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ORIGINAL RESEARCH

Exploring the efficacy and safety of laparoscopic liver resection in the treatment of early-stage male patients with liver cancer and tumor diameter $\leq$5 cm

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Abstract

Background: This study investigates the efficacy and safety of laparoscopic hepatectomy in male patients with hepatocellular carcinoma (HCC) and tumor diameter $\leq$5 cm. **Methods**: The clinical data of 100 male HCC patients treated at our hospital from January 2019 to January 2021 were retrospectively collected. According to the treatment methods, patients were divided into an observation group (50 cases) and a control group (50 cases). The control group underwent traditional open non-anatomical liver resection, while the observation group received laparoscopic non-anatomical liver resection. The safety and efficacy of the two surgical methods were compared. **Results**: The observation group demonstrated significantly reduced intraoperative blood loss, operation time, incision length, and hepatic portal occlusion time than the control group ($p < 0.001$). The observation group had shorter times to mobilization, initiation of oral feeding, and hospital discharge ($p < 0.001$). On postoperative day three, levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (TBIL) were significantly lower in the observation group ($p < 0.05$). Cluster of Differentiation 3^+ ($CD3^+$), $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ ratio were improved in the observation group one week post-surgery ($p < 0.05$). The complication rate was significantly lower in the observation group ($p < 0.05$). At 1 and 3 years post-surgery, the recurrence rate in the observation group was significantly lower ($p < 0.05$). The overall survival (OS) rates at one, two, and three years were 75.9%, 41.4% and 12.9% for the observation group and 55.5%, 14.4% and 0% for the control group ($p < 0.05$), respectively. The median survival times in the observation group was significantly longer than the control group ($p < 0.05$). **Conclusions**: Laparoscopic hepatectomy for HCC offers improved clinical outcomes, enhanced liver function, reduced complication rates, and favorable safety profiles compared to open hepatectomy.

Keywords

Laparoscopic hepatectomy; Hepatocellular carcinoma; Open hepatectomy

1. Introduction

Primary liver cancer ranks as the fourth most common malignant tumor in China by incidence and is the second leading cause of cancer-related deaths, posing a serious threat to public health and safety [1, 2]. Among these, hepatocellular carcinoma (HCC), the most prevalent subtype of primary liver cancer, accounts for approximately 85–90% of all cases [3, 4]. The pathogenesis of HCC is closely associated with genetic predisposition, chronic hepatitis B virus (HBV) infection, and hepatitis C virus (HCV) infection. HCC is characterized by a high degree of malignancy, poor prognosis, high recurrence rates, and significant metastatic potential, which greatly impacts patient health and survival [5, 6]. For patients diagnosed with HCC, a comprehensive treatment strategy primarily involving surgical intervention remains the cornerstone of management, with surgical resection playing a pivotal role [7]. While surgery procedures are inherently traumatic for patients, long-term outcomes demonstrate that patients derive significant benefits from surgical intervention. Surgical resection and liver transplantation are the standard treatment options for HCC. However, traditional open partial hepatectomy, though effective, is highly invasive and associated with prolonged postoperative recovery and significant physical burden [8, 9].

With the rapid advancement of minimally invasive surgical techniques, laparoscopic hepatectomy has emerged as a mainstream alternative in recent years. This approach is characterized by minimal trauma and faster recovery, and alignment with the principles of accelerated recovery surgery. As a result, laparoscopic hepatectomy has gained widespread acceptance among healthcare providers and patients alike [10]. Despite its clear short-term benefits, the long-term efficacy and safety of laparoscopic hepatectomy for HCC remain inadequately studied, particularly in the context of chronic HBV-related HCC.

Differences and connections between open surgery and laparoscopic surgery in treating HCC:

(1) Postoperative differences:

a. Degree of trauma and recovery period: Open surgery is a more invasive procedure that typically requires a longer postoperative recovery period. Patients experience significant pain and need a longer hospital stay, with a higher incidence of complications. The patient's immune function is also greatly affected, potentially delaying postoperative recovery. In contrast, laparoscopic surgery is a minimally invasive technique, causing less damage to surrounding tissues, with less bleeding and a lower risk of infection. The postoperative recovery period is shorter, significantly reducing hospital stay. These advantages make laparoscopic liver resection the preferred choice for an increasing number of patients.

b. Postoperative complications and immune function recovery: Open surgery, due to its high invasiveness and slow recovery, has a higher incidence of postoperative complications. In contrast, laparoscopic surgery, which is less invasive and allows for quicker recovery, has a significantly lower incidence of postoperative complications compared to open surgery. Additionally, laparoscopic surgery has a smaller impact on the immune system, helping patients to quickly restore immune function postoperatively, thus reducing the incidence of complications.

c. Survival rate and long-term recurrence: Although laparoscopic surgery has significant advantages in short-term postoperative recovery, the comparison of long-term efficacy, recurrence rates, and survival rates remains a matter of concern. Current studies suggest that laparoscopic liver resection has favorable effects on the long-term recurrence and survival rates of HCC patients. Some studies have found that patients in the laparoscopic group have better 3-year and 5-year survival rates compared to the open surgery group, which may be related to their lower incidence of postoperative complications and faster recovery speed. However, despite the high invasiveness of open surgery, it can still be effective for more complex cases or patients with larger lesions, and its long-term survival and recurrence rates in specific cases may be comparable to those of laparoscopic surgery.

(2) Relationship between open surgery and laparoscopic surgery: Despite the many advantages of laparoscopic liver resection, the two are not entirely independent. Both open surgery and laparoscopic surgery are treatment methods for HCC and rely on the removal of liver lesions. This means that factors such as the surgeon's technical skills, the patient's liver function, and the tumor's location and size can all impact the final surgical outcome. For some complex liver cancer cases, open surgery may still be necessary, especially when laparoscopic surgery cannot completely remove the tumor or encounters more complex liver anatomy. Additionally, the choice between open surgery and laparoscopic surgery is often based on the patient's specific condition. For instance, larger and deeper tumors may require open surgery to ensure complete resection, while laparoscopic surgery is often more advantageous for small liver cancers with a diameter $\leq$5 cm.

Laparoscopic surgery and open surgery show significant differences in the treatment of HCC. Due to its minimal invasiveness, faster recovery, and fewer complications, laparoscopic surgery has become the mainstream choice for modern liver resection surgeries. Although open surgery still has applicability in certain complex situations, laparoscopic liver resection demonstrates good safety and therapeutic efficacy for early-stage HCC patients, particularly male patients.

Chronic hepatitis B infection is a primary risk factor for the development of HCC. A notable feature of chronic hepatitis B related HCC patients is the pronounced gender disparity, with a male-to-female ratio of approximately 5–7:1 [11]. This significant difference is thought to be influenced by variations in testosterone and estrogen levels between sexes. Studies have shown that elevated androgen signaling and androgen receptor-mediated transcriptional activity in men are associated with a higher risk of HBV-related HCC [12]. Conversely, other researchers have suggested that low estrogen levels and reduced estrogen responsiveness may predispose individuals to liver cirrhosis and HCC, potentially explaining why male HBV carriers are more likely to progress to liver cancer than their female counterparts [13]. The interplay of these factors likely contributes to the observed gender disparity in HCC incidence. Given this context, it is essential for male patients to proactively seek early treatment for HCC and stay informed about relevant health measures. In summary, this study compares laparoscopic and open liver resection in male HCC patients, focusing on long-term recurrence, survival, and immune function outcomes.

2. Materials and methods

2.1 General information

Clinical data of 128 male patients with hepatocellular carcinoma (HCC) treated at our hospital between January 2019 and January 2021 were retrospectively collected. After propensity score matching (PSM) at a 1:1 ratio, 100 patients were included in the final analysis. These were divided into two groups: an observation group (50 patients) and a control group (50 patients). The patient inclusion process is outlined in Fig. 1.

PSM Process:

(1) Define study variables: First, identify the potential confounding variables that might affect the patient's treatment outcomes. These variables may include the patient's age, gender, underlying diseases, liver function status, tumor staging, *etc*.

(2) Calculate the propensity score: Use logistic regression or other appropriate statistical models to calculate the probability of each patient receiving treatment in the observation group or control group (*i.e.*, the propensity score). In this step, the treatment group (observation or control) is treated as the dependent variable, and the aforementioned confounding variables are used as independent variables.

(3) Match patients: Select matching method: In this study, a 1:1 matching ratio is used. For each patient in the observation group, find a control group patient with a similar propensity score. Matching process: Methods such as nearest neighbor matching or caliper matching can be used. In nearest neighbor matching, the patient with the closest propensity score is se-

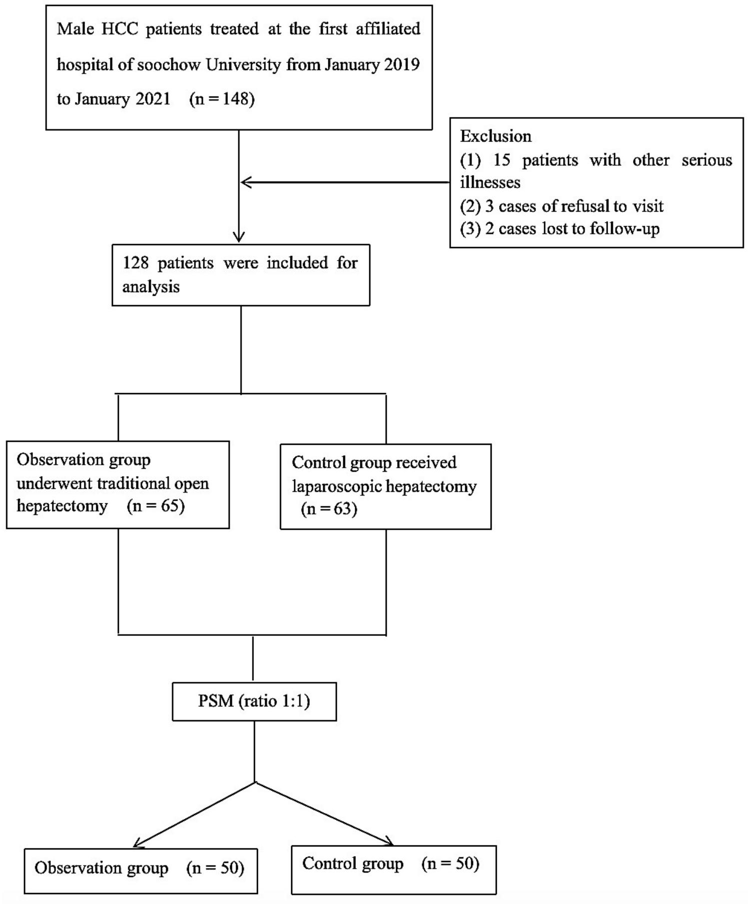

FIGURE 1. Flow chart of the study design and grouping. HCC: Hepatocellular carcinoma; PSM: propensity score matching.

lected for matching. When using caliper matching, the caliper width is set at 0.1 to ensure the quality of the matching results.

(4) Evaluate matching effects: After matching, check the balance of key confounding variables between the two groups before and after matching. Standardized mean difference can be used to assess balance, ensuring no significant differences between the two groups in baseline characteristics.

(5) Final analysis: After confirming the balance of confounding factors between the two groups, conduct subsequent statistical analysis to compare the treatment effects of the observation group and control group.

Inclusion Criteria: (1) Patients pathologically confirmed to have hepatocellular carcinoma; (2) No radiotherapy or adjuvant chemotherapy treatments were used before surgery; (3) Tumor size and location: Tumors that are smaller (generally less than 5 cm) and located at the liver's edge or in positions that are easily accessible are more amenable to laparoscopic resection; (4) Good liver function: Patients with a relatively good liver function score (*e.g.*, Child-Pugh score of Class A); (5) No severe comorbidities: Patients without serious cardiovascular or pulmonary diseases, diabetes, or other comorbidities that may affect the surgery; (6) Good liver anatomical structure: The liver's anatomy is relatively normal, without obvious cirrhosis or other structural abnormalities; (7) Early-stage liver cancer: Patients with early-stage liver cancer (*e.g.*, Barcelona Clinic Liver Cancer (BCLC) Stage A) are generally more suitable for laparoscopic surgery; (8) Patients' age and general health status: Relatively young and healthy patients, aged between 18 and 60 years, with good overall health condition.

Exclusion Criteria: (1) Combined damage to major organs (*e.g.*, heart, lungs, and kidneys) rendering surgery intolerable; (2) Concurrent malignancies in other organs and systems; (3) Presence of coagulation disorders, severe liver cirrhosis, immune system diseases, mental disorders, *etc.*; (4) Patients who voluntarily withdrew from treatment during the study.

2.2 Methods

2.2.1 Observation group

The observation group underwent laparoscopic non-anatomical liver resection. Patients were positioned in the supine position under general anesthesia, followed by routine disinfection and draping. A carbon dioxide (CO_2) pneumoperitoneum was established through a 2 cm puncture above the umbilicus, allowing the insertion of a 10 mm trocar and laparoscope. Based on computed tomography (CT) and magnetic resonance imaging (MRI) scan results, as well as intraoperative ultrasound (IOUS), 4 or 5 puncture sites were selected. IOUS, combined with laparoscopic exploration, was used to identify the location, size, number of cancer lesions, and their relationships with the bile ducts and blood vessels.

An ultrasound knife was employed to separate and cut the round ligament, falciform ligament, and, depending on the location of the cancer lesions, the affected side's coronary and triangular ligaments, ensuring adequate exposure of the surgical field. A hepatic hilum blocking band was placed at the first hepatic hilum to monitor the occlusion time. A proposed resection line was marked at least 2 cm away from the tumor edge using an electrocautery hook, and liver tissue was incised along the resection line with the ultrasound knife. The resected specimen was placed in a specimen bag and extracted through a small upper abdominal incision. If necessary, electrocautery or clamps were used to close the blood vessels and bile ducts on the liver surface. After cauterization with an electrocoagulation rod, the surface was irrigated with saline. A thorough laparoscopic inspection confirmed the absence of active bleeding or bile leakage. Hemostatic glue was then sprayed over the resected area, a drainage tube was placed, and the incision was sutured.

2.2.2 Control group

The control group underwent traditional open non-anatomical liver resection. Patients were positioned supine under general anesthesia, followed by routine disinfection and sterile draping. An upper abdominal reverse "L"-shaped incision was made for exploration. IOUS was performed to confirm the location, size and relationships of the cancer lesions with the bile ducts and blood vessels. If necessary, surrounding liver ligaments were freed, and the first hepatic hilum blood flow was occluded. The remaining procedural steps, including tumor resection, specimen handling, hemostasis, and placement of a drainage tube, were similar to those performed in the observation group.

2.3 Observation indicators

(1) Perioperative indicators: These included intraoperative blood loss, operation time, incision length, and hepatic portal occlusion time. Postoperative recovery indicators: time to get out of bed, time to resume eating, and length of postoperative hospital stay. (2) Liver function indicators: Liver function was assessed using an automatic biochemical analyzer (Hitachi Diagnostics, Model 3100, Tokyo, Japan) to measure alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBIL) levels were measured for both groups 1 day before surgery, and 3 and 7 days after surgery. (3) Immune functions indicators: Three and seven days post-surgery, 5 mL of venous blood was collected from each patient, and serum was separated. Flow cytometry was used to detect T lymphocyte subsets ($CD3^+$, $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ ratio). (3) Postoperative recovery comparison: Key metrics such as postoperative bed rest time, time to resume feeding, and postoperative hospitalization duration were compared between the two groups. (4) Postoperative complications: Complications were monitored and documented, including incision infection, thrombosis formation, pleural and abdominal effusion, postoperative bleeding, bile leakage, abdominal infection, liver failure, and liver dysfunction. (5) Follow-up and survival rates: both groups were followed to assess the recurrence rates, and survival rates at 1, 2 and 3 years after surgery. Postoperative recurrence: follow-up evaluations included enhanced abdominal CT scan, serum alpha-fetoprotein (AFP) levels, and liver function tests every 3 months after the first month post-surgery. Recurrence was defined as either a serum AFP level >400 ng/mL or a clear liver cancer lesion on CT imaging, excluding other potential causes such as pregnancy, chronic or active diseases, gonadal embryonic tumors, and gastrointestinal tumors. Overall survival (OS): OS was defined as the time from the start of treatment until death from any cause.

2.4 Variables and clinical definitions

Diabetes: Defined based on a history of diabetes in the electronic medical records or the use of anti-diabetic drugs. Hypertension: Defined based on a documented history of hypertension in the electronic medical records or the use of antihypertensive medications. The cutoff points for other analytical factors are based on previous reports: HBV DNA >20,000 IU/mL, and Child-Turcotte-Pugh (CTP) score >6. Other cutoff points for analytical factors are based on reference ranges from laboratory tests: elevated AFP: AFP >20 ng/mL; elevated glutathione reductase (GR): GR >73 U/L; low high-density lipoprotein (HDL): HDL ≤1.04 mmol/L; and elevated low-density lipoprotein (LDL): LDL >3.12 mmol/L.

2.5 Statistical methods

The data collected were analyzed using SPSS 21.0 statistical software (IBM, Armonk, NY, USA) and GraphPad Prism 8.0.2 software (GraphPad Software, Inc. San Diego, CA, USA). Normality tests were performed on the variables using the Shapiro-Wilk test. Normally distributed continuous variables are expressed as mean ± standard deviation (SD), and intergroup comparisons were performed using independent sample *t*-tests, and paired sample *t*-test were used for intra group comparisons. For skewed distribution or heteroscedastic data, the Mann-Whitney U test was used, and the median (M) and interquartile range (IQR) were reported (M (P25, P75)). Categorical variables were presented as percentages (%) and compared using chi-square tests. Propensity score matching (PSM) was performed in a 1:1 ratio with a matching tolerance of 0.1 to ensure the quality of the matching results. A multivariable Cox proportional hazards regression model was used to analyze the influencing factors. A *p*-value of $p < 0.05$ was considered statistically significant.

3. Results

3.1 General information

To minimize confounding bias and more accurately evaluate the effects of the intervention or treatment, this study utilized propensity score matching (PSM) to balance covariates that could potentially influence the outcomes between the two groups. Propensity scores were calculated for each individual, and treated individuals were matched with untreated individuals in a 1:1 ratio to create comparable control groups. The baseline characteristics of the two groups after matching are shown in Table 1. The results indicate that the groups were well-balanced, with no statistically significant differences observed ($p > 0.05$).

TABLE 1. Patients' baseline characteristics (continuous variables compared via *t*-test; categorical variables via chi-square test).

Variable	Pre-PSM				Post-PSM			
	Observation group (n = 65)	Control group (n = 63)	χ^2/t	*p*	Observation group (n = 50)	Control group (n = 50)	χ^2/t	*p*
Age (yr)	58.07 ± 8.54	58.66 ± 9.43	0.375	0.708	57.20 ± 6.25	57.45 ± 6.38	0.192	0.848
Disease course (mon)	5.28 ± 2.01	5.35 ± 1.96	0.199	0.842	4.10 ± 1.52	3.94 ± 1.63	0.507	0.613
Mean tumor diameter (cm)	3.50 ± 1.75	3.98 ± 1.23	1.801	0.074	3.28 ± 1.15	3.15 ± 0.98	0.610	0.543
Number of tumors	3.85 ± 0.73	3.68 ± 0.85	1.173	0.243	3.20 ± 0.78	3.12 ± 0.82	0.498	0.620
Child Pugh rating (A/B-C)	45/20	38/25	1.115	0.291	42/8	38/12	1.000	0.317
BCLC staging (A/B-C) (n (%))	42/23	35/28	1.096	0.295	32/18	33/17	0.044	0.834
Smoking history (%)	26 (40.00)	22 (34.92)	0.352	0.553	15 (30.00)	13 (26.00)	0.198	0.656
Family history of liver cancer (%)	5 (7.69)	8 (12.70)	1.000	0.317	3 (6.00)	5 (10.00)	0.543	0.461
Type 2 diabetes (%)	28 (43.08)	17 (26.98)	3.634	0.057	16 (45.71)	13 (43.33)	0.437	0.509
Essential hypertension (%)	30 (46.15)	19 (30.16)	3.464	0.063	12 (34.29)	11 (36.67)	0.056	0.812
Overweight (%)	22 (33.85)	17 (26.98)	0.711	0.399	15 (30.00)	13 (26.00)	0.198	0.656
Liver cirrhosis (%)	35 (53.85)	30 (47.62)	0.695	0.404	25 (50.00)	23 (46.00)	0.160	0.689
HBeAg (+)	18 (27.69)	15 (23.81)	0.252	0.616	14 (28.00)	12 (24.00)	0.208	0.648
HBV-DNA (IU/mL)	2860.75 ± 158.30	1791.37 ± 102.76	45.471	<0.001	2350.45 ± 102.54	2366.90 ± 98.37	0.818	0.415
AFP (ng/mL)	7.29 ± 1.15	5.57 ± 1.64	6.873	<0.001	8.56 ± 1.37	9.05 ± 1.25	1.838	0.069
GR (U/L)	82.00 ± 12.70	82.20 ± 11.90	0.096	0.923	75.60 ± 8.57	78.60 ± 9.06	1.700	0.092
CTP score	7.35 ± 1.25	7.50 ± 1.45	0.580	0.563	6.50 ± 1.75	7.05 ± 1.56	1.631	0.106
HDL (mmol/L)	1.09 ± 0.47	1.12 ± 0.43	0.415	0.679	1.10 ± 0.86	1.35 ± 0.67	1.630	0.107
LDL (mmol/L)	2.13 ± 0.89	2.03 ± 0.63	0.808	0.420	2.50 ± 0.53	2.41 ± 0.65	0.848	0.398

PSM: Propensity Score Matching; Pre-PSM: Pre-Propensity Score Matching; Post-PSM: Post-Propensity Score Matching; BCLC: Barcelona Clinic Liver Cancer; HBeAg: Hepatitis B e Antigen; HBV: hepatitis B virus; DNA: Deoxyribonucleic Acid; AFP: Alpha-fetoprotein; GR: Glutathione reductase; CTP: Child-Turcotte-Pugh; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

3.2 Cox regression analysis

3.2.1 Univariate Cox analysis of HCC-related factors

The hazard function of the Cox model can be expressed as: $h(t \mid X) = h_0(t) \times \exp(\beta^T X)$.

(t | X): the hazard function at time (t) given covariates (X) (*i.e.*, the instantaneous rate of the event occurring). $h_0(t)$: the baseline hazard function, representing the basic risk in the absence of any covariate effects. β: the vector of regression coefficients, representing the effect of each covariate on the hazard. X: the vector of covariates, including one or more explanatory variables (such as age, gender, treatment group, *etc.*). $\beta^T X$: the inner product of the covariate vector and the regression coefficient vector.

The univariate Cox regression analysis identified several significant risk factors for HCC. Male gender (p = 0.016), a family history of liver cancer (p = 0.006), hypertension (p = 0.028), a CTP score > 6 ($p < 0.001$), elevated AFP levels ($p < 0.001$), elevated GR levels ($p < 0.001$), decreased HDL levels (p = 0.008), and increased LDL levels (p = 0.027) were all found to be significant risk factors for HCC (Table 2).

3.2.2 Multivariate Cox analysis of HCC-related factors

The multivariate Cox regression analysis identified several independent risk factors for the occurrence of HCC. These included male gender (p = 0.005), family history of liver cancer ($p < 0.001$), essential hypertension (p = 0.002), elevated AFP (p = 0.001), elevated GR levels (p = 0.046), decreased HDL (p = 0.027), and increased LDL (p = 0.003) (Table 3).

3.3 Comparison of perioperative indicators

The observation group demonstrated significantly better perioperative outcomes compared to the control group. Specifically, intraoperative blood loss, the requirement for blood transfusion, operation time, incision length, and hepatic portal occlusion time were all significantly lower in the observation group ($p < 0.05$). Additionally, postoperative recovery metrics, including the time to get out of bed, time to resume feeding, and duration of postoperative hospital stay, were significantly shorter in the observation group than in the control group ($p < 0.05$), Figs. 2,3,4).

3.4 Liver function indicators

On postoperative day 1, 3, and 7, liver function indicators, including ALT, AST and TBIL levels, were significantly lower in the observation group compared to the control group ($p < 0.05$) (Figs. 5,6). These results indicate better preservation of liver function in patients undergoing laparoscopic hepatectomy.

3.5 Immune function

At day 3 and 7 after surgery, the observation group had higher levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ than the control group, while $CD8^+$ was lower than the control group ($p < 0.05$, Figs. 7,8).

3.6 Complications

The incidence of complications in the observation group was lower than in the control group ($p < 0.05$) (Table 4).

TABLE 2. Single factor Cox proportional hazards analysis of factors related to the occurrence of hepatocellular carcinoma.

Variable	HR	95% CI	*p*
Male	1.57	1.09–2.26	0.016
Smoking history	1.05	0.77–1.44	0.761
Family history of liver cancer	1.85	1.20–2.85	0.006
Type 2 diabetes	0.93	0.69–1.29	0.654
Essential hypertension	1.42	1.04–1.94	0.028
Overweight	1.09	0.79–1.51	0.612
HBeAg (+)	0.72	0.50–1.05	0.088
HBV-DNA >20,000 IU/mL	0.91	0.66–1.26	0.568
AFP	3.19	2.34–4.36	<0.001
GR	2.01	1.43–2.84	<0.001
CTP score >6	2.00	1.43–2.80	<0.001
HDL	1.52	1.12–2.07	0.008
LDL	1.54	1.05–2.26	0.027

HR: Hazard Ratio; CI: Confidence Interval; HBeAg: Hepatitis B e Antigen; HBV-DNA: Hepatitis B Virus- Deoxyribonucleic Acid; AFP: Alpha-fetoprotein; GR: Glutathione reductase; CTP: Child-Turcotte-Pugh; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

TABLE 3. Multivariate Cox proportional hazards analysis of factors related to the occurrence of hepatocellular carcinoma.

Variable	HR	95% CI	*p*
Male	1.73	1.18–2.54	0.005
Family history of liver cancer	2.23	1.40–3.55	<0.001
Type 2 diabetes	0.74	0.52–1.05	0.093
Essential hypertension	1.69	1.22–2.34	0.002
Overweight	1.13	0.80–1.61	0.470
AFP	2.83	2.04–3.94	0.001
GR	1.53	1.01–2.31	0.046
CTP score >6	1.38	0.97–1.98	0.077
HDL (mmol/L)	1.46	1.04–2.04	0.027
LDL (mmol/L)	2.29	1.33–3.93	0.003

HR: Hazard Ratio; CI: Confidence Interval; AFP: Alpha-fetoprotein; GR: Glutathione reductase; CTP: Child-Turcotte-Pugh; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

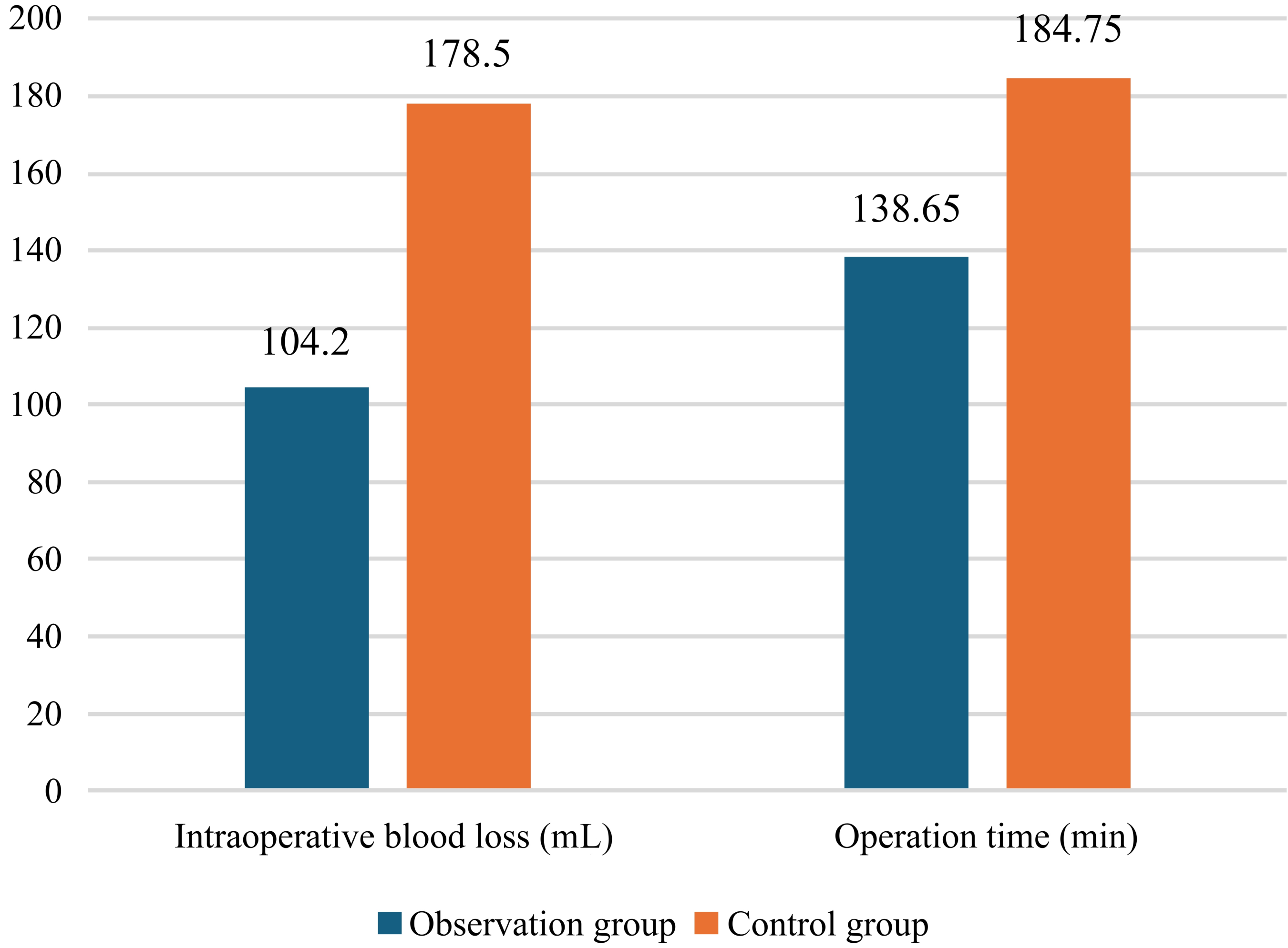

FIGURE 2. Comparison of intraoperative blood loss and operation time between the observation and control group.

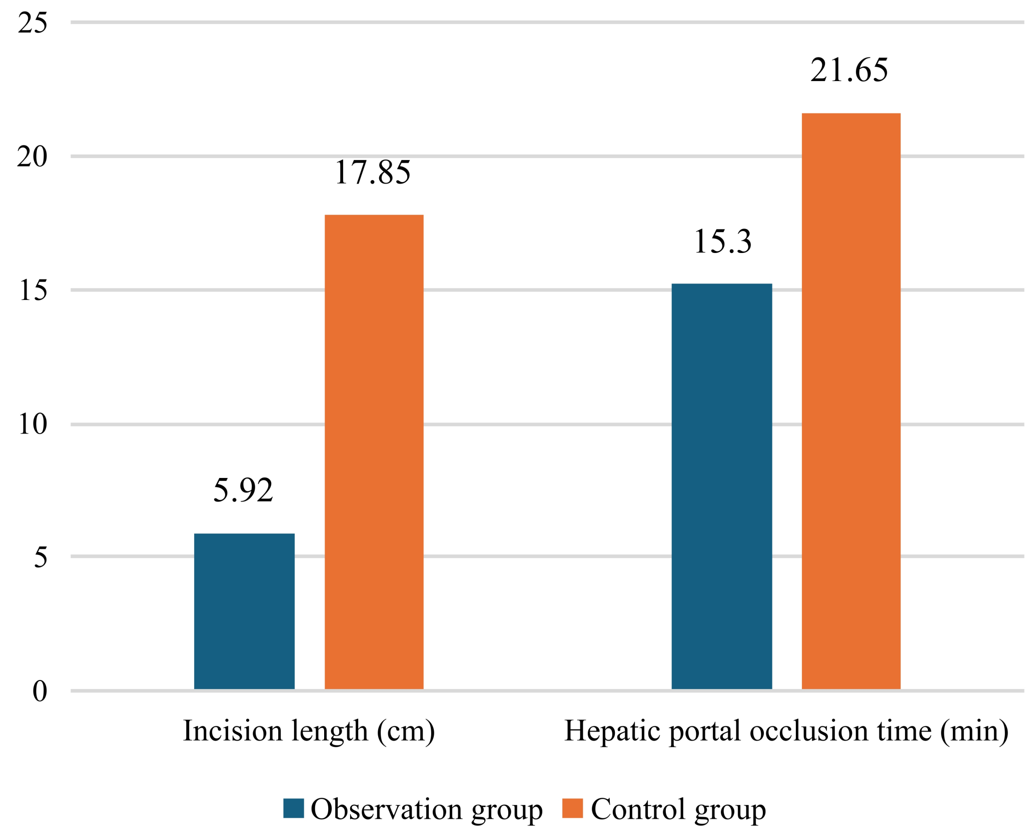

FIGURE 3. Comparison of incision length and hepatic portal occlusion time between the observation and control group.

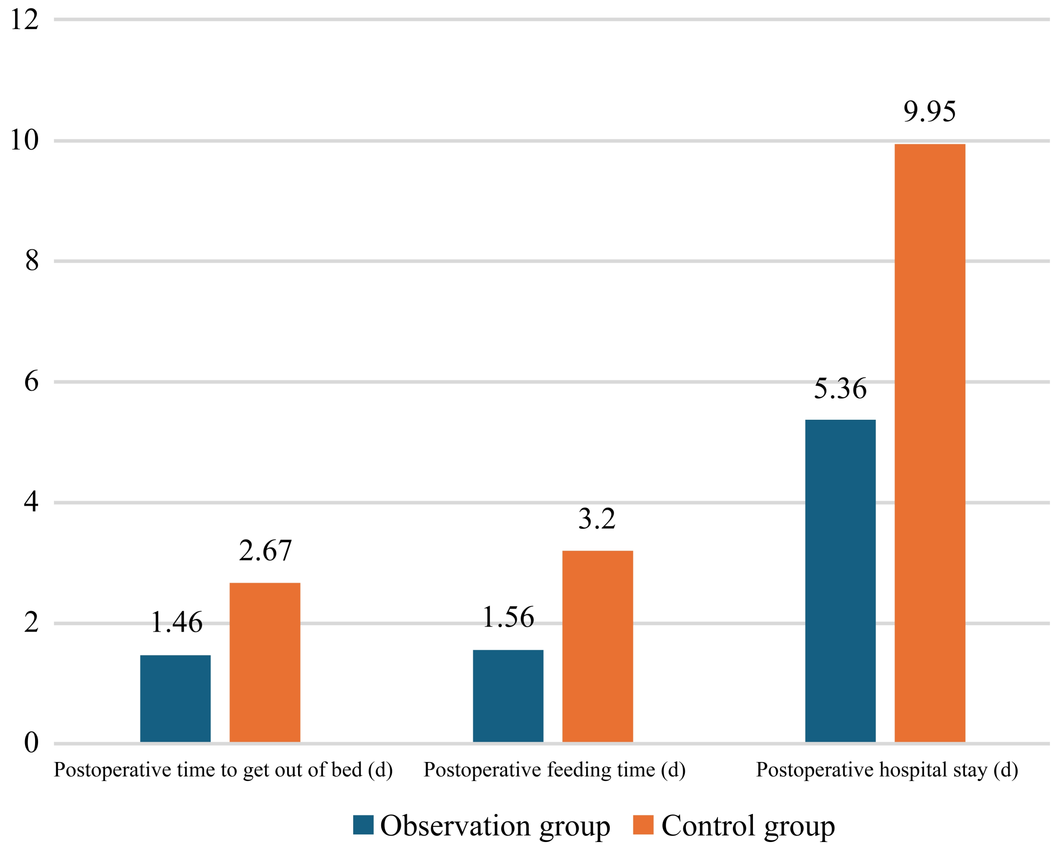

FIGURE 4. Comparison of postoperative time to get out of bed, feeding time and hospital stay between the observation and control group.

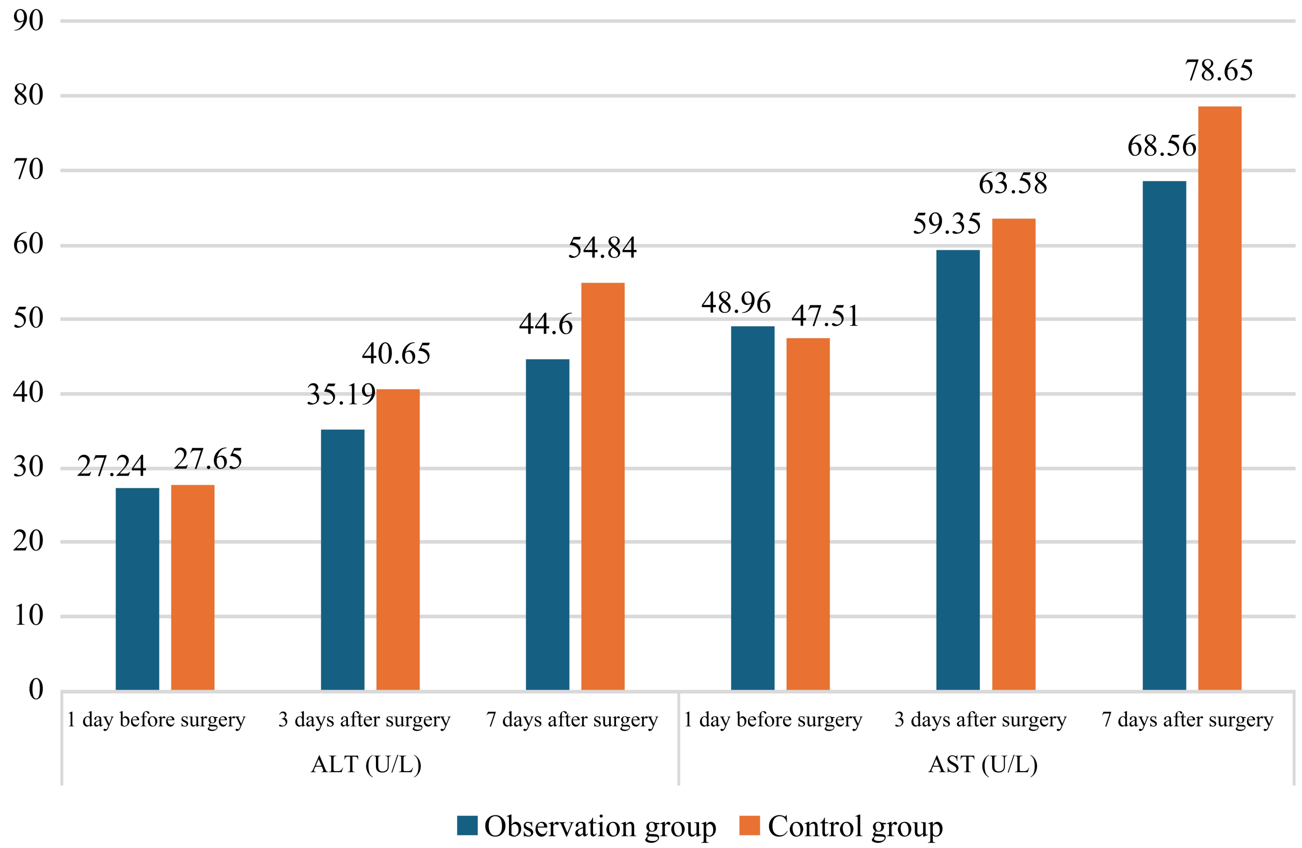

FIGURE 5. Comparison of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) before surgery and after surgery between the observation and control group.

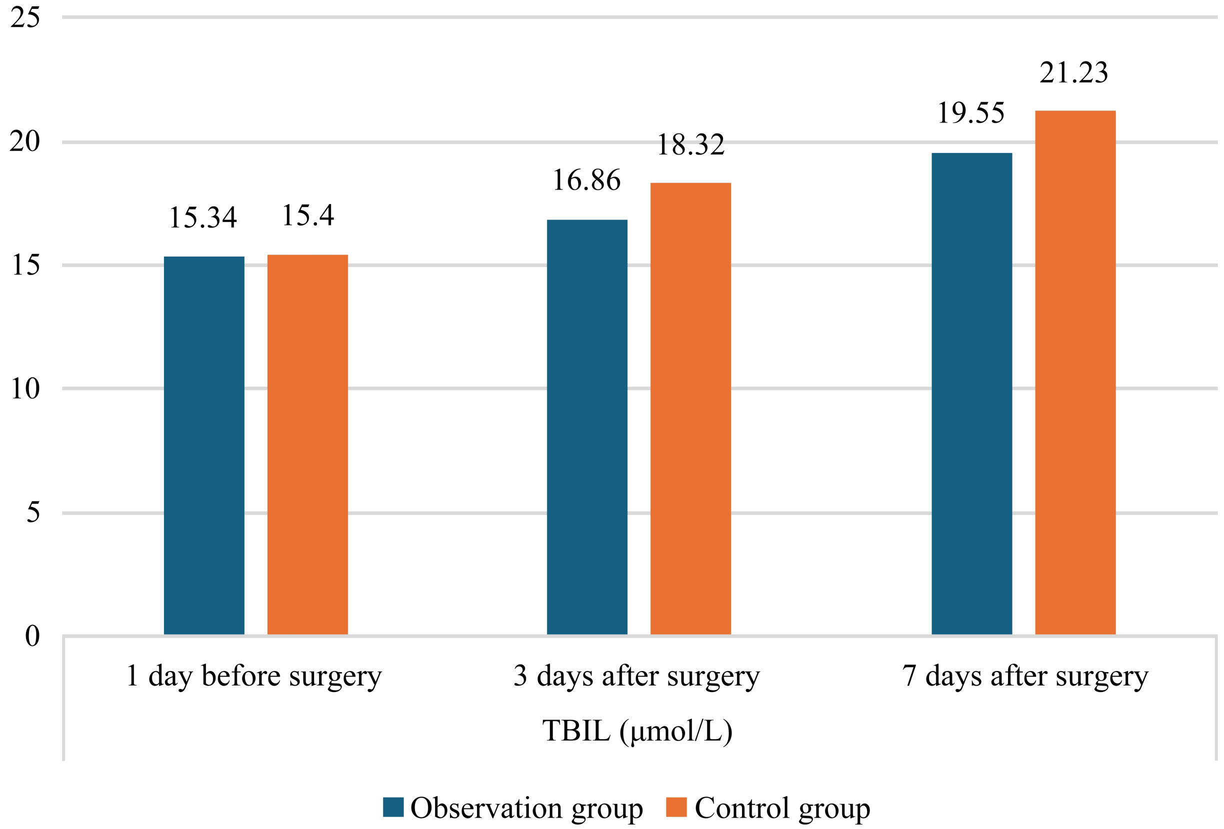

FIGURE 6. Comparison of total bilirubin (TBIL) before surgery and after surgery between the observation and control group.

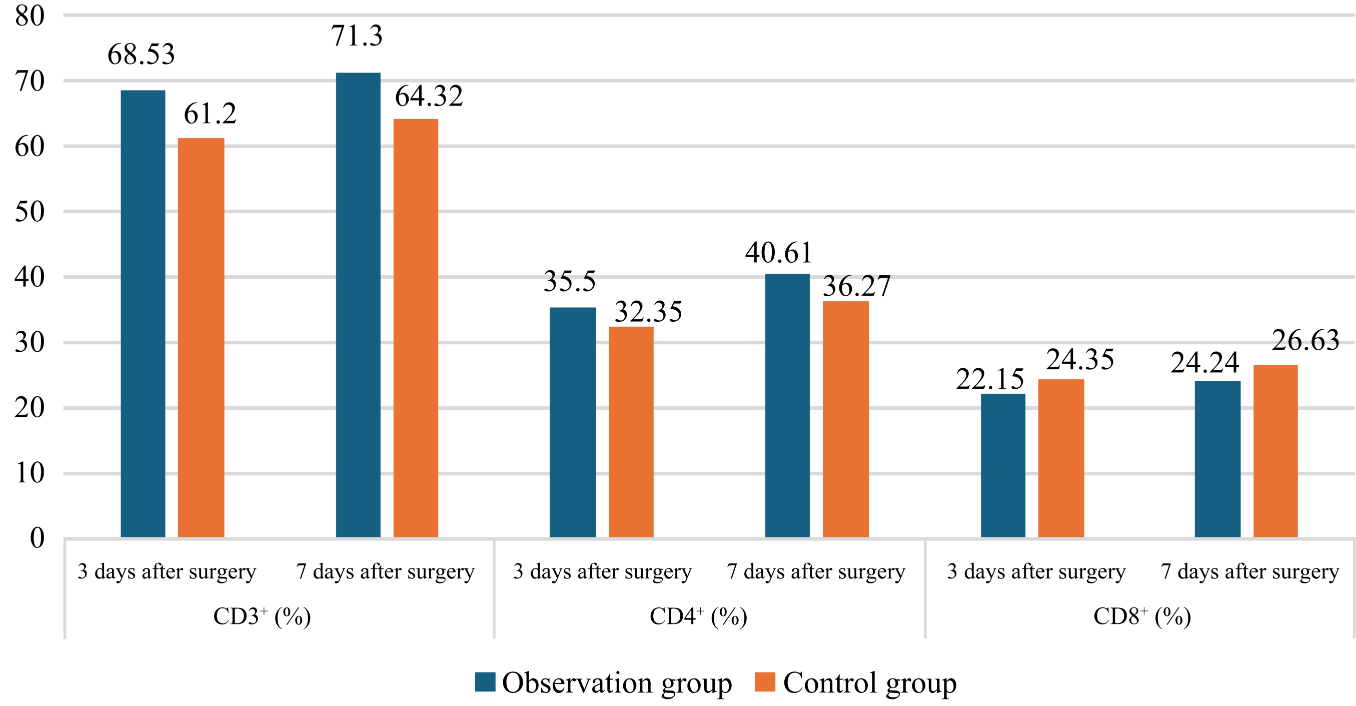

FIGURE 7. Comparison of Cluster of Differentiation (CD) 3^{+}, $CD4^{+}$ and $CD8^{+}$ at day 3 and 7 after surgery between the observation and control group.

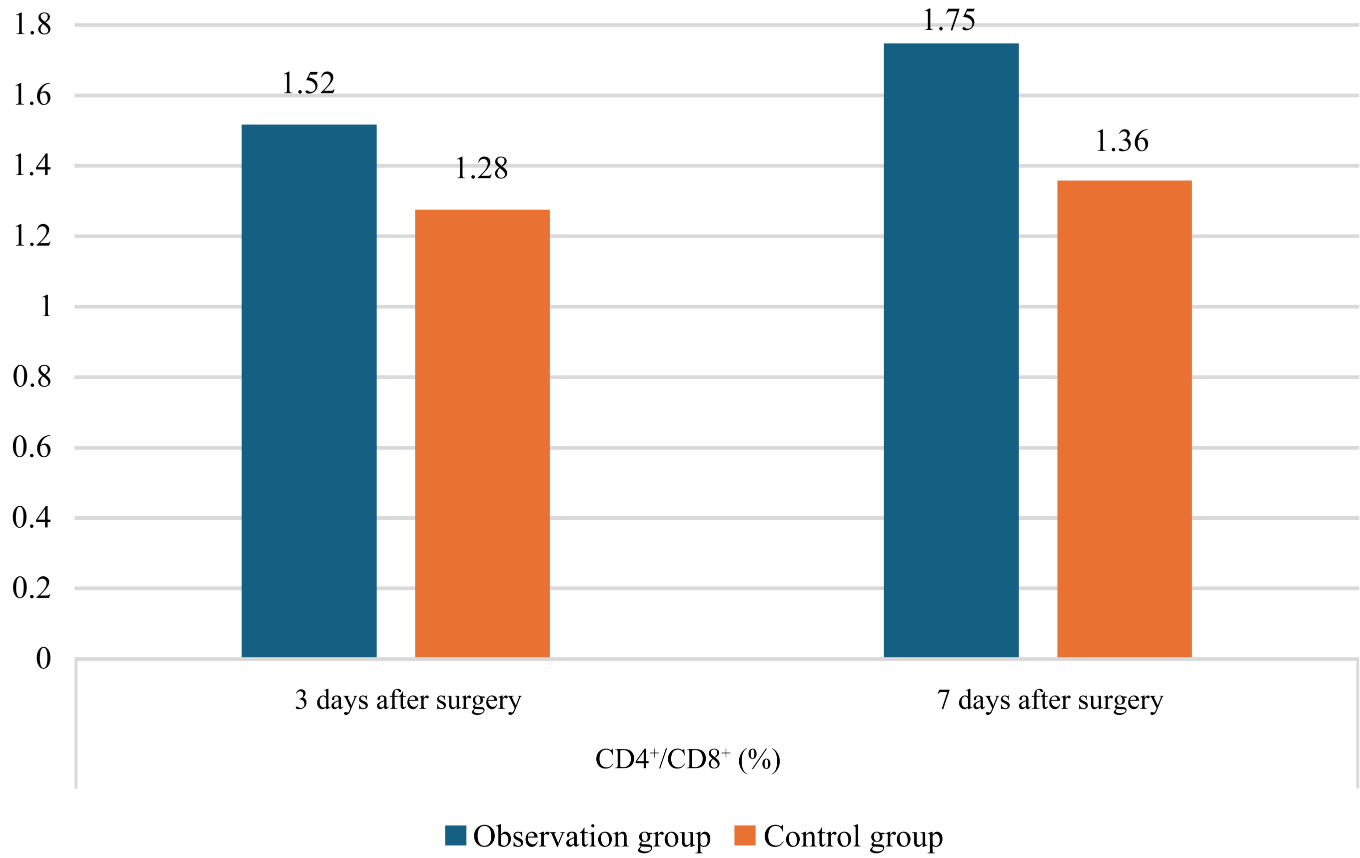

FIGURE 8. Comparison of postoperative Cluster of Differentiation (CD) 4^{+} to $CD8^{+}$ ratio between the observation and control group.

TABLE 4. Comparison of complication rates between the observation and control group.

Complications	Observation group, n (%)	Control group, n (%)
Infection of incisional wound	0	4 (8.00)
Thrombosis formation	2 (4.00)	5 (10.00)
Postoperative bleeding	1 (2.00)	2 (4.00)
Bile leakage	0	2 (4.00)
Liver failure	2 (4.00)	3 (6.00)
Liver dysfunction	0	3 (6.00)
Total	5 (10.00)	19 (38.00)
Chi-square test, χ^2	χ^2 = 10.746	p-value = 0.001

3.7 Postoperative recurrence situation

Six months after surgery, no significant difference was observed in the recurrence rate between the two groups (χ^2 = 2.041, p = 0.150 > 0.05). However, at 1 and 3 years post-surgery, the recurrence rate in the observation group was significantly lower than in the control group (χ^2 = 6.618, p = 0.010; χ^2 = 9.091, p = 0.003, both $p < 0.05$, Table 5).

3.8 Prognostic analysis

Kaplan-Meier survival curve: For a given survival time (t) and the number of events that occur, the Kaplan-Meier survival function (S(t)) can be expressed as:

$$S(t) = \prod_{i:t_i \leq t} (1 - \frac{d_i}{n_i})$$

S(t): the survival probability at time (t).

t_i: the time point at which the event (*e.g.*, death) occurs.

d_i: the number of individuals experiencing the event at time point (t_i).

n_i: the number of individuals at risk at time point (t_i) (*i.e.*, those still alive before this time point, including those who have not experienced the event).

In terms of overall survival (OS), the observation group had 1, 2 and 3-year OS rates of 75.9%, 41.4% and 12.9%, respectively, while the control group had OS rates of 55.5%, 14.4% and 0% (χ^2 = 4.4564, p = 0.035; χ^2 = 25.4804, p < 0.001; χ^2 = 6.3829, p = 0.011). The median survival times were 18.5 months (95% CI = 12.9–24.1) for the observation group and 12.5 months (95% CI = 10.4–14.6) for the control group. The difference between the two groups was statistically significant (χ^2 = 4.843, p = 0.028, $p < 0.05$, Fig. 9). See Fig. 10 for the nomogram.

4. Discussion

With the rapid advancement of minimally invasive techniques, laparoscopic surgery has gradually replaced traditional open surgery. Laparoscopic hepatectomy is now widely recognized and adopted [14, 15], offering notable advantages such as reduced incision length, minimized blood loss, and faster postoperative recovery. Continuous improvements in medical equipment and technology in recent years have further enhanced the advantages of laparoscopic techniques [16].

The observation group had significantly less intraoperative blood loss, shorter operation times, smaller incision lengths and reduced hepatic portal occlusion time compared to the control group. Additionally, postoperative time to get out of bed, resume eating, and the length of postoperative hospital stay were all significantly shorter in the observation group. These findings suggest that laparoscopic resection can improve clinical perioperative indicators. The reasons for these improvements lie in the magnification capability of laparoscopic surgery, which provides a clear, magnified image of the surgical field - up to six times greater than the naked eye, thus ensuring a clear surgical field for the surgeon. This enhanced visualization enables detailed observation of the liver's internal ductal structures, helping to avoid damage to major blood vessels and bile ducts during lesion resection. Furthermore, this clarity aids in preserving the normal function of the remaining liver tissue, potentially improving patient outcomes and extending survival time [17, 18].

The observation group also experienced significantly less intraoperative blood loss compared to the control

TABLE 5. Comparison of postoperative recurrence situation (n (%)) (categorical variables via chi-square test).

Group	n	Six months after surgery	One year after surgery	Three years after surgery
Observation group	50	0.000	10 (20.00)	20 (40.00)
Control group	50	2 (4.00)	22 (44.00)	35 (70.00)
Chi-square, χ^2	-	2.041	6.618	9.091
p-value	-	0.150	0.010	0.003

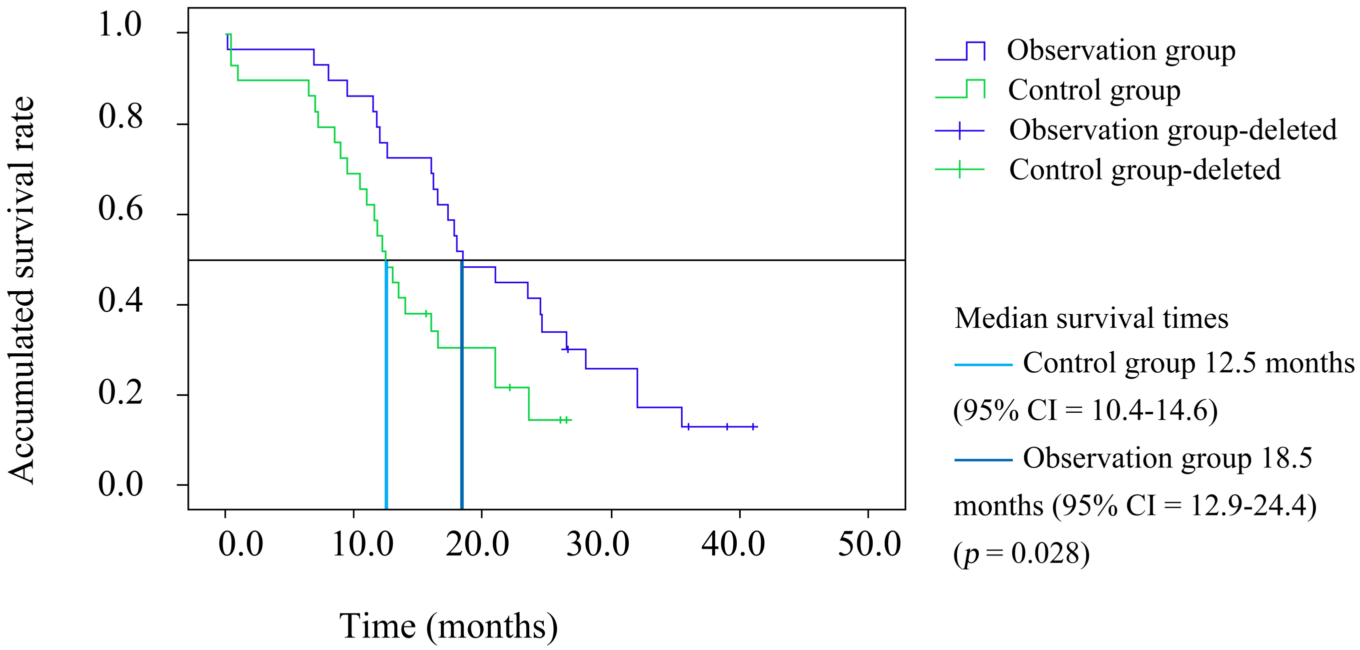

FIGURE 9. Overall survival curves for the observation and control groups post surgery. CI: Confidence interval.

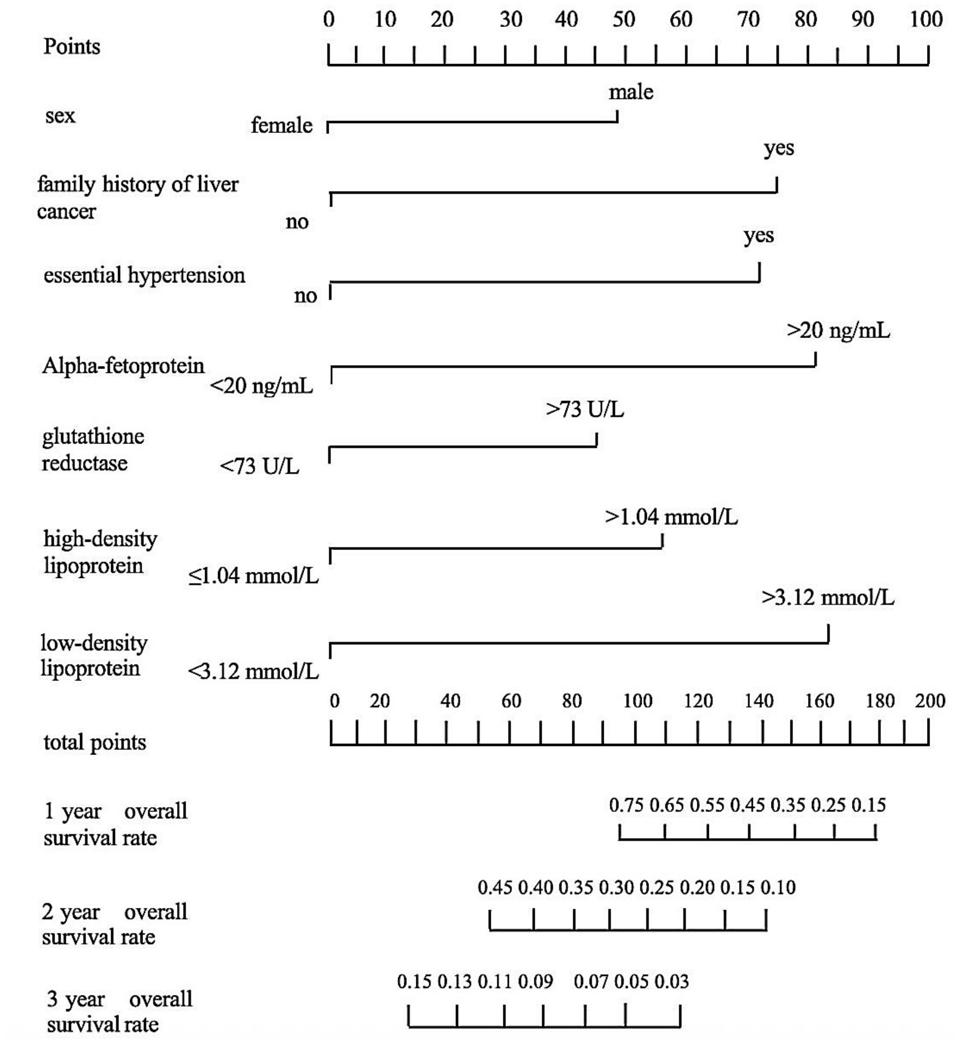

FIGURE 10. Nomogram.

group, which can be attributed to effective management of hepatic blood flow and central venous pressure by the anesthesiologist. Maintaining appropriate pneumoperitoneum pressure and the judicious use of laparoscopic instruments are crucial in minimizing blood loss. Moreover, choosing suitable methods to control hepatic blood flow, accurately identifying the bleeding site, and promptly implementing effective hemostatic measures are critical to the success of laparoscopic hepatectomy. The clearer visual field provided by laparoscopy allows for precise identification of arterial and venous pathways, thereby reducing intraoperative bleeding [19]. Laparoscopy, being a minimally invasive technique, typically involves smaller incisions compared to open surgery. The use of a five-port approach in the upper abdomen results in much smaller incisions than those in open surgery [20]. Operation time and hepatic portal occlusion time are also significantly reduced. These benefits are due to the use of pneumoperitoneum, which expands the surgical space and the magnification effect of the laparoscope, which aids in the precise removal of cancerous lesions and small metastases within the liver. As a minimally invasive procedure, laparoscopic surgery results in smaller incisions, less postoperative pain, shorter operation times, and minimal interference with the intra-abdominal environment and major blood vessels, thereby significantly optimizing perioperative indicators. Laparoscopic partial hepatectomy shortens ischemic time in liver tissues and reduces hepatic portal occlusion time, effectively preventing damage to surrounding tissues [21]. Consequently, postoperative recovery rate is faster, and liver function restores quickly, allowing patients to regain their health sooner. Additionally, because laparoscopic surgery is performed within a closed abdominal space, it avoids visceral exposure and moisture evaporation. Sterilized instruments make minimal contact with the viscera, reducing local inflammatory responses and stress reactions contributing to faster postoperative recovery, including shortening postoperative feeding time and a lower risk of postoperative infections. Although laparoscopic surgery involves multiple small abdominal incisions, these incisions are widely spaced and do not require cutting abdominal wall muscles or nerves. This results in less pain and facilitates earlier ambulation, which in turn promotes recovery of digestive function and nutritional intake [22]. Overall, laparoscopic surgery significantly reduces the size of the incision, minimizes damage to major arteries and bile ducts, decreases blood loss and infection rates, and enhances patient prognosis and recovery speed. Therefore, laparoscopic hepatectomy is associated with faster postoperative recovery [23].

In a study by Lee YH *et al*. [24], a retrospective analysis of primary HCC patients who underwent liver resection at Hualien Tzu Chi Hospital from January 2013 to December 2019, in which patients with HCC located in favorable positions (anterolateral segments) were divided into laparoscopic liver resection (LH) and open liver resection (OH) groups, reported similar findings. The results showed that the laparoscopic group had a lower transfusion rate, shorter postoperative hospital stay, and lower 90-day readmission rate. Compared to open hepatectomy (OH), laparoscopic liver resection (LH) was favored as the preferred surgical approach for HCC in favorable positions, owing to its reduced transfusion requirements, shorter recovery times, and lower readmission rates. Moreover, even in advanced stages, LH has proven to be a safe and effective surgical option. These results are in agreement with our study, further supporting the conclusion that laparoscopic partial liver resection minimizes physical trauma, reduces the impact on the body, and promotes faster recovery compared to traditional open surgery.

Hisamune Sakai [25] compared laparoscopic anatomical liver resection (LAR) with open anatomical resection (OAR) for HCC, focusing on perioperative and long-term oncological outcomes. Patients undergoing anatomical liver resection as initial treatment for primary HCC were divided into LAR and OAR groups, and surgical outcomes between the two groups were compared. The results demonstrated that, compared with the OAR group, patients in the LAR group experienced significantly reduced blood loss, shorter operative time, lower postoperative complication rates, and shorter hospital stays. These findings further support the notion that LAR improves perioperative outcomes and clinical indicators. Therefore, LAR is considered a safe, feasible, and oncologically acceptable approach for selected patients with HCC.

Assessing liver function damage is crucial for evaluating the efficacy of hepatectomy. Serum ALT, AST and TBIL levels are primary indicators for assessing liver function damage. ALT and AST are primarily located within hepatocytes. When the liver is damaged, these enzymes are released into the bloodstream, resulting in elevated levels of ALT and AST [26]. At day 3 and 7 after surgery, the observation group exhibited lower levels of ALT, AST and TBIL compared to the control group, suggesting that laparoscopic hepatectomy promotes better postoperative liver function recovery. This could be attributed to the fact that laparoscopy reduces compression on the liver during the procedure, thereby minimizing liver damage. Laparoscopic hepatectomy involves less trauma and has a smaller impact on postoperative liver function. The liver resection process during laparoscopic surgery is more precise than that in open hepatectomy, with greater attention to liver separation, hemostasis, and suturing. During laparoscopic liver resection, large blood vessels and bile ducts are avoided, preserving the blood supply to the remaining liver tissues, which helps prevent unnecessary liver damage and supports liver function recovery [27]. Furthermore, compared to open surgery, laparoscopic partial hepatectomy for treating HCC can inhibit inflammatory responses and slow the progression of liver fibrosis, further promoting liver function recovery. Laparoscopic partial hepatectomy avoids traction, cutting, and other stress responses on the tissues and blood vessels surrounding the lesion, thereby suppressing the secretion of inflammatory mediators by monocytes and the release of liver fibrosis markers such as Procollagen Type III N-terminal Peptide (PIIIP), Hyaluronic Acid (HA) and Procollagen Type I C-terminal Peptide (PICP) [28]. As a result, this technique facilitates postoperative liver function recovery. Studies have reported that on the seventh day following laparoscopic hepatectomy, levels of ALT, AST, TBIL, C-reactive protein, tumor necrosis factor-alpha, and interleukins are significantly lower compared to open hepatectomy. These findings suggest that laparoscopic hepatectomy reduces hepatocyte damage and inflammatory responses, with minimal impact on the immune system [29].

In the observation group, which underwent laparoscopic liver resection, the levels of $CD3^+$, $CD4^+$ and the $CD4^+/CD8^+$ ratio were higher, while $CD8^+$ levels were lower compared to the control group. The differences in immune cell subsets ($CD3^+$, $CD4^+$, $CD8^+$) and the $CD4^+/CD8^+$ ratio between the two groups could be attributed to several factors: (1) Postoperative Recovery and Complications: Laparoscopic surgery is associated with less postoperative pain, shorter recovery times, and quicker return to normal physiological functions. This faster recovery could allow the immune system to recover more rapidly, resulting in higher counts of $CD4^+$ (helper T cells) and $CD3^+$ (total T cells). (2) Immune Response: $CD4^+$ cells play a critical role in the immune response by promoting B cell antibody production and activating $CD8^+$ cells (cytotoxic T cells). The higher $CD4^+/CD8^+$ ratio in the observation group may reflect a more robust immune response due to laparoscopic surgery [30]. (3) Changes in $CD8^+$ Cells: $CD8^+$ cells are crucial in anti-tumor immunity. The lower $CD8^+$ count in the observation group could be a result of immune modulation associated with laparoscopic surgery. This reduction may indicate a lower postoperative inflammatory response, suggesting that laparoscopic surgery could potentially reduce immune suppression and inflammation. These results suggest that laparoscopic surgery has advantages in immune modulation.

This aligns with a study by Tao Z *et al.* [31], in which 80 elderly cancer patients were randomly assigned to either a laparoscopic treatment group or a conventional open surgery group. The experimental group received laparoscopic complete mesocolic excision combined with oral Ubenimex, while the control group received conventional open surgery. The results showed that after treatment, immune molecular levels in the experimental group were significantly higher than those in the control group. This supports the findings of our study, demonstrating that laparoscopic resection offers better treatment outcomes for elderly cancer patients compared to conventional open surgery and is worthy of clinical promotion.

The complication rate in the observation group was lower, indicating that laparoscopic hepatectomy is safer. This can be attributed to the clear anatomical delineation of the liver's ductal structures during surgery, which reduces unnecessary damage to preserved blood vessels and bile ducts. Additionally, the use of electrocautery hemostasis during surgery allows timely cleaning of bile, blood, and tissue fluid from the wound surface, ensuring a clear surgical field and enhancing operational safety. Laparoscopic precision liver resection ensures that damage to surrounding tissues is avoided, and minor wounds are kept within a controllable range. The use of imaging techniques during surgery further helps to avoid important hepatic structures such as arteries, veins, and bile ducts, thereby reducing the risk of postoperative complications [32, 33].

Six months after surgery, there were no significant differences in the recurrence rates between the two groups ($p >$ 0.05). However, at 1 and 3 years post-surgery, the recurrence rate in the observation group was significantly lower than in the control group ($p < 0.05$). The observed differences in recurrence rates at 1 and 3 years can be attributed to the following factors: (1) Surgical technique differences: Minimally invasive nature: Laparoscopic surgery, being minimally invasive, typically involves smaller incisions, fewer postoperative complications, and less pain. These advantages may lead to a faster recovery of normal physiological functions, improve overall health and reduce the risk of recurrence. Liver Preservation: Laparoscopic techniques allow for more precise control over resection margins, reducing damage to surrounding healthy tissue and preserving liver function, which may lower the risk of recurrence. (2) Postoperative recovery and management: Faster recovery: Laparoscopic surgery generally allows for quicker recovery, earlier resumption of eating, and quicker ambulation, reducing the risk of postoperative complications (*e.g.*, infections, liver failure) and decreasing recurrence rates. Monitoring and follow-up: Faster recovery enables more timely follow-up, including imaging and tumor marker monitoring, which aids in the earlier detection and management of recurrence. (3) Immune regulation: Immune function: As previously mentioned, laparoscopic surgery may exert a more favorable regulatory effect on the immune system, promoting the activation and proliferation of $CD4^+$ T cells, enhancing immune surveillance against tumors, and thereby reducing the risk of recurrence. (4) Postoperative tumor management: Comprehensive treatment: Patients who undergo laparoscopic liver resection may receive more active follow-up treatments (*e.g.*, adjuvant therapy, regular monitoring), which could further reduce the risk of recurrence.

An Zhi Wang [34] conducted a study in which HCC patients were divided into two groups: one received laparoscopic portal area fluorescence-guided anatomical resection (LPTAR), while the other underwent conventional anatomical resection (CAR). Postoperative assessments revealed significant differences in recurrence-free survival (RFS), overall survival (OS), and perioperative outcomes between the two groups. The LPTAR group showed superior perioperative parameters, with wider resection margins, reduced intraoperative blood loss, and fewer postoperative complications. Furthermore, the RFS rate was significantly improved in the LPTAR group. One, three, and five-year RFS rates were significantly higher than those of the CAR group. The authors concluded that precise preoperative planning and standardization of the LPTAR technique prolonged RFS and enhanced surgical safety. These findings are consistent with this study and support the observation that laparoscopic liver resection is associated with fewer postoperative complications and higher recurrence-free survival rates.

The 1, 2 and 3-year OS rates for the observation group were 75.9%, 41.4% and 12.9%, respectively, while the control group had OS rates of 55.5%, 14.4% and 0%. The median survival times were 18.5 months for the observation group and 12.5 months for the control group. The difference between the two groups was statistically significant ($p < 0.05$). The observed significant differences in OS and median survival time between the two groups may stem from multiple factors. Below is a detailed analysis: (1) Impact of surgical approach: Laparoscopic liver resection, a minimally invasive procedure, involves smaller incisions, less postoperative pain, and quicker recovery times. These advantages may contribute to fewer complications and improved overall health, which may enhance survival rates. Postoperative Complications: Open surgery generally carries a higher risk of complications (*e.g.*, infections, liver failure), which can adversely affect recovery and survival outcomes. (2) Postoperative recovery and quality of life: Laparoscopic surgery typically enables quicker recovery and earlier initiation of adjuvant therapies (*e.g.*, chemotherapy, radiation), which may improve survival rates. Patients who undergo minimally invasive surgery generally experience a better quality of life postoperatively, which can enhance treatment adherence and foster a positive outlook, thereby positively influencing survival outcomes. (3) Tumor Characteristics and Biology: Tumor Size and Staging: Different surgical techniques may be more appropriate for tumors of different sizes and stages. Laparoscopic surgery is generally preferred for early-stage liver cancer, while open surgery may be required for advanced cases. Tumor microenvironment: The choice of surgical approach may influence the tumor microenvironment and immune response, which could, in turn, affect both recurrence and overall survival. (4) Postoperative monitoring and management: Patients who undergo laparoscopic surgery generally benefit from more frequent postoperative monitoring, which enables the earlier detection of recurrence or complications, allowing for timely interventions that improve survival. After laparoscopic surgery, patients often receive more proactive follow-up treatments (*e.g.*, local ablation, chemotherapy), which play a critical role in improving long-term survival outcomes.

This study makes several important contributions to the field of HCC treatment:

(1) Gender-specific investigation. This study focuses specifically on male patients with hepatocellular carcinoma, helping to address a gap in the existing literature regarding sex-specific outcomes. Given the known differences in incidence and prognosis between male and female HCC patients, a targeted analysis of therapeutic efficacy and safety in male patients is of considerable clinical relevance.

(2) Evaluation of laparoscopic techniques. This study is the first to systematically evaluate the efficacy and safety of non-anatomical laparoscopic liver resection in male HCC patients and to compare it with traditional open non-anatomical resection. The findings provide empirical evidence supporting the broader application of laparoscopic techniques in HCC surgery, especially in the pursuit of more minimally invasive approaches to improve patients' quality of life.

(3) Comprehensive assessment of clinical parameters. Through the evaluation of multiple clinical indicators—such as intraoperative blood loss, operative time, length of hospital stay, and liver function markers—this study offers a multidimensional comparison between the two surgical approaches. The results substantiate the advantages of laparoscopic surgery in terms of both safety and efficacy, thereby offering valuable data for clinical decision-making.

(4) Survival and recurrence outcomes. The study demonstrates that patients undergoing laparoscopic surgery had significantly better one- and three-year overall survival rates compared to those receiving open surgery. This provides new clinical insight, suggesting that laparoscopic techniques may help improve long-term prognosis in HCC patients.

(5) Immune function analysis. This study also explores postoperative immune responses, showing that $CD3^+$ and $CD4^+$ cell levels were higher in the laparoscopic group, whereas $CD8^+$ cell levels were lower compared to the control group. These findings suggest that laparoscopic surgery may positively influence immune function, offering a novel perspective for future research on the interplay between surgical methods and immune modulation.

(6) Limitations and future directions. The study acknowledges limitations such as sample size and variations in surgical technique. It highlights the need for future multi-center, large-scale prospective studies to validate these findings, thereby guiding the next phase of clinical and translational research in HCC treatment.

In summary, this study provides new clinical evidence supporting the application of laparoscopic liver resection in male HCC patients. It demonstrates improved short-term outcomes, lower complication rates, and better recurrence-free survival, thus contributing meaningfully to the advancement of surgical oncology and minimally invasive hepatobiliary surgery. These findings offer a solid foundation for both clinical practice and future research in the field.

Significance of the Study on open *vs.* laparoscopic surgery for HCC:

(1) Selection of surgical approach and patient safety. This study clearly demonstrates that laparoscopic liver resection (LLR) outperforms traditional open surgery in several clinical indicators, such as intraoperative blood loss, surgical time, incision length and portal blocking time. These findings suggest that laparoscopic surgery offers significant advantages in reducing trauma and minimizing postoperative complications. For HCC patients, selecting a safer surgical approach can significantly improve postoperative recovery and quality of life, providing an important reference for clinical practice.

(2) Postoperative recovery and survival improvement. The study shows that the laparoscopic group had significantly shorter times to ambulation, feeding, and hospital stay compared to the open surgery group. These results indicate that laparoscopic surgery may help accelerate postoperative recovery. Moreover, the laparoscopic group exhibited better survival rates at one and three years. This emphasizes the potential of laparoscopic surgery in improving long-term survival, offering clinicians a more targeted choice when developing treatment plans.

(3) Advantages in postoperative liver function recovery. The study further observed that the laparoscopic group had significantly lower levels of ALT, AST and TBIL postoperatively compared to the open surgery group, indicating that laparoscopic surgery may provide a protective effect on liver function. This result is particularly relevant for HCC patients with pre-existing liver dysfunction, highlighting the importance of considering liver function status in surgical decision-making and its impact on postoperative recovery.

(4) Reduction in complication rates. The laparoscopic group experienced a lower complication rate than the open surgery group. This finding provides essential safety data when choosing a surgical approach. Particularly in liver cancer patients, reducing postoperative complications not only improves pa-

tients' quality of life but may also decrease the need for further treatments, thereby reducing healthcare costs.

(5) Implications for future research. The results of this study lay the groundwork for further comparative research between laparoscopic and open surgical techniques. Future studies could involve large-scale, prospective, randomized controlled trials to further validate the long-term effects and safety of laparoscopic liver resection, as well as to explore the impact of different surgeons' skill levels on surgical outcomes. Such studies will help guide the refinement and personalization of surgical treatment for HCC.

The study has several limitations. The sample size was relatively small, and there was insufficient examination of patients' baseline disease conditions and general data. The relatively small sample size and single-center design may limit the generalizability of the findings. Additionally, potential risk factors influencing postoperative complications were not deeply explored, and further analysis is needed to improve surgical and clinical management.

Future Research Directions: (1) Long-Term follow-up studies: Although the results indicate a lower recurrence rate in the laparoscopic liver resection group at 1-year and 3-year follow-ups, future studies should focus on longer follow-up periods to assess the impact of this surgery on long-term survival rates and recurrence. Long-term data will provide a clearer understanding of the sustained benefits and potential risks of laparoscopic liver resection. (2) Multicenter studies: To enhance the external validity of the results, multicenter studies should be conducted, involving diverse patient population patients from different regions and healthcare institutions. This would allow for a more comprehensive comparison of surgical outcomes and improve the broader applicability of the results. (3) Comparing the efficacy of different techniques: It may be valuable to compare the effectiveness and safety of laparoscopic liver resection with other minimally invasive techniques, such as robot-assisted surgery, to further optimize the surgical treatment of liver cancer. (4) Optimization of postoperative rehabilitation plans: The impact of postoperative rehabilitation protocols on patient recovery should be studied, focusing on the effects of early mobilization, nutritional support, and other rehabilitation measures. Understanding these factors could help shorten hospital stays, enhance recovery, and improve overall quality of life for patients undergoing laparoscopic liver resection.

5. Conclusions

In summary, laparoscopic hepatectomy for treating HCC improves clinical symptoms, facilitates liver function recovery, and enhances postoperative recovery. It is a promising approach that demonstrates good safety and efficacy. This surgical technique warrants further clinical implementation and research, and it is worthy of clinical promotion.

AVAILABILITY OF DATA AND MATERIALS

The author declares that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

SPC—designed the study and carried them out; supervised the data collection; analyzed the data; interpreted the data; prepared the manuscript for publication and reviewed the draft of the manuscript. The author has read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of the First Affiliated Hospital of Soochow University (Approval no. 2024-681). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

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