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Original Article

Efficacy and safety of laparoscopic hepatectomy procedures for treatment of primary hepatic carcinoma

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Abstract: Objective: The aim of the current study was to investigate efficacy and safety levels of laparoscopic hepatectomy (LH) for treatment of primary hepatic carcinoma (PHC). Methods: Sixty-four patients with PHC were selected as observation subjects. They were divided into the control group (n=30) and research group (n=34), according to surgical methods. Patients in the control group were treated with open hepatectomy (OH) procedures, while patients in the research group were treated with LH. The two groups of patients were observed, comparing incision lengths, intraoperative blood loss, operative times, hospitalization times, postoperative pain scores, postoperative extubation times, fasting times, liver function, and postoperative complications, as well as postoperative 1-year survival and recurrence rates. Results: Compared with the control group, patients in the research group showed shorter incision lengths, less intraoperative blood loss, and shorter operative times (all $P<0.05$). Compared with the control group, patients in the research group showed lower pain scores and shorter postoperative extubation times, fasting times, and hospitalization times (all $P<0.05$). On the 1st and 7th days after the operation, ALT, AST, and TIBL levels in the research group were lower than those in the control group (all $P<0.05$). Incidence rates of postoperative complications in the research group were lower than those in the control group ($P<0.05$). There were no significant differences in postoperative 1-year survival, recurrence, and metastasis rates between the two groups (all $P>0.05$). Conclusion: LH is effective for treatment of PHC. Compared with OH, LH has distinct advantages, including shorter operative times, smaller incisions, less blood loss, faster postoperative recoveries, milder pain, fewer complications, and higher safety levels. Thus, this method has high application value.

Keywords: Primary hepatic carcinoma, laparoscopic hepatectomy, survival rate

Introduction

Primary hepatic carcinoma (PHC) is a common malignant tumor. According to 2015 statistics, there were 782,500 new cases, worldwide, with the 6th highest incidence. There were 745,500 deaths, worldwide, with the 2nd highest mortality in 2012 [1]. A high-prevalence area of PHC is China. In China, incidence rates account for more than 50% of the worldwide total. Annual deaths are approximately 300,000 to 400,000, accounting for about 51% of the worldwide total [2]. PHC is commonly treated by surgical resection. This disease is prone to intrahepatic recurrence, even after radical resections, with a postoperative recurrence rate of 64.3% and a 5-year overall survival rate of 47.6% [3]. The liver is supplied with blood from hepatic artery and portal veins. With abundant blood supply, wound surfaces are prone to massive hemorrhaging during hepatectomy procedures [4, 5].

Laparoscopic techniques have been recognized by many doctors and patients. They have been widely used in surgery due to the advantages of minimal invasiveness, less hemorrhaging, and fast recovery times. During laparoscopic hepatectomy (LH) procedures for PHC, hard instruments are necessary because the exposure of tissue and hemostasis cannot be manual. Hepatic portal occlusion is also difficult [6, 7]. Therefore, safety and efficacy levels of LH for treatment of PHC remain controversial. The current study examined these levels, aiming to provide reference for similar studies.

Materials and methods

General information

Sixty-four patients with PHC, admitted to First Affiliated Hospital of Gannan Medical University, from January 2015 to February 2018, were selected as observation subjects.

Inclusion criteria: (1) Patients confirmed by imaging, laboratory, and postoperative pathological examinations, meeting diagnostic criteria for PHC in the *Clinical Diagnosis and Staging Criteria for Primary Liver Cancer* formulated by the Chinese Society of Liver Cancer, Chinese Anti-Cancer Association in 2001 [8]; (2) Patients with single lesions ≤ 6 cm in diameter; (3) Patients with normal cardiopulmonary function able to tolerate surgery; (4) Patients without ascites, intrahepatic metastasis, jaundice, or distant metastasis; and (5) Patients providing informed consent.

Exclusion criteria: (1) Patients with abnormal coagulation function; (2) Patients ≥ 80 years old; (3) Patients complicated with other malignant tumors; (4) Patients that received other major surgeries within six months; (5) Lactating women; (6) Patients with surgical contraindications; and (7) Patients complicated with mental diseases. The patients were divided into the control group (n=30) and research group (n= 34), according to surgical methods. The current study was approved by the Medical Ethics Committee of First Affiliated Hospital of Gannan Medical University.

Methods

Patients in the control group were treated with open hepatectomy (OH) procedures. The patients were generally anesthetized. An incision was made, layer by layer, below the right costal margin, entering the abdominal cavity and dissociating the hepatic lobe. Liver blood flow was blocked or semi-blocked based on tumor location. Afterward, Glisson's capsule was cut 2 cm outside the margin of the lesion, removing the lesion and part of the normal liver tissue, and preventing residue. Hemostasis and washing of the wound surface were routinely performed. Fibrin glue was sprayed. The drainage tube was inserted when there was no active hemorrhaging on the section. Finally, the abdominal cavity was closed, completing the surgery.

Patients in the research group were treated with LH. A Germany STORZ laparoscope 260-03BA and other corollary equipment were used. The patients were generally anesthetized and placed in a horizontal position. A 1 cm incision was made at the upper margin of the umbilicus to insert a Veress needle. Medical CO_2 was used to form pneumoperitoneum at 12-14 mmHg. A 10 mm trocar and a laparoscopic cold light source at 30° were inserted. A 10 mm trocar was inserted into a 1 cm incision below the xiphoid process of the patients with the lesion on the surface of the right liver or into a 1 cm incision below the costal margin of the left midclavicular line of patients with the lesion on the surface of the left liver. Next, 5 mm trocars were, respectively, inserted into incisions made at the midaxillary line below the left and right costal margins at a horizontal level. These trocars were, respectively, inserted into incisions made below the costal margin of the right midclavicular line and at the left midaxillary line at the level of the umbilicus. Ultrasound technology was used to determine the specific location of the lesion, assessing its relationship with the surrounding tissue. The lesion was fixed using graspers and perihepatic ligaments were incised, dissociating the hepatic lobe. Ultrasonic scalpels were used to cut off the lesion 1 cm outside the margin of the lesion. Titanium clips were used to block the bile ducts or large blood vessels on the section, completely excising the tumor and surrounding normal tissue. Bleeding on the section was arrested with electric coagulation or ultrasonic scalpels. Hemostatic dressings were also packed. The drainage tube was placed and the surgical instruments were withdrawn. Lesion specimens excised from both groups were sent for examination. After the operation, fluid infusion, hemostasis, anti-infection, and liver protection methods were routinely performed.

Evaluation criteria

(1) Incision lengths, intraoperative blood loss, and operative times were compared between the two groups; (2) Hospitalization times, postoperative pain scores, postoperative extubation times, and fasting times were compared between the two groups. Patient pain was scored according to the Visual Analogue Scale (VAS). Grade 0 indicates painless and 0 points. Grade 1 indicates mild pain and 1 point. Patient pain levels were tolerable. Sleeping habits and

Table 1. Comparison of general information ($\overline{x}$ ± sd, n)

	Research group (n=34)	Control group (n=30)	χ^2/t	P
Gender (male/female)	24/10	21/9	0.003	0.959
Average age (years old)	52.70 ± 5.70	51.40 ± 5.20	0.921	0.361
BMI (kg/m^2)	23.02 ± 3.30	23.06 ± 3.50	0.047	0.963
Average lesion diameter (cm)	4.22 ± 0.95	4.43 ± 0.89	0.909	0.367
Child-Pugh classification of liver function			0.072	0.485
A	30	28		
B	4	2		
Location			0.372	0.542
Right liver	25	24		
Left liver	9	6		
Pathological types			0.822	0.663
Hepatocyte type	30	28		
Cholangiocyte type	1	1		
Mixed type	3	1		
Differentiation			0.125	0.940
Highly differentiated	14	12		
Moderately differentiated	17	15		
Poorly differentiated	3	3		
Hepatitis B virus genes			0.083	0.772
Positive	25	23		
Negative	9	7		
TNM staging of hepatic carcinoma			0.219	0.896
I	22	21		
II	7	5		
III	5	4		

Note: BMI, body mass index.

Table 2. Comparison of intraoperative conditions ($\overline{x}$ ± sd)

Group	Incision length (cm)	Intraoperative blood loss (mL)	Operative time (min)
Research group (n=34)	4.38 ± 1.52	153.67 ± 54.82	120.64± 35.33
Control group (n=30)	18.79 ± 2.87	360.49 ± 88.96	138.42 ± 36.75
t	25.517	11.340	1.972
P	<0.001	<0.001	<0.001

daily lives were not affected. Grade 2 indicates moderate pain and 2 points. Patient pain was obvious and sleep was affected. They required pain killers and sedatives. Grade 3 indicates severe pain and 3 points. Patient pain was intense and accompanied by vegetative nerve functional disturbance. Sleep was seriously affected, requiring anesthetics. There were 6 total points. Higher scores indicate more obvious pain; (3) Liver function was compared between the two groups. A total of 3 mL of venous blood was collected in the morning on the 1st and 7th days after the operation, detecting levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBIL) using a fully automatic biochemical analyzer from Beckman Coulter, USA; (4) Incidence of postoperative complications was compared between the two groups; (5) Finally, 1-year survival, recurrence, and metastasis rates were compared between the two groups. Recurrence refers to new lesions in the liver tissue. Metastasis refers to new lesions in other parts of the liver or outside the liver.

Statistical analysis

SPSS 19.0 was used to analyze study data. Normality tests were performed on measurement data using Kolmogorov-Smirnov tests. Measurement data, conforming to normal distribution, are expressed by mean ± standard

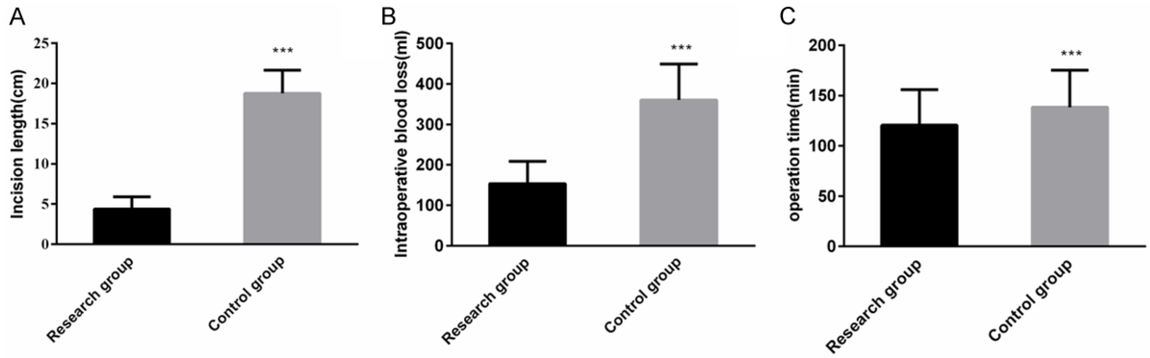

Figure 1. Comparison of intraoperative conditions. A: Incision length; B: Intraoperative blood loss; C: Operation time. Compared with the control group, ***P<0.001.

Table 3. Comparison of postoperative recovery ($\bar{x}$ ± sd)

Group	Pain score (point)	Postoperative extubation time (d)	Fasting time (d)	Hospitalization time (d)
Research group (n=34)	0.84 ± 0.26	1.62 ± 0.68	1.93 ± 0.54	7.63 ± 1.02
Control group (n=30)	1.56 ± 0.47	3.80 ± 0.89	2.81 ± 0.65	15.78 ± 1.24
t	7.701	11.083	5.914	28.838
P	<0.001	<0.001	<0.001	<0.001

deviation ($\bar{x}$ ± sd) and were tested by independent t-tests. Count data are expressed by the number of cases/percentage (n/%) and were tested by χ^2. P<0.05 indicates statistically significant differences.

Results

Comparison of general information

There were no significant differences between research and control groups in gender, age, lesion diameter, Child-Pugh classification of liver function, location, pathological types, differentiation, positive rate of hepatitis B virus genes, and BMI (all P>0.05). More details are shown in **Table 1**.

Comparison of intraoperative conditions

Compared with the control group, patients in the research group showed shorter incision lengths, less intraoperative blood loss, and shorter operative times (all P<0.05). More details are shown in **Table 2** and **Figure 1**.

Comparison of postoperative recovery

Compared with the control group, patients in the research group showed lower pain scores, as well as shorter postoperative extubation times, fasting times, and hospitalization times (all P<0.05). More details are shown in **Table 3** and **Figure 2**.

Comparison of liver function

Before the operation, there were no significant differences between research and control groups in ALT, AST, and TIBL levels (all P>0.05). On the 1st and 7th days after the operation, these three levels in the research group were lower than those in the control group (all P<0.05). More details are shown in **Table 4** and **Figure 3**.

Comparison of postoperative complications

Total incidence rates of postoperative complications in the research group were lower than those in the control group (P<0.05). More details are shown in **Table 5**.

Comparison of postoperative survival, recurrence, and metastasis rates

There were no significant differences in postoperative 1-year survival, recurrence, and metastasis rates between research and control groups (all P>0.05). More details are shown in **Table 6**.

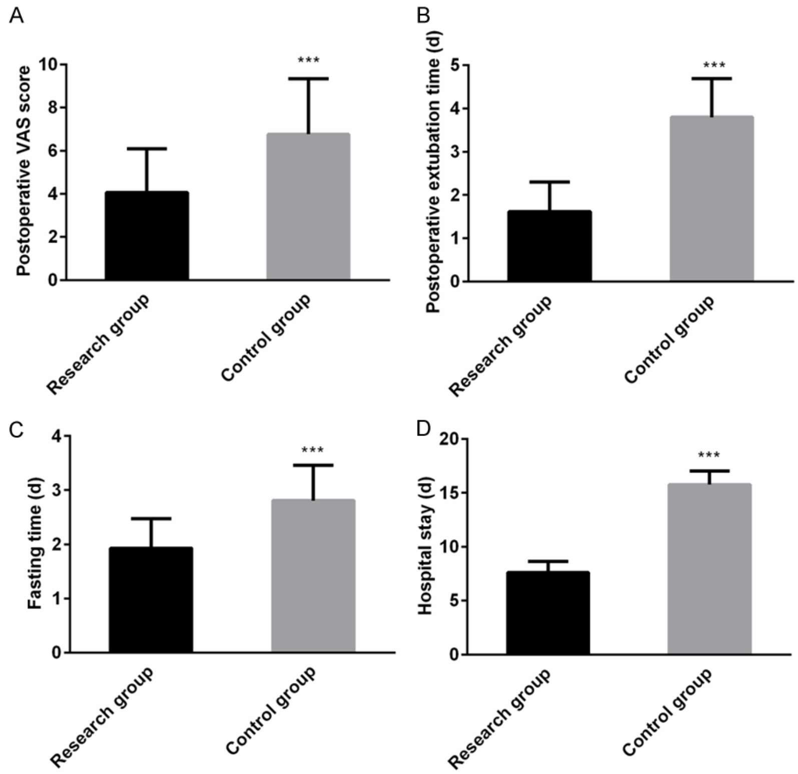

Figure 2. Comparison of postoperative recovery. A: Postoperative VAS score; B: Postoperative extubation time; C: Fasting time; D: Hospital stay. Compared with the control group, ***P<0.001.

Table 4. Comparison of liver function ($\bar{x}$ ± sd)

	ALT (U/L)	AST (U/L)	TIBL (μmol/L)
Research group (n=34)			
Before operation	64.08 ± 12.21	57.43 ± 11.95	18.78 ± 4.27
1 d after operation	95.21 ± 38.72	78.16 ± 28.23	20.11 ± 0.83
7 d after operation	40.46 ± 16.57	20.64 ± 9.33	14.13 ± 0.39
Control group (n=30)			
Before operation	66.79 ± 13.76	58.01 ± 12.26	19.14 ± 4.34
1 d after operation	283.49 ± 32.67	243.68 ± 24.35	24.59 ± 1.12
7 d after operation	92.28 ± 35.19	27.96 ± 10.38	16.88 ± 0.61
t_1/P_1	0.835/0.407	0.191/0.849	0.334/0.740
t_2/P_2	20.356/<0.001	24.318/<0.001	18.317/<0.001
t_3/P_3	7.681/<0.001	2.971/0.004	21.741/<0.001

Note: ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin. t_1/P_1 was comparison of two groups before operation, t_2/P_2 was comparison of two groups 1 day after operation, t_3/P_3 was comparison of two groups 7 days after operation.

Discussion

PHC refers to malignant tumors originating in the liver. This disease has high incidence, recurrence, and mortality rates [9, 10]. It is caused by many factors, including a history of hepatitis, family history of liver cancer, and smoking [11, 12]. Surgery is currently the main treatment for PHC. Traditional OH is effective in treating PHC. However, this method may cause infections, biliary fistula, pleural effusion, and subphrenic hydrops/abscesses, affecting patient prognosis [13, 14]. In a meta study on 1,113 patients with PHC, incidence of complications after traditional OH was 30.77% [15]. Laparoscopic techniques have been gradually recognized and popularized for treatment of PHC. However, they are difficult to apply to hepatectomies due to the complex anatomical relationship between the liver and adjacent tissues and organs, as well as the abundant blood supply.

LH for treatment of PHC enlarges the surgical field. It defines lesion location, peripheral blood vessels, and bile ducts, providing the basis for formulating operative plans. It also defines pathways and extensions of excisions and realizes a fine operation. This helps prevent massive hemorrhaging and biliary fistula, reduces damage to the surrounding tissue caused by the operation, and provides help for hepatectomies in special parts with deep lesion location and abundant blood supply [16]. LH excises liver cancer tissues using ultrasonic scalpels. It disintegrates the liver tissue utilizing high frequency ultrasonic concussion. This causes little damage to the connective tissue and reduces hemorrhaging [17]. Present results indicate that, compared

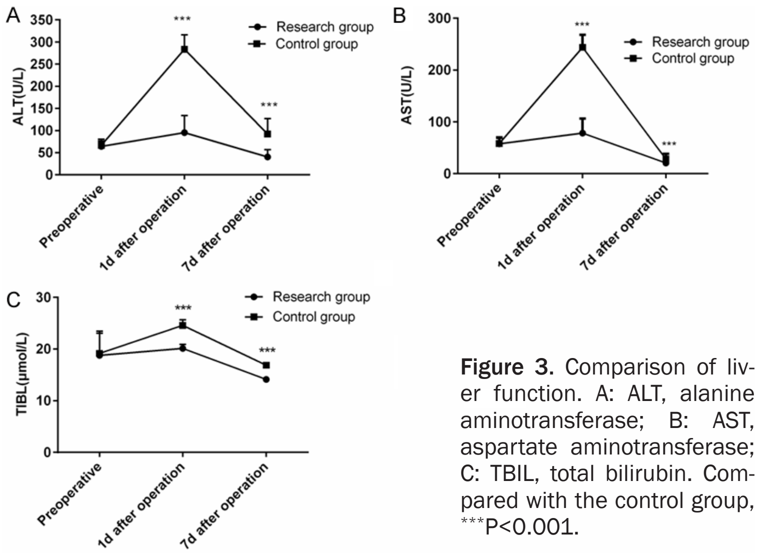

Figure 3. Comparison of liver function. A: ALT, alanine aminotransferase; B: AST, aspartate aminotransferase; C: TBIL, total bilirubin. Compared with the control group, ***P<0.001.

Table 5. Comparison of postoperative complications (n, %)

Group	Research group (n=34)	Control group (n=30)	χ^2	P
Hemorrhage	1 (2.94)	2 (6.67)	0.012	0.482
Biliary fistula	1 (2.94)	2 (6.67)	0.012	0.482
Infection	0 (0.00)	3 (10.00)	1.680	0.059
Pleural effusion	1 (2.94)	1 (3.33)	0.000	1.000
Subphrenic abscess	0 (0.00)	1 (3.33)	0.000	1.000
Total incidence rate	3 (8.82)	9 (30.00)	5.915	0.015

Table 6. Comparison of postoperative survival, recurrence, and metastasis rates (n, %)

Group	1-year survival rate	1-year recurrence rate	1-year metastasis rate
Research group (n=34)	33 (97.06)	4 (11.76)	2 (5.88)
Control group (n=30)	28 (93.33)	5 (16.67)	2 (6.67)
χ^2	0.012	0.041	0.151
P	0.482	0.574	0.897

with the control group, patients in the research group had shorter incision lengths, less intraoperative blood loss, and shorter operative times. Results suggest that LH for treatment of PHC has the advantages of smaller incisions, less blood loss, and shorter operative times. This is possibly because the laparoscope can realize a fine operation. Pneumoperitoneum pressure is helpful in reducing blood flow in the veins and abdominal organs, as well as hemorrhaging of the cut surface of the liver [18].

In the current study, compared with the control group, patients in the research group had lower VAS scores, as well as shorter postoperative extubation times, fasting times, and hospitalization times. Present results are consistent with the findings of previous studies [19, 20]. Small incisions and short operative times in LH reduce intraoperative blood oozing from the wound surface and intraoperative blood loss, accelerate postoperative recovery, and reduce postoperative pain [21]. LH avoids long-term exposure of abdominal organs and reduces loss of moisture in the serosal surface of the gastrointestinal tract during surgery. LH instruments avoid stimulation of the gastrointestinal tract caused by manual turnover of organs during surgery. This factor is beneficial to postoperative recovery of gastrointestinal function and shortening of postoperative fasting times [22].

In this study, on the 1st and 7th days after the operation, ALT, AST, and TIBL levels in the research group were lower than those in the control group. Results suggest that LH, compared with OH, causes less damage to the liver tissue, with less influence on liver function, as well as faster postoperative recovery of liver function and higher safety levels. Incidence of postoperative complications in the research group was lower than that in the control group, consistent with the findings of a previous report [23]. Results suggest that LH reduces postoperative hemorrhaging, infections, bile fistula, and other complications. According to long-term follow-ups, there were no significant differences in 1-year survival, recurrence, and metastasis rates between research and control groups. This is consistent with the results of previous studies [24]. Results indicate that the survival rate of patients with PHC after LH is the same as that after OH. However, postoperative recurrence and metastasis may occur after both LH and OH. Thus, postoperative follow-ups and monitoring should be strengthened. In addition, the sample size was quite small in the current study. There may be bias in screening cases. Whether LH is suitable for elderly patients with PHC requires further study. Sample size should also be enlarged, obtaining more valuable results.

In summary, LH is effective for treatment of PHC. Compared with OH, LH has distinct advantages, including shorter operative times, smaller incisions, less blood loss, faster postoperative recoveries, milder pain, fewer complications, and higher safety levels. Thus, this method has high application value.

Disclosure of conflict of interest

None.

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