of consciousness, and extubation time, but also key parameters including perioperative stress response, inflammatory markers, postoperative cognitive dysfunction, and complication rates. This multidimensional analysis provides a robust scientific basis for optimizing anesthetic management in this high-risk population.

Nevertheless, several limitations should be acknowledged. First, the relatively limited sample size may affect the generalizability of the findings. Second, this was a single-center study, and potential regional or demographic biases cannot be excluded. Moreover, elderly patients often present with comorbidities, fragile cardiovascular systems, and increased susceptibility to postoperative cognitive dysfunction or side effects of inhaled anesthetics. The requirement for advanced anesthesia equipment may also restrict the widespread application of CIVIA. Future research should therefore employ larger, multicenter cohorts with more rigorous study designs to validate these findings. Individualized anesthetic strategies tailored to the specific conditions of elderly patients with liver disease will be essential to further enhance surgical safety and postoperative recovery.

Conclusion

This study systematically evaluated the effects of CIVIA and TIVA in elderly patients with liver disease undergoing hepatectomy. By comprehensively analyzing multiple indicators, we demonstrated that CIVIA offers significant advantages in improving recovery quality, attenuating stress response, reducing the incidence of postoperative cognitive dysfunction, and lowering postoperative complication rates. CIVIA may thus be considered a preferred anesthetic regimen for hepatectomy in elderly patients with liver disease.

Disclosure of conflict of interest

None.

Address correspondence to: Juan Liu, Department of Anesthesiology, Beijing Chaoyang Hospital, Capital Medical University, Beijing 100020, China. Tel: +86-010-85231330; E-mail: chaoyangyiylj@126.com

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