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ORIGINAL ARTICLE

A comparative study of laparoscopic precise hepatectomy with conventional open hepatectomy in the treatment of primary hepatocellular cancer

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Summary

Purpose: *To compare the short-term efficacy and safety of laparoscopic precise hepatectomy and conventional open hepatectomy in the treatment of primary hepatocellular cancer.*

Methods: *90 patients with primary hepatocellular cancer admitted to our hospital from September 2015 to September 2017 were collected and divided into the laparoscopic precise hepatectomy group (experimental group, n=45) and conventional open hepatectomy group (control group, n=45). The differences in operation time, intraoperative blood loss, postoperative time with drainage tubes, perioperative blood transfusion, postoperative hospital stay, postoperative liver function indicators, postoperative complications and 1-year tumor recurrence rate and survival rate after operation between the two groups were compared.*

Results: *The general clinical features of the two groups of patients were comparable, and there was no perioperative death. The operation time in the experimental group was longer than that in the control group (106.5±26.4 min vs. 95.2±21.3 min, p=0.028). The intraoperative blood loss in the experimental group was less than that in the control group (204.3±34.9 mL vs. 285.2±39.9 mL, p<0.001). The postoperative time with drainage tubes (6.2±1.7 days vs. 7.1±2.1 days, p=0.028) and postoperative hospital stay (8.1±2.5 days vs. 12.2±3.3 days, p<0.001) in the experimental group were significantly shorter than those in the control group. The levels of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the experimental group were significantly lower than those in the control group (p<0.05), while the levels of albumin (ALB) and total bilirubin (TBIL) in the former were obviously higher than those in the latter (p<0.05). The incidence rate of postoperative complications in the experimental group (15.6%) was evidently lower than that in the control group (35.6%; p=0.030). There was no significant difference in the 1-year recurrence rate between the two groups (p=0.086), and the 1-year survival rate in the experimental group was notably higher than in the control group (p=0.019).*

Conclusion: *Laparoscopic precise hepatectomy for the treatment of primary hepatocellular cancer significantly reduces intraoperative blood loss, shortens hospital stay, causes less trauma to patients and liver function damage, improves the 1-year survival rate, and has a lower incidence rate of complications than the traditional laparotomy, so it is worthy of clinical promotion.*

Key words: *laparoscopic precise hepatectomy, primary hepatocellular cancer*

Introduction

Primary hepatocellular cancer originates from malignant transformation of hepatocytes or the intrahepatic bile duct epithelium. It has high morbidity and mortality rates, with about 1 million new cases added every year worldwide and a death toll of about 600,000, ranking fifth among malignant

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tumors [1]. Operation is the main method for the treatment of primary hepatocellular cancer. Traditional hepatectomy is based on surgical dissection of liver segments. However, with the continuous understanding of liver anatomy and the continuous progress of imaging techniques, traditional hepatectomy is facing severe challenges due to severe trauma and poor prognosis after operation [2,3].

With the development of liver surgery techniques, many authors have analyzed different aspects of precise hepatectomy. In other words, through accurate assessment of liver anatomy and liver function before operation, fine operation and excellent postoperative management, the liver tumor focus is completely removed, the integrity of the remaining liver structure and function is largely preserved, and minimum trauma is caused [4]. Before hepatectomy, the feasibility and risk of resection of large liver cancer need to be predicted to achieve the best efficacy with the minimum risk. Laparoscopic precise hepatectomy is a minimally operation based on the development of modern laparoscopic techniques. It is characterized by small trauma, effective resection of lesions, maximum preservation of liver tissues and good prognosis [5].

In this study, the clinical efficacy of laparoscopic precise hepatectomy and open hepatectomy in the treatment of primary hepatocellular cancer were prospectively compared. The operation time, intraoperative blood loss, perioperative blood transfusion, postoperative time with drainage tubes, postoperative hospital stay, postoperative liver function indexes, postoperative complications and the 1-year tumor recurrence and survival rates after operation were recorded, and the short-term clinical efficacy and safety of the two surgical methods were compared.

Methods

General data

The clinical data of 90 patients with primary hepatocellular cancer treated in our Department from September 2015 to September 2017 were collected and analyzed, including 45 patients in the laparoscopic precise hepatectomy group (experimental group) and 45 patients in the conventional hepatectomy group (control group).

Inclusion criteria

Patients aged ≤75 years, receiving no anti-tumor treatment such as chemotherapy before operation, with primary hepatocellular carcinoma pathologically confirmed after operation, with no serious organ dysfunction, with stable blood pressure and blood glucose control before operation, in grade A or B Child-Pugh or elevated to grade A or B after liver non-operative treatment, and with more than 1-year follow-up after operation.

Exclusion criteria

Patients undergoing emergency surgery or endoscopic surgery, with metastatic tumors, with tumors that had been widely metastasized, with abnormal liver function through examinations before operation and ineffective results in liver protection treatment (whose Child-Pugh grade did not reach grade A or B after conservative treatment), or with portal vein tumor thrombus visible to naked eye. The comparison of general clinical data between the two groups is shown in Table 1. There were no significant differences in the preoperative basic conditions between the two groups, which were comparable. All the selected patients complied with the Helsinki Declaration. They were informed based on the obligation and signed the informed consent. This study was approved by the Ethics Committee of First Peoples Hospital of Jingzhou.

Preoperative assessment

Routine blood examination, biochemical tests, coagulation, immune function and other laboratory examinations and the cardiopulmonary function were performed before operation to evaluate the general health status of the patients. The number, size, location and obvious metastasis of the tumor were evaluated via B-mode ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) in the abdomen, liver, gallbladder, pancreas and spleen. Before operation, liver function reserve was determined by the Child-Pugh grading and indocyanine green (ICG) excretion test. The retention rate of ICG at 15 min in both groups was significantly less than 15%. Siemens 64-slice spiral CT was used to perform three-dimensional reconstruction of the patient's liver and accurately locate the primary hepatocellular cancer focus in two-dimensional CT imaging. The size of the tumor and the distance between the tumor and the hepatic artery and between the hepatic vein and the portal vein were measured. A reasonable tumor resection range was designed based on clinical practice, and then the surgical simulation function of the planning system was applied to carry out surgical simulation. At the same time, the resection liver volume and residual liver volume were predicted. Then, the residual liver functional volume was evaluated to meet the patient's compensation possibility after surgery, and various surgical resection schemes were designed and compared.

Operation modes

Laparoscopic precise hepatectomy: Patients were placed in supine position, with feet higher than the head, and artificial CO_2 pneumoperitoneum was established, with the pneumoperitoneum pressure set at 11-13 mmHg (1 mmHg= 0.133 kPa). Five- or six-hole hepatectomy was performed, with the lesion at 2 cm below the umbilicus as the observation hole, that at 2-3 cm below the rib edge of the left clavicle line in the left lobe of the liver as the main operation hole, and that at 2-3 cm below the xiphoid apophysis in the right lobe of the liver as the main operation hole. The ultrasonic scalpel was used to cut the round ligament and the falciform ligament of the liver in sequence. When the lesion was located in the left lobe of the liver, the hepatogastric ligament or the left lobe ligament of the liver should be removed, and when the lesion was located in the right liver, the right coronary ligament should be removed. A conventional vascular occlusion band was placed at the first hepatic portal. According to two-dimensional CT imaging and angiography, the artery and vein of the resected hepatic segment were selectively embolized with gelatin sponge particles (50-100 mg). Ischemic hepatic segments were seen after the regional hepatic segment vascular embolization. If the embolization was difficult, ultrasound was used to make a resection marker line at 1 cm outside the edge of the tumor. According to the principle of non-tumor, the ultrasonic scalpel was applied to remove at least 1 cm around the lesion, and then the lesion was sent for inspection to clean the wound surface. Bipolar electrocoagulation was used to stop bleeding. If the blood vessels were thicker, the 5-0 Prolene suture would be used.

Conventional open hepatectomy: An accurately middle L-shaped incision was made, and the remaining operations were the same as those in the observation group.

Observational indicators

Perioperative indicators: operation time (from the beginning of skin cutting to the end of skin sewing), intraoperative blood loss (suction volume of a suction bottle-volume of intraoperative flushing fluid), perioperative blood transfusion and postoperative time with drainage tubes.

Postoperative indicators: postoperative hospital stay, postoperative liver function indicators, postoperative complications (incision infection, lung infection, abdominal infection, ascites, bile leakage, liver failure, intestinal obstruction, etc.) and the 1-year tumor recurrence and survival rates after operation. After discharge, the patients were followed up once in the 1st, 2nd, 3rd, 4th, 5th, 6th, 9th and 12th month, respectively, and those who survived for more than 1 year were followed up once every 6 months. The follow-up period ended in Septem-

Table 1. Demographics and general clinical data of all studied patients

Parameters	*Experimental group n=45, n (%)*	*Control group n=45, n (%)*	*p value*
Gender (Male/Female)	24/21	29/16	0.392
Age (years), mean±SD	56.74±8.71	53.58±10.12	0.115
Number of tumors			0.509
1	27 (60.0)	31 (68.9)	
2-3	18 (40.0)	14 (31.1)	
Tumor diameter (cm), mean±SD	2.7±1.7	3.2±1.9	0.192
Tumors' location			0.688
II	9 (20.0)	12 (26.7)	
III	12 (26.7)	8 (17.7)	
IV	7 (15.6)	9 (20.0)	
V	10 (22.1)	7 (15.6)	
VI	7 (15.6)	9 (20.0)	
ICG-R15, mean±SD	7±5	8±6	0.393
Cirrhosis	23 (51.1)	18 (40.0)	0.290
Child-Pugh class			0.385
A	26 (57.8)	30 (66.7)	
B	19 (42.2)	15 (33.3)	
TNM stage			0.413
T1N0M0	25 (55.6)	28 (62.2)	
T2N0M0	20 (44.4)	17 (37.8)	
AFP (ng/mL)			0.200
>400	29 (64.4)	23 (51.1)	
<400	16 (35.6)	22 (48.9)	
HBsAg (+)	35 (77.8)	31 (68.9)	0.340
ALT (U/L), mean±SD	43.11±21.09	39.22±17.41	0.343
TBIL (μmol/L), mean±SD	20.82±3.74	20.13±3.31	0.357

ICG-R15: Indocyanine Green retention rate at 15 min; TNM: Tumor, Lymph Node, Metastasis; AFP: Alpha fetoprotein; HBsAg: Hepatitis B surface antigen; ALT: Alanine transaminase; TBIL: Total bilirubin ber 2018. The follow-up included the general condition of the patients, the level of alpha-fetoprotein (AFP), liver function, B-mode ultrasound in the liver, gallbladder, pancreas and spleen, and CT or MRI examination if necessary.

Statistics

SPSS 22.0 (IBM, Armonk, NY, USA) was used for statistical analyses. Measurement data were expressed as mean ± standard deviation (x±s), and the comparison between groups was tested by the t-test. Count data were expressed as percentages (%), and x^2 test was used for the comparison between groups. P<0.05 showed statistically significant difference. Kaplan-Meier method was used to plot survival curves, and log-rank test was used to compare survival differences between the two groups. P<0.05 showed statistically significant differences.

Results

Preoperative general conditions

In this study, 90 patients with primary hepatocellular cancer were studied, including 53 males (58.9%) and 37 females (41.1%), aged 34-76 years (mean 54.52±10.35). In the experimental group, there were 27 cases (60.0%) with single tumor and 18 cases (40.0%) with multiple tumors, and the average tumor diameter was 2.7±1.7 cm. Besides, there were 23 cases (51.1%) complicated with liver cirrhosis. In the control group, 31 cases (68.9%) with single tumor and 14 cases (31.1%) with multiple tumors had average tumor diameter 3.2±1.9 cm. In addition, there were 18 cases (40%) complicated with liver cirrhosis. The lesions were located between segment II and VI in Couinaud segmentation, and were confined to the half liver. In the two groups, the tumors were located in segment II in 9 cases (20.0%) and 12 cases (26.7%), segment III in 12 cases (26.7%) and 8 cases (17.7%), segment IV in 7 cases (15.6%) and 9 cases (20.0%), segment V in 10 cases (22.1%) and 7 cases (15.6%), and segment VI in 7 cases (15.6%) and 9 cases (20.0%), respectively. The ICG-R15 in the two groups was 7±5% and 8±6%, respectively. In the experimental group, there were 26 cases (57.8%) in Child-Pugh grade A and 19 cases (42.2%) grade B. In the TNM staging, there were 25 cases (55.6%) in T1N0M0 and 20 cases (44.4%) in T2N0M0. In the control group, there were 30 cases (66.7%) in Child-Pugh grade A and 15 cases (33.3%) in grade B. In the TNM staging, there were 28 cases (62.2%) in T1N0M0 and 17 cases (37.8%) in T2N0M0. There were no significant differences in the comparisons of liver function indicators between the two groups before operation (p>0.05;Table 1).

Comparisons of perioperative indicators

The operation time of patients in the experimental group was longer than that in control group (106.5±26.4 min *vs.* 95.2±21.3 min), showing a significant statistical difference (p=0.028). The intraoperative blood loss in the former was less than that in the latter (204.3±34.9 mL *vs.* 285.2±39.9 mL; p<0.001). There was no statistically significant difference in the perioperative blood transfusion volume between the two groups (p>0.05). The postoperative time with drainage tubes (6.2±1.7 days *vs.* 7.1±2.1 days, p=0.028) and the postoperative hospital stay (8.1±2.5 days *vs.* 12.2±3.3 days, p<0.001) in the experimental group were remarkably shorter than those in control group. The incidence rates

Table 2. Comparison of parameters related to surgery

Parameters	*Experimental group (n=45)*	*Control group (n=45)*	*p value*
Operation time (min)*	106.5±26.4	95.2±21.3	0.028
Blood loss (mL)*	204.3±34.9	285.2±39.9	0.001
Blood transfusion volume (mL)*			
226.9±61.1	251.6±69.3	0.076	
Postoperative catheter drainage time (days)*	6.2±1.7	7.1±2.1	0.028
In-hospital time (days)*	8.1±2.5	12.2±3.3	0.001
Complication**	7 (15.6)	16 (35.6)	0.030
Incision infection**	0 (0)	1 (2.2)	
Pulmonary infection**	3 (6.7)	5 (11.1)	
Abdominal infection**	1 (2.2)	2 (4.4)	
Ascites**	3 (6.7)	6 (13.3)	
Biliary fistula**	1 (2.2)	3 (6.7)	
Hepatic failure**	2 (4.4)	4 (8.9)	
Ileus**	0 (0)	1 (2.2)	

*mean±SD, ** n (%)

of postoperative complications in the two groups were 15.6% and 35.6%, respectively, and the difference was statistically significant (p=0.030). In the two groups after operation, there were 0 case and 1 case (2.2%) complicated with incision infection, 3 cases (6.7%) and 5 cases (11.1%) complicated with pulmonary infection, 1 case (2.2%) and 2 cases (4.4%) complicated with abdominal infection, 3 cases (6.7%) and 6 cases (13.3%) complicated with ascites, 1 case (2.2%) and 3 cases (6.7%) complicated with biliary fistula, 2 cases (4.4%) and 4 cases (8.9%) complicated with hepatic failure, and 0 case and 1 case (2.2%) complicated with intestinal obstruction (Table 2).

Recovery of liver function after operation

The levels of ALT and AST in the two groups of patients after operation were significantly lower than those before operation. The levels of serum ALT on the 1st, 3rd and 5th day after operation in the experimental group were evidently lower than those in the control group (26.11±13.15 U/L *vs.* 32.78±17.29 U/L, p=0.042, 23.38±10.70 U/L *vs.* 28.91±13.80 U/L, p=0.036, and 20.63±8.23 U/L *vs.* 25.59±7.19 U/L, p=0.013) (Figure 1A). The levels of serum AST on the 1st, 3rd and 5th day after operation in the experimental group were obviously lower than those in the control group (21.58±11.80 U/L *vs.* 27.90±12.56 U/L, p=0.016, 15.37±12.91 U/L *vs.* 21.07±10.80 U/L, p=0.026), and 11.18±10.56 U/L *vs.* 16.53±9.47 U/L, p=0.013) (Figure 1B). On the 3rd and 5th day after operation, the serum albumin (ALB) levels in the experimental group were notably higher than those in the control group (47.48±8.50 g/L *vs.* 42.57±9.15 g/L, p=0.010, and 53.34±8.74 g/L *vs.* 48.63±8.97 g/L, p=0.013) (Figure 1C). On the 1st, 3rd and 5th day after operation, the serum total bilirubin (TBIL) levels in the experimental group were markedly higher than those in the control group (19.55±3.04 μmol/L *vs.* 18.18±2.89 μmol/L, p=0.031, 18.58±2.14 μmol/L *vs.* 16.77±2.81 μmol/L, p=0.019, and 17.18±2.94 μmol/L *vs.* 15.71±2.58 μmol/L,

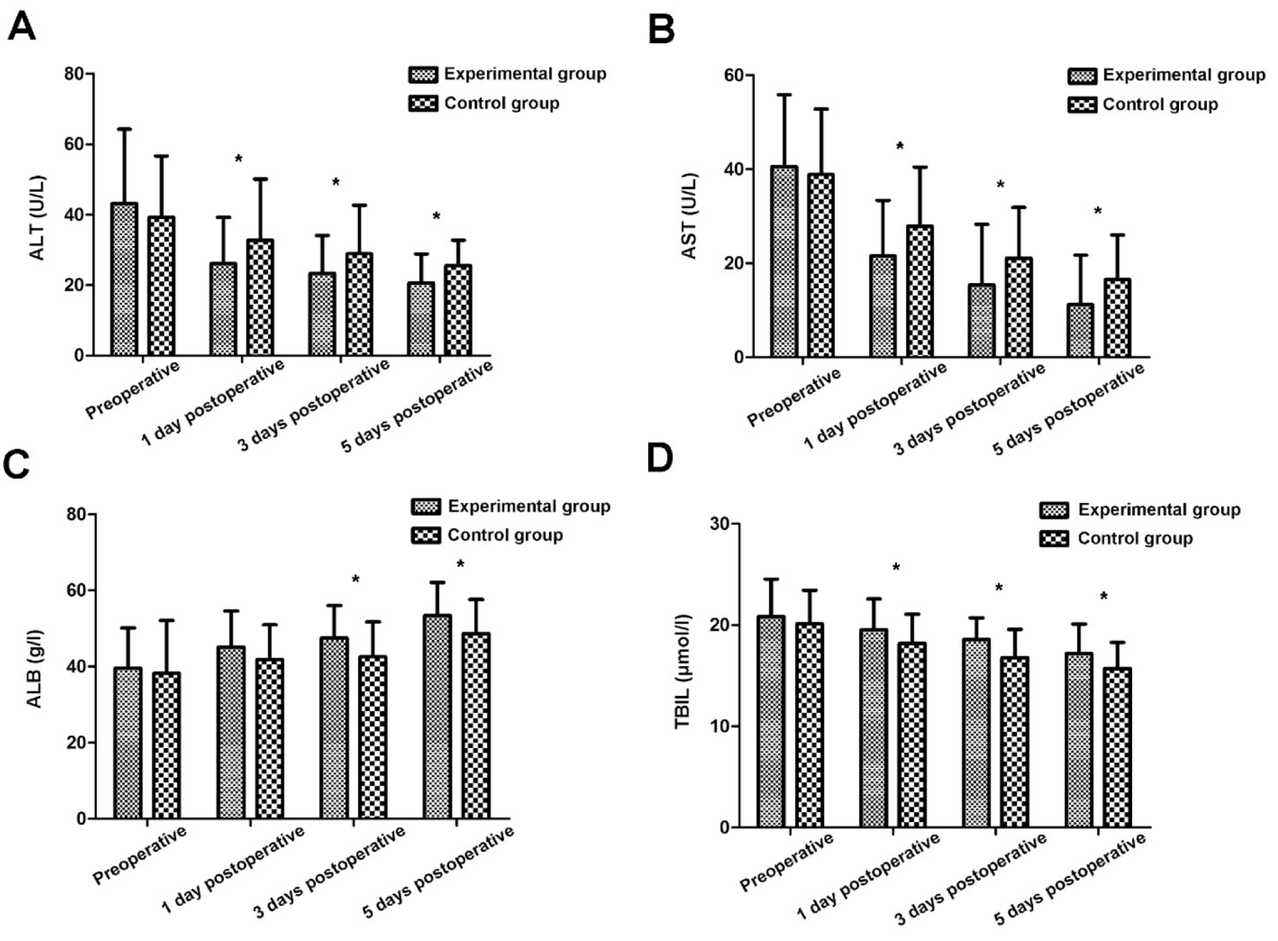

Figure 1. Comparison of postoperative liver function indexes of the patients in the two groups. **A:** ALT (postop 1, 3, 5 days) levels of patients in the experimental group were significantly lower than in the control group. **B:** AST (postop 1, 3, 5 days) levels of patients in the experimental group were significantly lower than in the control group. **C:** ALB (postop 3, 5 days) levels of patients in the experimental group were significantly higher than in the control group. **D:** TBIL (postop 1, 3, 5 days) levels of patients in the experimental group were significantly higher than in the control group (*p<0.05).

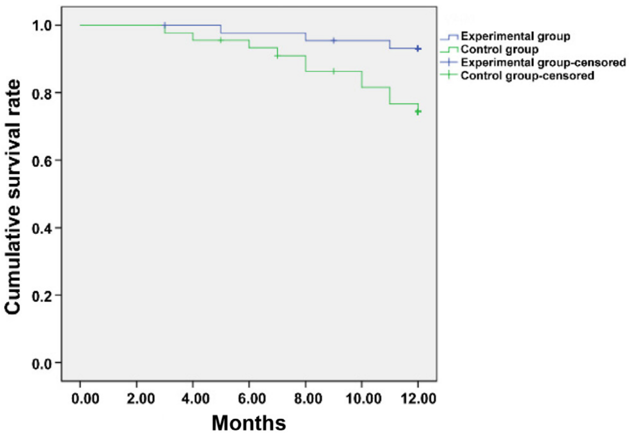

Figure 2. Kaplan-Meier one-year survival of patients in the experimental group and the control group. The one-year survival rate of patients in the experimental group was significantly higher than in the control group (p=0.019).

p=0.021) (Figure 1D). The above results revealed that the operation in the experimental group caused little damage to the liver function, and the liver function recovered well after the operation.

Follow-up results of the patients' survival

After 12 months follow-up, 2 cases were lost to follow-up in the experimental group at 3 and 9 months after operation and 3 cases in the control group at 5, 7 and 9 months after operation. Four patients in the experimental group had recurrence of liver cancer at 4, 6, 9 and 12 months after operation with a recurrence rate of 9.3 % (4/43) and 3 deaths at 5, 8 and 11 months after operation. In the control group, liver cancer recurred in 10 patients at 3, 5, 6, 8, 9 and 12 months after operation, with a recurrence rate of 23.8% (10/42), and 11 patients died at 3, 4, 6, 7, 8, 10, 11 and 12 months after operation. There was no significant difference in the tumor recurrence rate between the two groups (p=0.086). The 1-year Kaplan-Meier survival curves of the experimental group and control group are shown in Figure 2. The log-rank test revealed that there was a statistically significant difference in the 1-year survival rate between the two groups (p=0.019).

Discussion

The risk factors for primary hepatocellular cancer are complex, and most of them originate from hepatitis, cirrhosis and other diseases. At present, surgical resection of the neoplastic focus is the first choice in clinical practice. Traditional laparotomy needs a large operating space, which contributes to the in-time handling and controlling of sudden massive bleeding with high safety. With the continuous development and improvement of surgical techniques in recent years, the operation has also moved from blind hepatectomy, regular hepatectomy, local hepatectomy and anatomical hepatectomy to precise hepatectomy [6,7]. The therapeutic concept of laparoscopic precise hepatectomy is based on minimally invasive surgery. On the basis of radical resection of the lesion, trauma to residual tissues is minimized, the function of residual liver tissues is ensured, and the prognosis and quality of life of patients are effectively improved [8,9].

In this study, laparoscopic precise hepatectomy was compared with conventional open hepatectomy in the treatment of primary hepatocellular cancer. The operation time in the experimental group was longer compared with the control group, but the intraoperative blood loss, postoperative time with drainage tubes and postoperative hospital stay in the experimental group were shorter than in the control group. This is because laparoscopic precise hepatectomy is based on a detailed assessment of the patient's liver function before operation, the lesion site is precisely localized, and the distribution of liver blood vessels is known beforehand according to angiography [10,11]. In this study, three-dimensional CT imaging, ultrasound, MRI and other means were used for evaluation before operation, and 64-slice spiral CT was adopted to perform three-dimensional imaging. The hazard in the laparoscopic operation is bleeding during the operation. An ultrasonic scalpel was used to avoid bulky blood vessels to bleed through preoperative three-dimensional CT imaging, and there was no smoke during the operation, which could affect the visual field, and the hemostatic effect was better than that of conventional hepatectomy. During operation, arterial embolization was performed on the liver segment of the focus to block the blood flow of this segment, not affecting the liver function after operation, and effectively reducing the blood reperfusion injury of the remaining liver [12,13].

The liver function indicators such as AST, ALT, ALB and TBIL in the experimental group were higher than in the control group, indicating that laparoscopic precise hepatectomy causes less trauma to liver function than conventional open hepatectomy [14]. The survival rate in the experimental group was remarkably higher than in the control group, which was related to factors such as small damage to liver function caused by precise hepatectomy, ensuring the margin distance of tumor resection and the reduction of the intrahepatic spread of the tumor. There was no significant difference in the tumor recurrence rate between the two groups, which might be related to the selected cases. In the study, the sample size of cases was small, so there might be some biases. The exact efficacy still needs to be studied in larger-sample cases.

The incidence rate of postoperative complications in the experimental group was significantly lower than in the control group. This is due to the fact that precise hepatectomy avoids the resection of liver tissues other than lesions, and the preoperative three-dimensional imaging of liver anatomy avoids important structures such as the biliary tract, arteries and veins, thus reducing the incidence rate of postoperative complications. Due to the short hospital stay, the time of patients staying in bed was decreased, and the incidence rate of lung infection was reduced. At the same time, due to the small trocar port, the incidence rate of incision infection was reduced. The patients recovered quickly after operation, the hospital stay was shortened, and their financial burden also declined [15,16].

This study has found that laparoscopic precise hepatectomy for the treatment of primary hepatocellular cancer caused less trauma and liver function damage, with high safety, and it could improve the 1-year survival rate. The incidence rate of complications after laparoscopic precise hepatectomy was lower than after conventional open hepatectomy, so it is worthy of clinical promotion. However, the long-term efficacy of laparoscopic precise hepatectomy for primary hepatocellular cancer patients still needs multi-center and large-sample clinical research.

Conclusions

Laparoscopic precise hepatectomy for primary hepatocellular cancer significantly reduces intraoperative blood loss, shortens hospital stay, causes less trauma to patients and liver function damage, improves the 1-year survival rate and has a lower incidence rate of complications than traditional laparotomy, so it is worthy of clinical promotion.

Conflict of interests

The authors declare no conflict of interests.

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