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Research article

Effect of total intravenous-based immediate extubation on patient outcomes in adult liver transplantation: A retrospective cohort study

Yan-Jun Chu [a,1], Hui Zhang [a,1], Bing-Xin Jin [a], Yu-Fan Liu [a], Yong-Xing Yao [a,b,*]

[a] *Department of Anesthesia, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, People's Republic of China*
[b] *Key Laboratory of Clinical Evaluation Technology for Medical Device of Zhejiang Province, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, People's Republic of China*

A R T I C L E I N F O

Keywords:
Total-intravenous anesthesia
Immediate extubation
Balanced anesthesia
Liver transplantation
Postoperative infection
Retrospective

A B S T R A C T

Background: Although step-down emergence and extubation are universally practiced after liver transplantation (LT), prolonged mechanical ventilation and positive end-expiratory pressure may enhance predisposition to ventilator-associated complications and may be associated with inferior outcomes.
Methods: We screened 339 patients who underwent LT in this retrospective cohort study. After propensity score matching, 35 patients in Group F (total intravenous-based immediate extubation, TIIE) and 107 patients in Group C (balanced anesthesia with step-down extubation) with balanced and comparable pre- and intraoperative profiles were selected for analysis. Patients in Group F received propofol- and remifentanil-based total intravenous anesthesia, followed by immediate tracheal extubation. Patients in Group C received sevoflurane-based balanced anesthesia and were step-down extubated in the intensive care unit. The primary outcomes were postoperative respiratory support time and length of postoperative ICU stay. Other postoperative outcomes were compared between the two groups.
Results: Group F had significantly shorter postoperative respiratory support time than Group C (median, 0.08 vs 17 h; $P < 0.001$). The duration of postoperative intensive unit care stay in Group F was significantly shorter than that in Group C (mean, 5.84 vs 7.08 days; $P = 0.019$). Group F had a lower incidence of bacterial infection (20.0 % vs 42.1 %; $P = 0.019$) than Group C. No significant differences in continuous renal replacement therapy use (2.86 % vs 13.08 %; odds ratio, 0.195; $P = 0.088$), early mortality rate, percentage reduction of bilirubin, the incidence of exploratory laparotomy, pneumonia, or thrombosis were observed between groups.
Conclusion: TIIE is safe, effective, and associated with a lower incidence of postoperative bacterial infection.

* Corresponding author. Department of Anesthesia, First Affiliated Hospital, Zhejiang University School of Medicine, 79 Qingchun Road, Hangzhou, 310003, People's Republic of China.
E-mail address: yaoyongxing@zju.edu.cn (Y.-X. Yao).
[1] Chu YJ and Zhang H contributed equally.

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1. Introduction

Liver transplantation (LT) is the treatment of choice for end-stage liver disease, including metabolic liver disease, acute or chronic liver failure, and hepatocellular carcinoma [1]. The number of LTs has increased over the last 20 years, and anesthesia techniques have evolved [2,3]. Conventionally, the protocol for step-down emergence and extubation after a period of ventilation support is recommended following general anesthesia in LT. This approach is widely adopted not only because of the evident surgical stress, significant volume replacement, and inner environment disturbance resulting from the operation but also because of the presence of multiple pre-existing organ dysfunctions in the population [4]. However, prolonged mechanical ventilation and positive end-expiratory pressure after surgery may enhance predisposition to ventilator-associated complications. Although controversial, mechanical ventilation could potentially reduce cardiac output, affect venous outflow, and impact liver function recovery, which is critical in LT [5,6]. In contrast, studies have demonstrated that early extubation not only enhances comfort, decreases intrathoracic pressure, and reduces pulmonary complications but also reduces hospitalization costs; prolonged ventilator support, along with the treatment of ventilator-related complications, accounts for a substantial proportion of the overall cost [7–9]. Therefore, fast-track anesthesia and care steps have been tentatively implemented in some centers. In addition to the economic advantages, fast-track anesthesia also suggests potential clinical benefits postoperatively [10,11].

Anesthetic agents and management affect patient outcomes [12]. Inhalational anesthetics are suggested to be associated with more postoperative stress than intravenous anesthetics, and postoperative stress is considered a key factor in provoking systemic inflammation and immunosuppression [13–15]. Conversely, in total intravenous anesthesia, the depth of sedation can be monitored more easily, and the recovery profile of cognitive function is superior to that of inhalational anesthetic-based balanced anesthesia [16]. Additionally, total intravenous anesthesia has been reported to decrease postoperative nausea and vomiting, shorten the time to discharge, and potentially offer benefits in terms of tumor recurrence [17,18].

Fast-track anesthesia and immediate extubation were introduced at the turn of this century and have since been widely practiced in cardiac surgery [19–21]. However, the management of immediate extubation is much more meticulous and team-involved in LT [22–24]. To date, few studies have investigated the effect of total intravenous-based immediate extubation (TIIE) on patient outcomes in LT [25]. The present study aimed to compare the safety and efficacy of TIIE and balanced anesthesia for LT. Therefore, we investigated the postoperative outcomes of patients who received TIIE and balanced anesthesia with step-down extubation to compare the safety and efficacy of adult LT.

2. Methods

2.1. Study cohort

2.1.1. Ethical considerations

This study was approved by the Ethics Committee of our hospital (No. 2022-891) and adhered to the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective study design.

2.2. Inclusion and exclusion criteria

The inclusion criteria were as follows: 1) adult patients aged 18–80 years, 2) patients who underwent LT, and 3) transplant surgeons and anesthesiologists with at least five years of experience in LT. The clinical exclusion criteria included preoperative hepatic encephalopathy (West Haven criteria $\geq$ II).

2.3. Clinical data

We retrospectively analyzed the data of 339 adult patients who underwent LT at our institution between July 2017 and September 2022. The patients were divided into two groups according to the type of anesthesia they received: Group F (TIIE; 38 patients) and Group C (balanced anesthesia with step-down extubation; 301 patients). All patients were diagnosed with end-stage liver disease. Preoperative clinical data, including sex, age, etiology of liver disease, comorbidity (diabetes mellitus, hypertension), body mass index (BMI), American Society of Anesthesiologists (ASA) classification, model for end-stage liver disease (MELD) score, partial pressure of arterial oxygen/fraction of inspired oxygen (PO_2/FiO_2), and partial pressure of arterial carbon dioxide (PCO_2), were recorded in both groups. The MELD score was calculated using the following formula: [0.957 $\times$ log e (creatinine mg/dL) + 0.378 $\times$ log e (bilirubin mg/dL) + 1.120 $\times$ log e (INR) + 0.643] $\times$ 10 + 0.64 x (biliary or alcoholic 0, others 1).

Intraoperative factors, including propofol dosage, duration of surgery, duration of anesthesia, total amount of transfusion during surgery (including packed red blood cells, fresh frozen plasma, and fluid), intraoperative autologous blood transfusion volume, blood loss, hourly urine output, blood pH at the end of surgery (EOS), and EOS lactate concentration, were recorded in both groups.

The primary outcomes were postoperative respiratory support time and postoperative intensive care unit (ICU) stay. Other postoperative outcomes included the duration of hospitalization, hospitalization costs, percentage reduction of bilirubin seven days after surgery, incidence of early mortality, bacterial infection, continuous renal replacement therapy (CRRT) use, pneumonia, thrombosis, and exploratory laparotomy during postoperative hospitalization. The total hospitalization costs included intra- and postoperative costs, ICU stay, and treatment complications. The percentage reduction in bilirubin level 7 days after surgery was calculated as follows:

Percentage reduction in bilirubin 7 days after surgery = (postoperative bilirubin peak level - bilirubin level at 7 days after surgery)/

postoperative bilirubin peak level.

Early mortality was defined as in-hospital all-cause mortality within the first 30 days of hospitalization. Postoperative bacterial infections included pulmonary and bloodstream infections. According to previous reports, bacterial infections were defined as a positive culture of a pathogenic microorganism in any sample [26], which includes blood-borne, respiratory, or other-oriented infections.

2.4. Anesthesia procedure and pain management

All patients underwent orthotopic liver transplantation (piggyback or classic) under general anesthesia. Prophylactic anti-infective treatment before and after the operation was administered in all the patients. Cephalosporin and penicillin were used as antibiotics.

Standard monitoring, including a 5-lead electrocardiogram, invasive blood pressure, bispectral index (BIS), temperature, and oxygen saturation, was performed for all patients. Patients in Group F received etomidate (0.3 mg/kg) and fentanyl (5 μg/kg). Tracheal intubation was performed with rocuronium (0.9 mg/kg). Patients in Group C received etomidate (0.3 mg/kg) combined with fentanyl (5 μg/kg) or sufentanyl (0.5 μg/kg). Tracheal intubation was performed with rocuronium (0.9 mg/kg) or vecuronium (0.15 mg/kg). After tracheal intubation, a central line catheter was placed through the internal jugular vein for hemodynamic monitoring and rapid infusion, and the second radial artery was cannulated for blood sampling. Under a 50 %–70 % oxygen/air mixture, mechanical ventilation was controlled in the partial pressure of the end-tidal CO_2 range of 30–35 mmHg, with a tidal volume of 8–10 mL/kg and a respiratory rate of 10–14 breaths/min. Anesthesia in Group F was maintained with propofol (starting at 5–6 mg/kg/h), remifentanil (0.2–0.4 μg/kg/min), and cis-atracurium (0.06–0.12 mg/kg/h) infusion, while in Group C, which consisted of inhaled sevoflurane (1–1.5 %) and propofol infusion, supported by remifentanil infusion (0.1–0.3 μg/kg/min) or intermittent fentanyl (2 μg/kg) and sufentanyl (0.2 μg/kg) injection and a muscle relaxant (cis-atracurium, [0.06–0.12 mg/kg/h]). Anesthetic management was performed according to clinical judgment and institutional care standards such that a targeted BIS of 40–60 was maintained. Packed red blood cells were administered to maintain the hematocrit between 25 % and 30 %. Freshly frozen plasma, cryoprecipitates, and platelets were transfused to improve intraoperative coagulopathy under thromboelastography guidance and laboratory coagulation parameters. Norepinephrine (0.1–0.5 μg/kg/min) and/or epinephrine (0.1–0.5 μg/kg/min) were infused to maintain hemodynamic stability after caval clamping. Calcium chloride was administered when the serum calcium levels dropped to <80 % of the normal lower limit. Sodium bicarbonate was administered when the serum base excess was below −6. After caval unclamping and liver reperfusion, fibrinogen and prothrombin complexes were administered based on the laboratory parameters and clinical judgment.

Immediate extubation was defined as tracheal extubation in the operating room within 20 min after surgery. The attending anesthesiologist decided to extubate after consulting with the surgeons toward the end of the surgery. The criteria for extubation were as follows [27]: recovery of consciousness; compliance with verbal commands; tidal volume, >6 mL/kg; respiratory rate, 10–18/min; partial pressure of end-tidal CO_2, <50 mm Hg; oxygen saturation, >95 % (with $FiO_2 \leq 40$ %); hemodynamic stability; normothermia; reversal of neuromuscular blockade by neostigmine (0.05 mg/kg); and adequate hemostasis in the surgical field. The patients were subsequently transferred to the ICU for further care.

All patients in Group F were incisionally infiltrated with 0.375 % ropivacaine, and long-acting opioids, including fentanyl and tramadol, were administered for postoperative analgesia. All patients received patient-controlled analgesia with sufentanyl or oxycodone. Awake patients were closely monitored and evaluated for postoperative pain status using the numerical rating scale (NRS). If analgesia is inadequate (NRS ≥4), 50–100 mg of tramadol will be administered for rescue analgesia.

Patients without plans for immediate extubation or those who failed to fulfill the extubation criteria were transferred to the ICU for mechanical ventilation support. The sedation protocol and weaning from mechanical ventilation were performed in the ICU at the discretion of the attending physician.

2.5. Statistical analysis

All statistical analyses were performed using the SPSS software version 22.0. Propensity score matching (PSM) analysis was used to eliminate selection bias between the two groups. In the PSM analysis, the following variables were considered potential confounders between the groups and were adjusted for age, blood loss, hourly urine output, and EOS pH. Propensity scores were calculated by bivariate logistic regression using a 1:4 ratio matching with a caliper width of 0.2 based on the nearest-neighbor matching method without replacement. PSM revealed that the relevant preoperative and intraoperative clinical factors were well-balanced. Multivariable logistic regression analysis was performed to determine the association between perioperative factors and hospitalization costs. The one-sample Kolmogorov–Smirnov test was used to determine the normality of the continuous variable distributions. Continuous variables with a normal distribution are presented as mean ± standard deviation (SD), and non-normal variables are presented as medians (interquartile range [IQR]). An independent *t*-test was used to evaluate differences between normally distributed continuous variables. Values greater than the upper quartile +1.5 times the interquartile spacing or less than the lower quartile - 1.5 times the interquartile spacing were defined as outliers. Continuous variables with a non-normal distribution were compared using the Mann–Whitney *U* test. For categorical variables, frequencies were compared using the Pearson χ^2 test or Fisher exact test. Statistical significance was set at $P < 0.05$. PASS software version 2021 was used to calculate the actual power.

3. Results

Forty-five of the 384 patients who were assessed for eligibility between July 2017 and September 2022 were excluded from the study because of severe encephalopathy. In total, 339 adult patients were enrolled in this study. Thirty-eight patients were allocated to Group F (received TIIE), and 301 were allocated to Group C (balanced anesthesia with step-down extubation) (Fig. 1).

Baseline parameters, including age (median, 50.0 vs 55.0; $P = 0.010$), blood loss (median, 1500 vs 1000; $P = 0.029$), hourly urine output (median, 333 vs 1963; $P < 0.001$), and EOS pH (median, 7.419 vs 7.385; $P = 0.007$), were heterogeneous between the groups. Therefore, PSM was conducted. After PSM, 35 patients in Group F were matched with 107 patients in Group C. All characteristics were well-matched in the PSM cohort (Table 1).

There was no significant difference in prophylactic anti-infective treatment between the two groups (Supplementary Table 1). The dosage of propofol used in Group F was significantly higher than that used in Group C (mean, 2371 vs 1995 mg; $P = 0.02$, Supplementary Table 2). Group F had significantly shorter postoperative respiratory support time than Group C (median, 0.08 vs 17 h; $P < 0.001$). The difference in postoperative ICU stay was significant between the two groups (mean, 5.84 vs 7.08; $P = 0.019$) after excluding three outliers in Group F (14, 14, and 23 days) and three outliers in Group C (17, 21, and 32 days). The incidence of bacterial infection was significantly lower in Group F than in Group C (20.0 % vs 42.1 %; odds ratio (OR), 0.344; 95 % confidence interval (CI), 0.183–0.858; $P = 0.019$). However, CRRT use (2.9 % vs 13.1 %; OR, 0.195; 95 % CI, 0.025–1.543; $P = 0.088$) was slightly lower in Group F than in Group C. The duration of postoperative hospitalization (median, 23 vs 25 days; $P = 0.194$) was slightly shorter, and hospitalization costs (mean, 243, 979 vs 275, 429 RMB; $P = 0.294$) were slightly lower in Group F than in Group C. The percentage reduction in bilirubin 7 days after surgery (median, 56 % vs 52 %; $P > 0.05$), the incidence of early mortality (2.86 % vs 1.87 %; $P > 0.05$), pneumonia (20 % vs 32.7 %; $P > 0.05$), thrombosis (5.7 % vs 8.4 %; $P > 0.05$), and exploratory laparotomy (8.6 % vs 10.3 %; $P > 0.05$) were similar in both groups (Table 2).

Multivariable logistic regression analysis was performed to determine the effects of perioperative factors, including patient age, duration of surgery, blood loss, hourly urine output, EOS pH, duration of postoperative ICU stay, and hospitalization costs. The analysis revealed that linear regression was effective ($R^2 = 0.183$) and that a longer ICU stay was associated with a significant increase in hospitalization costs ($P < 0.001$) (Table 3).

4. Discussion

In this study, potential confounding factors for PSM were selected according to previous reports [28–32]. After matching, the parameters were statistically balanced in terms of age, comorbidities, body mass index (BMI), MELD score, preoperative PO_2/FiO_2, PCO_2, duration of surgery, intraoperative blood product transfusion, blood loss, hourly urine output, and EOS pH. No significant differences were observed in these factors between the two groups. Therefore, the data on postoperative outcomes were comparable.

In our study, in addition to the expected natural results of immediate extubation, such as a significant reduction in the duration of postoperative respiratory support and a significant reduction in ICU stay, the incidence of bacterial infection was also significantly lower (20.0 % vs 42.1 %, $P = 0.019$) in Group F than in Group C. The incidence of CRRT use decreased by 78 % in Group F compared to that in Group C (2.9 % vs 13.1 %), although the difference was not statistically significant. The duration of hospitalization was shorter, and hospitalization costs were also lower in Group F than in Group C (8 % and 11.4 % reduction, respectively), suggesting that the TIIE bundle may exhibit economic advantages over conventional balanced anesthesia. Multivariable logistic regression analysis showed a

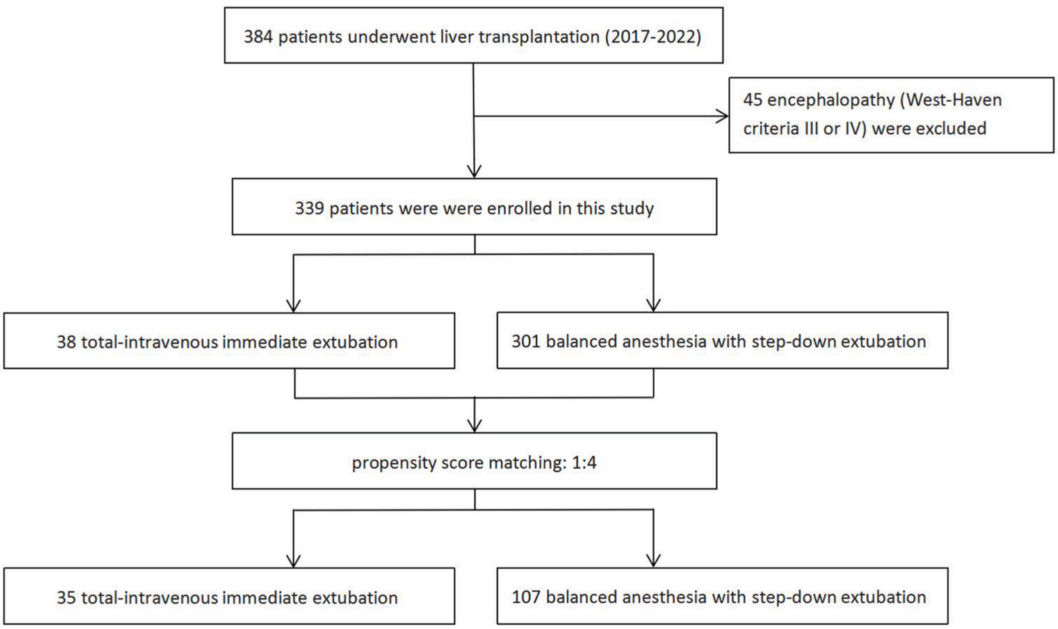

Fig. 1. Study flow-chart.

Table 1
Preoperative data and intraoperative parameters of two groups.

Variables	Before PSM			After PSM		
	Group F	Group C	*P*	Group F	Group C	*P*
	n = 38 (%)	n = 301 (%)		n = 35 (%)	n = 107 (%)	
Sex						
Female	7 (18.4)	61 (20.3)	0.884	6 (17.1)	23 (21.5)	0.579
	31 (81.6)	240 (79.7)		29 (82.9)	84 (78.5)	
Male						
Etiology						
Cirrhosis	19 (50.0)	166 (55.1)	0.082	17 (48.6)	58 (54.2)	0.302
	9 (23.6)	95 (31.6)		9 (25.7)	31 (29.0)	
Cirrhosis complicated with liver cancer						
Liver cancer	8 (21.1)	21 (7.0)		7 (20.0)	9 (8.4)	
Acute liver failure	2 (5.3)	19 (6.3)		2 (5.7)	9 (8.4)	
Comorbidity						
Diabetes mellitus	3 (7.9)	40 (13.3)	0.381	3 (8.6)	13 (12.1)	0.561
	4 (10.5)	45 (15.0)	0.477	4 (11.4)	14 (13.1)	0.798
Hypertension						
ASA classification						
III	31 (81.6)	223 (74.1)	0.230	28 (80.0)	79 (73.8)	0.457
	6 (15.8)	76 (25.2)		6 (17.1)	27 (25.2)	
IV						
V	1 (2.6)	2 (0.7)		1 (2.9)	1 (1)	
BMI, kg/m^2	22.3 (3.14)	22.7 (3.36)	0.481	22.3 (2.93)	22.6 (3.19)	0.611
Mean (SD)						
	50 (18.5)	55 (13.5)	0.010	51 (19)	51 (15)	0.624
Age (y)						
Median (IQR)						
MELD score Median (IQR)	10.8(12.58)	12.9(13.3)	0.174	11(12)	12.5(14)	0.527
	353 (103)	333 (88)	0.132	353 (101)	325 (82)	0.066
Operation duration (min)						
Median (IQR)						
	395 (98)	377 (94)	0.113	395 (92)	365 (92)	0.098
Anesthesia duration (min)						
Median (IQR)						
	5240 (1733)	5317.7 (2270)	0.503	5210 (1740)	5330 (2340)	0.751
Total amount of transfusion (mL)						
Median (IQR)						
	800 (1200)	900 (1546)	0.965	800 (1200)	1100 (1600)	0.941
Packed red blood cell (mL)						
Median (IQR)						
	1260 (713)	1340 (815)	0.877	1260 (750)	1400 (730)	0.923
Fresh frozen plasma (mL)						
Median (IQR)						
	0 (300)	0 (112.5)	0.295	0 (300)	0 (250)	0.584
Autologous blood transfusion volume (mL)						
Median (IQR)						
	1500 (1000)	1000 (973)	0.029	1500 (1000)	1000 (1200)	0.072
blood loss (mL)						
Median (IQR)						
	333 (258)	193 (163)	<0.001	329 (257)	281 (207)	0.168
Hourly urine output (mL/h)						
Median (IQR)						
	7.419 (0.096)	7.385 (0.090)	0.007	7.41 (0)	7.4 (0)	0.210
EOS Ph						
Median (IQR)						
	3.75 (3.4)	3.9 (3.5)	0.776	3.5 (3)	3.6 (3)	0.696
EOS lactate						
Median (IQR)						
	450 (78)	438 (110)	0.099	454 (80)	445 (107)	0.282
PO_2/FiO_2 (SD)						
	34.7 (5.3)	34.6 (6.0)	0.897	35.0 (5.2)	34.4 (4.7)	0.519
PCO_2 (SD)						

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; EOS, end-of-surgery; MELD, model for end-stage liver disease; PO_2, partial pressure of oxygen; FiO_2, fraction of inspired oxygen; PCO_2, partial pressure of carbon dioxide.

significant linear correlation between the duration of ICU stay and hospitalization costs, indicating that the use of TIIE in LT improves resource utilization. Lastly, no increase in the incidence of early mortality, exploratory laparotomy, pneumonia, or thrombosis was observed in Group F, indicating that total TIIE is safe and effective during adult LT.

Table 2
The postoperative outcomes of the two groups.

Variables	Group F	Group C	Odds Ratio (95%CI)	*P*	Power
	n = 35 (%)	n = 107 (%)			
Respiratory support time (h) Median (IQR)	0.08 (0)	17 (10)	/	<0.001	1.0
ICU stay (d) Mean (SD)	5.84 (2.35)	7.08 (3.15)	/	0.019	0.79
Postoperative hospital stays (d) Median (IQR)	23 (9)	25 (12)	/	0.194	0.27
Hospitalization costs (RMB) mean (SD)	243979 (91481)	275429 (168243)	/	0.294	0.40
Bacterial infection	7 (20)	45 (42.1)	0.344 (0.183–0.858)	0.019	0.71
CRRT use	1 (2.9)	14 (13.1)	0.195 (0.025–1.543)	0.088	0.36
Percentage reduction of bilirubin 7 days after surgery (%) Median (IQR)	52 (65)	56 (48)	/	0.804	0.09
Early mortality	1 (2.86)	2 (1.87)	1.544 (0.136–17.564)	0.724	0.05
Pneumonia	7 (20)	35 (32.7)	0.514 (0.205–1.292)	0.153	0.31
Thrombosis	2 (5.7)	9 (8.4)	0.660 (0.136–3.211)	0.604	0.05
Exploratory laparotomy	3 (8.6)	11 (10.3)	0.818 (0.215–3.188)	0.768	0.04

Abbreviations: CI, confidence interval; CRRT, continuous renal replacement therapy; ICU, intensive care unit.

Table 3
Multivariable logistic regression analysis of hospitalization costs by perioperative factors.

	R	R^2	Durbin-Watson		
	0.428	0.183	2.04		
	Denormalization coefficient		Standardization coefficient	T	*P*
	beta	Standard error	Beta		
ICU stay (d)	12651	2929	0.347	4.319	0.000
Operation duration (min)	−142	172	−0.075	−0.823	0.412
Bleeding volume (mL)	18.4	10.2	0.164	1.798	0.074
EOS pH	−158805	226220	−0.059	−0.702	0.484
Age (y)	1535	1132	0.11	1.356	0.177
Hourly urine output (mL/h)	41.4	89.5	0.038	0.462	0.645

Abbreviations: CRRT, continuous renal replacement therapy; EOS, end of surgery; ICU, intensive care unit.

Prolonged mechanical ventilation has been consistently associated with an increased incidence of adverse events [33,34]. A longer duration of intubation has been associated with ICU admission, which may lead to the occurrence of ventilation-associated pneumonia and increase the risk of nosocomial infections [35–38]. Furthermore, positive pressure ventilation, particularly with positive end-expiratory pressure, may reduce cardiac output and splanchnic blood flow, potentially affecting graft liver function recovery [6,39]. Our results revealed no significant effect of immediate extubation on the reduction of bilirubin levels after surgery, suggesting that total TIIE has no obvious effect on graft function. Lastly, reducing the duration of ICU stay is considered crucial for improving prognosis, as long-term ICU stay may result in sustained physical, cognitive, and/or mental health impairments [22,40,41]. Therefore, early extubation provides clinical benefits in the management of patients undergoing LT.

The quality of emergence after general anesthesia significantly influences the feasibility of immediate extubation. In the early postoperative stage, patients anesthetized with propofol tend to emerge clear-headed, whereas those administered volatile anesthetics are sometimes confused, which may greatly jeopardize immediate extubation after major surgeries [17]. Therefore, to obtain a clear-headed emergence, in the current study, Group F received total intravenous anesthesia with propofol and remifentanil. All patients in Group F fully regained consciousness, demonstrated compliance with verbal instructions, and exhibited no signs of agitation or delirium. This outcome underscores the reliability of fast-track anesthesia in this context.

Postoperative infection is an important factor affecting survival rates after LT transplantation, with total intravenous anesthesia showing potential benefits over conventional balanced anesthesia [42,43]. In the present study, the incidence of bacterial infection was reduced from 42.1 % in Group C to 20.0 % in Group F, indicating that total intravenous-based fast-track anesthesia affects the incidence of postoperative bacterial infection in LT. However, the reduction in infections was largely not solely due to a reduction in ventilator-associated pneumonia, as the pneumonia difference between the groups was not statistically significant. Studies have reported that the incidence of surgical site infections in patients undergoing colorectal surgery and postoperative pulmonary complications in neck surgery is lower with propofol-based intravenous anesthesia than with volatile anesthesia [44,45]. A recent report revealed that extubation in the operating room had no effect on postoperative moderate-to-severe infectious complications [22]. Multiple factors might be attributable to the incidence of infection; therefore, the exact reason remains to be evaluated, one of which might be due to the anesthetic agents rather than anesthesia methods.

Sevoflurane-induced balanced anesthesia remains the mainstay in LT; however, concerns regarding potential nephrotoxicity have been raised since its introduction into clinical use [46,47]. In contrast, propofol- and remifentanil-based intravenous anesthesia might produce better renal protection by preserving antioxidant ability and attenuating the inflammatory response [48–50]. Franzén et al. reported that sevoflurane anesthesia reduced urine output and sodium excretion while increasing plasma renin levels compared to propofol anesthesia [47]. A meta-analysis showed that volatile anesthesia is associated with a higher incidence of postoperative acute renal injury than propofol anesthesia [51]. In contrast, animal studies have revealed that propofol exerts organ-protective effects by suppressing neutrophil chemotaxis and phagocytosis [52,53]. Clinical studies in nephrectomy showed that compared with sevoflurane or desflurane, the use of propofol was associated with a lower incidence of postoperative acute kidney injury and chronic kidney dysfunction upstaging [54]. In this study, we were surprised to find that the incidence of CRRT use decreased by 78 % in Group F compared to that in Group C. Although the precise cause remains unknown, the decision to not administer sevoflurane and to increase the use of propofol and remifentanil may explain this difference.

Our results also revealed a reduction in the duration of ICU stay, duration of hospitalization, and hospitalization costs in Group F, confirming that TIIE improves resource utilization. Multivariate regression analysis revealed a significant correlation between the duration of ICU stay and hospitalization costs, indicating that the difference in costs was primarily due to the difference in the use of mechanical ventilation after surgery, which is also consistent with the findings of other studies [22].

5. Strengths and limitations

This study had several strengths and limitations. This is the first study to demonstrate the benefits of TIIE in adult patients undergoing LT using PSM. Although previous reports have discussed either total intravenous anesthesia or fast-track anesthesia protocols individually, our research highlights the combined benefits of both methodologies [22,55]. Second, PSM was used to control for selection biases. After PSM, no significant differences in relevant preoperative clinical data or intraoperative factors were observed between the two groups; therefore, the postoperative outcome data were comparable.

Nevertheless, this study had several limitations. Our study was retrospective in nature, which may limit our ability to establish a causal relationship between TIIE and the outcomes we observed. Despite the use of PSM, inadvertent confounding factors may have affected outcomes. Furthermore, the strictly limited sample size may limit the statistical power to detect potentially significant differences in outcomes between the two groups. Finally, the study was conducted at a single center, which may also restrict the generalizability of the findings to other centers with different patient populations, resources, and expertise. Therefore, randomized prospective studies with larger sample sizes are warranted to confirm our results.

6. Conclusions

TIIE is safe and effective and is associated with a lower incidence of infection. Studies with larger sample sizes and well-designed trials are warranted to further investigate its clinical significance in this population.

CRediT authorship contribution statement

Yan-Jun Chu: Writing – original draft, Formal analysis, Data curation. **Hui Zhang:** Writing – review & editing, Formal analysis, Data curation. **Bing-Xin Jin:** Data curation. **Yu-Fan Liu:** Data curation. **Yong-Xing Yao:** Writing – review & editing, Conceptualization.

Data availability statement

The data will be made available upon reasonable request.

Institutional review board statement

Ethical approval was obtained from the Ethics Committee of the First Affiliated Hospital of Zhejiang University (no. 2022-891).

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2025.e42108.

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