Original Article

Comparison of the short-term outcomes of open and laparoscopic hepatectomy in the treatment of recurrent hepatocellular carcinoma: a single-center retrospective study

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Background: To retrospectively analyze the short-term outcomes between open hepatectomy (OH) and laparoscopic hepatectomy (LH) in the treatment of recurrent hepatocellular carcinoma (HCC). The objective is to develop the optimal surgical method for patients with recurrent liver cancer after operation.

Methods: We retrospectively reviewed the data of 165 HCC patients whose cancer recurred after hepatectomy between January 2015 and March 2021 at our medical center. According to the inclusion and exclusion criteria, a total of 74 patients were eventually enrolled in this study.

Results: Tumors located in S1, S7, or S8 and larger tumor diameters were more frequent in the OH group, and the difference was statistically significant. Furthermore, there were notable differences between the LH and OH groups in terms of intraoperative blood loss (140.00 *vs.* 348.68 mL, P<0.001), mean operation time (150.95 *vs.* 203.28 min, P=0.024), and mean postoperative hospital stay (6.76 *vs.* 11.28 days, P=0.014). There were no statistically significant differences in the remaining characteristics between the two groups. There was no significant difference in recurrence-free survival and overall survival between the two groups.

Conclusions: Compared with OH, LH can significantly reduce the amount of intraoperative blood loss and shorten the operation time and postoperative hospital stay. At the same time, laparoscopic surgery may be a better surgical approach for patients with tumors of smaller diameter located in segments 2 to 6.

Keywords: Hepatocellular carcinoma (HCC); laparoscopic; hepatectomy; recurrence; short-term outcomes

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Introduction

The incidence and mortality of hepatocellular carcinoma (HCC) are rapidly increasing worldwide. According to the analysis of global cancer statistics, HCC is the seventh most diagnosed cancer (4.7%) and the second leading cause of cancer-related deaths (8.2%) (1). For HCC patients with good liver function, hepatectomy is effective and the only possible curative treatment method, and plays a major role in treatment guidelines (2,3). However, due to the high postoperative recurrence rate of HCC, its overall survival rate remains low.

According to previous experience, repeat hepatectomy is safe and feasible for HCC recurrence. Due to complex

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postoperative adhesions and changes in anatomical markers, repeat hepatectomy is usually performed through an open approach. Laparoscopic techniques and instruments have advanced over the course of more than 20 years, and the number of patients with HCC undergoing laparoscopic hepatectomy (LH) has continued to grow exponentially (4,5). LH has achieved good efficacy in primary liver cancer resection and compared with open surgery, LH possesses a growing number of advantages, such as less intraoperative hemorrhage, fewer postoperative complications, and shorter hospital stays (6-10). However, the short-term outcomes of LH in the treatment of recurrent liver cancer are still controversial, and no consensus has been reached.

The purpose of this study was to compare the short-term efficacy of open and LH in the treatment of recurrent HCC. In this study, we retrospectively analyzed the clinical and pathological data of patients with recurrent liver cancer who underwent LH and compared them with those who underwent open hepatectomy (OH). We present the following article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2576/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of The Affiliated Lihuili Hospital (Project Identification Code: KY2019PJ024). Individual consent for this retrospective analysis was waived.

Highlight box

Key findings

- Tumors located in S1, S7, or S8 and larger tumor diameters were more frequent in the OH group. There were notable differences between the LH and OH groups in terms of intraoperative blood loss, operation time and postoperative hospital stay.

What is known and what is new?

- Compared with OH, LH can significantly reduce the amount of intraoperative blood loss, shorten the operation time and postoperative hospital stay. Also, LH may be a better surgical approach for patients with tumors of smaller diameter located in segments 2 to 6.
- The results of this study may provide more surgical options for patients with recurrent liver cancer.

What is the implication, and what should change now?

- Open surgery is not necessary for the secondary operation of patients with recurrence of liver cancer after surgery, and laparoscopic surgery is also feasible for some patients. This study provides a reliable basis for the selection of surgical methods for patients with recurrent liver cancer in the future.

Patient selection

We retrospectively reviewed the data of 165 patients who were diagnosed with HCC between January 2015 and March 2021 at The Affiliated Lihuili Hospital. These patients had previously undergone hepatectomy and returned to our hospital due to tumor recurrence. To select the appropriate method of reoperation, all recurrent patients in this study were evaluated by preoperative computed tomography (CT) or magnetic resonance imaging (MRI) and other imaging examinations. Patients were excluded for the following reasons: (I) patients with missing clinical data; (II) patients who did not undergo surgery; (III) those who underwent transplants; and (IV) those who received other abdominal surgeries. With the above patients excluded, the final number of patients included was 74. A diagram demonstrating the patient selection process is shown in *Figure 1*.

All patients in this study received telephone or outpatient follow-up. Re-examination was conducted monthly within six months after radical HCC resection, every three months from six months to one year, and every six months after one year. Follow-up data were mainly collected for recent imaging changes. Postoperative tumor-free survival was defined as the time from radical surgery for HCC to tumor recurrence (including intrahepatic and extrahepatic recurrence), and overall survival was defined as the time from radical surgery for HCC to death or the last follow-up time. The end point of follow-up was death or until the end of follow-up. The last follow-up was on December 31, 2021.

Variables

Patient data including demographic, preoperative, operative, pathologic, and postoperative information were collected and analyzed. Demographic variables included age, sex, body mass index (BMI), first surgical method, and performance status (PS). Preoperative data included hepatitis B virus (HBV) infection, antiviral therapy, albumin (ALB), total bilirubin (TB), direct bilirubin (DB), alpha-fetoprotein (AFP), international normalized ratio (INR), and Child-Pugh classification. The grading

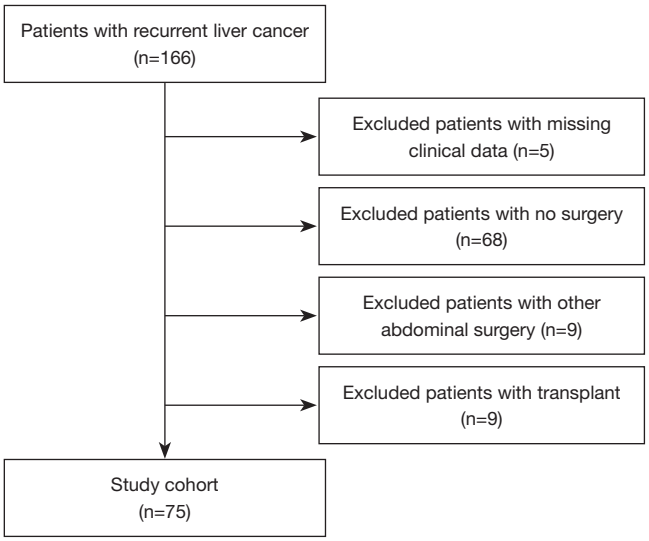

Figure 1 Diagram demonstrating the study cohort selection.

of abdominal adhesions, tumor location, liver texture, liver cirrhosis, blood loss, blood transfusion, plasma transfusion, and operation time were included as operative variables. Postoperative variables included fasting time, tumor size, tumor number, tumor differentiation, tumor grade (T grade), Barcelona Clinic Liver Cancer (BCLC), complications, and postoperative hospital stay.

According to the standard range of each indicator, Child-Pugh classification was categorized into two groups (A, B), as were ALB (<35.0, ≥35.0 g/L), TB (<17.1, ≥17.1 mmol/L), DB (<6.8, ≥6.8 mmol/L), and AFP (<400, ≥400 ng/mL). The grading of abdominal adhesions was categorized into four groups [Group 0: no adhesion; Group 1: thin layer adhesion can be obtuse separation; Group 2: thin layer adhesion can be sharp and easily separated; Group 3: extensive vascular adhesion requires careful and sharp separation; and Group 4: dense adhesions carry the risk of damage to the internal organs (10)]. The tumor location was categorized into two groups (segments 1, 7, 8 and segments 2–6), as the LH of tumors in segments 1, 7, and 8 are reportedly technically difficult (11). The tumor grade was categorized into four groups (well differentiated, moderately differentiated, poorly differentiated, and undifferentiated). T staging was based on the American Joint Committee on Cancer (AJCC) guideline.

Statistical analysis

Continuous data are expressed as the mean ± standard deviation or median and interquartile range (IQR), and the Mann-Whitney U test was used to perform the difference test. The software SPSS 22.0 (IBM Corp., Armonk, NY, USA) and R language (version 4.0.4; The R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis, and P<0.05 was defined as statistically significant. This study was reviewed by the hospital ethics committee and complied with the guidelines of the government agencies responsible for the center.

Results

Baseline characteristics

A total of 74 patients with recurrent hepatectomy were included in this study, all of whom were confirmed to have HCC based on their pathology findings. Among them, 21 patients underwent LH (LH group), and 53 patients underwent OH (OH group). The baseline characteristics of patients in both groups are compared in *Table 1*. There were no statistically significant differences between the LH and OH groups in terms of the patients' sex, age, BMI, PS, HBV infection, antiviral therapy, Child-Pugh classification, ALB, TB, DB, INR, AFP, or first operation.

Comparison of intraoperative-related characteristics

The same medical team treated both groups. There were no statistically significant differences between the LH and OH groups in terms of the patients' abdominal adhesions, liver texture, blood transfusion, or plasma transfusion. Tumors located in S1, S7, or S8 were more frequent in the OH group, and the difference was statistically significant. Intraoperative blood loss in the LH and OH groups were 140.00±176.95 and 348.68±288.89 mL, respectively, and the difference between the two groups was statistically significant. The operation times of the LH and OH groups were 150.95±86.23 and 203.28±89.06 min, respectively, and this difference was statistically significant (*Table 2*).

Postoperative characteristics

The clinicopathological and surgical outcomes are shown in *Table 3*. The mean tumor sizes of the LH and OH groups were 2.27±1.08 and 4.00±2.94 cm, respectively, and the difference between the two groups was statistically significant. The postoperative hospital stay duration was markedly higher in the OH group (11.28±6.82 days) than

Table 1 Patients' characteristics in the LH and OH groups

Variable	Group (n=74)		P value
	LH (n=21)	OH (n=53)	
Age	63.33±12.22	63.28±11.59	0.987
Gender			1.000
Male	18	44	
Female	3	9	
BMI	24.34±3.46	23.55±3.50	0.383
PS			0.074
0	19	36	
1	2	17	
HBV infection			0.707
Yes	18	47	
No	3	6	
Antiviral therapy			0.265
No	4	5	
Entecavir	15	36	
Other	2	12	
Child-Pugh			0.554
A	21	50	
B	0	3	
ALB (g/L)			1.000
<35.0	3	8	
≥35.0	18	45	
TB (mmol/L)			0.253
<17.1	16	33	
≥17.1	5	20	
DB (mmol/L)			0.151
<6.8	18	35	
≥6.8	3	18	
INR	1.08±0.14	1.08±0.08	0.852
AFP (ng/mL)			0.499
<400	16	44	
≥400	5	9	
First operation			0.718
OH	19	44	
LH	2	9	

Quantitative data were expressed by means plus or minus standard deviation. LH, laparoscopic hepatectomy; OH, open hepatectomy; BMI, body mass index; PS, performance status; HBV, hepatitis B virus; ALB, albumin; TB, total bilirubin; DB, direct bilirubin; INR, international normalized ratio; AFP, alpha-fetoprotein.

Table 2 Univariate analysis of intraoperative characteristics in the LH and OH groups

Variable	Group (n=74)		P value
	LH (n=21)	OH (n=53)	
Grading of abdominal adhesions			0.908
Grade 1	1	2	
Grade 2	0	0	
Grade 3	11	30	
Grade 4	9	21	
Tumor location			0.008
S1, S7, S8	3	26	
S2–6	18	27	
Liver texture			0.851
Soft	7	16	
Middle	6	13	
Hard	8	24	
Blood loss (mL)	140.00±176.95	348.68±288.89	<0.001
Blood transfusion (mL)	28.57±130.93	84.91±210.67	0.171
Plasma transfusion (mL)	22.86±130.93	102.64±262.73	0.066
Operation time (min)	150.95±86.23	203.28±89.06	0.024

Quantitative data were expressed by means plus or minus standard deviation. LH, laparoscopic hepatectomy; OH, open hepatectomy.

in the LH group (6.76±7.46 days) (P=0.014). There were no statistically significant differences between the LH and OH groups in terms of the patients' liver cirrhosis, tumor number, tumor differentiation, T grade, BCLC, fasting time, complications, recurrence-free survival, or overall survival (*Figure 2*).

Discussion

Since the world's first successful LH in 1991, and with the improvement of laparoscopic equipment and instruments, the application scope of LH has gradually expanded to include the early resection of tumors on the left lateral lobe and right surface of the liver to resection of the left and right halves of the liver. Furthermore, totally laparoscopic caudate lobectomy (12) and totally laparoscopic associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) (13) have also been reported.

The advantages of laparoscopic surgery in shortening the

Table 3 Univariate analysis of postoperative characteristics in the LH and OH groups

Variable	Group (n=74)		P value
	LH (n=21)	OH (n=53)	
Liver cirrhosis			0.516
Yes	14	31	
No	7	22	
Mean tumor size (cm)	2.27±1.08	4.00±2.94	<0.001
Tumor number			0.170
Single	17	33	
Multiple	4	20	
Tumor differentiation			0.891
Well	1	4	
Moderately	10	28	
Poorly	10	20	
Undifferentiated	0	1	
T			0.311
T1a	11	18	
T1b	6	15	
T2	4	16	
T3	0	4	
BCLC			0.053
A	21	43	
B	0	10	
Fasting time (h)	25.67±23.32	26.59±28.07	0.894
Postoperative hospital stay (d)	6.76±7.46	11.28±6.82	0.014
Complications			0.313
No	21	48	
Yes	0	5	

Quantitative data were expressed by means plus or minus standard deviation. LH, laparoscopic hepatectomy; OH, open hepatectomy; T, tumor; BCLC, Barcelona Clinic Liver Cancer.

hospital stay, reducing intraoperative bleeding, and relieving postoperative pain are increasingly prominent. Moreover, a large number of retrospective studies have also found that the long-term efficacy of laparoscopic HCC resection is comparable to that of open surgery (14-17).

Owing to the high postoperative recurrence rate of HCC, its overall survival rate remains low. For recurrent HCC with good liver function and sufficient residual liver volume, surgical resection is still the first choice (18). However, for recurrent liver cancer, most medical centers still choose traditional open resection, and the main reasons for this may be as follows: (I) after one or more operations for recurrent liver cancer, the liver anatomical morphology changes; (II) abdominal adhesions increase the difficulty of surgery and the probability of surgical injury; and (III) recurrent liver cancer often has multiple foci with deep locations, which makes surgical resection difficult.

A history of abdominal surgery has been considered a relative contraindication to laparoscopic surgery (19). With the continuous improvement of laparoscopic instruments and the increasingly rich experience of surgeons, domestic and foreign scholars have begun to explore the possibility of laparoscopic resection of recurrent liver cancer. A meta-analysis conducted by Cai *et al.* in China found that the laparoscopic surgery group was significantly superior to the open surgery group in terms of mean operative time, intraoperative blood loss, postoperative complication rate, and postoperative hospital stay (19), and these findings are consistent with the results of another meta-analysis by Perunovic *et al.* (20). Noda *et al.* (5). retrospectively analyzed 20 recurrent liver cancer patients who underwent laparoscopic resection and compared them with those who underwent open resection. They found that the laparoscopic group had lower intraoperative blood loss, mean postoperative hospital stay, and postoperative complication rate compared to those in the open group.

Our retrospective study found that intraoperative blood loss, mean operative time, and mean postoperative hospital stay in the laparoscopic group were markedly lower than those in the open group (140.00 *vs.* 348.68 mL, P<0.001; 150.95 *vs.* 203.28 min, P=0.024; 6.76 *vs.* 11.28, respectively, P=0.014). We also found that patients with recurrent liver cancer who underwent LH had smaller tumor diameters and more superficial tumor locations (the tumors were located in segments 2–6). Therefore, for patients with smaller tumor diameters and more superficial tumor locations, LH resection may be a better surgical method. The conclusions of our study are consistent with the findings of Jeong *et al.* (21) .

This retrospective study has some shortcomings that should be noted. Firstly, this is a single-center study, and a multicenter study is still needed. Secondly, the number of included cases in this study is small, and thus, the sample size needs to be increased to increase the accuracy and

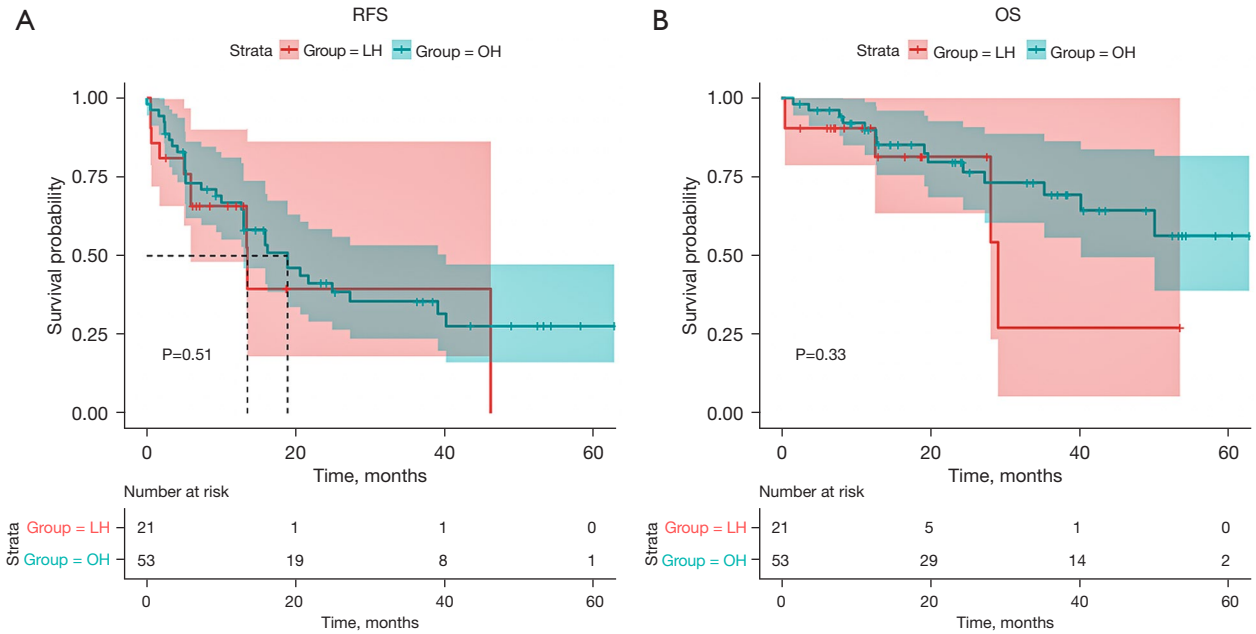

Figure 2 RFS and OS curves of the LH and OH groups. RFS, recurrence-free survival; LH, laparoscopic hepatectomy; OH, open hepatectomy; OS, overall survival.

reliability of the results. Thirdly, prospective randomized controlled studies are still needed to further verify the effect of laparoscopic surgery in the resection of recurrent liver cancer.

Conclusions

Compared with OH, LH can significantly reduce the amount of intraoperative blood loss and shorten the operation times and postoperative hospital stays of patients. At the same time, laparoscopic surgery may be a better surgical approach for patients with smaller tumor diameters located in segments 2 to 6. However, for tumors that are larger in diameter or are located in segments 1, 7, and 8, OH may be a safer surgical method. Therefore, a detailed preoperative evaluation is particularly important and can provide a basis for the selection of the appropriate surgical methods. In addition, laparoscopic surgery for recurrent HCC is still in the exploratory stage, and as the technology continues to evolve, it is expected to be accepted and implemented by more medical centers.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2576/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2576/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2576/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was

conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of The Affiliated Lihuili Hospital (Project Identification Code: KY2019PJ024). Individual consent for this retrospective analysis was waived.

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