

Long-term outcomes of laparoscopic hepatectomy for hepatocellular carcinoma at Viet Duc University Hospital from 2019 to 2023

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Abstract

Introduction: Laparoscopic liver resection is a challenging procedure, yet it is increasingly applied in the treatment of hepatocellular carcinoma (HCC), including our center. Our aim is to evaluate the impact of laparoscopic hepatectomy for hepatocellular carcinoma regarding the long-term outcomes.

Patients and Methods: A combined retrospective-prospective cohort study of 41 HCC patients who underwent laparoscopic hepatectomy at the Organ Transplantation Center, Viet Duc University Hospital from January 2019 to December 2023.

Results: Liver resection for tumors >5 cm accounted for 24.4%, with 63.4% of cases classified as high difficulty (Ban Daisuke score). The mean operative time was 192 minutes, and the intraoperative blood transfusion rate was 18.9%. The mean disease-free survival was 44.5 ± 3.19 months, with 1-, 2-, 3-, and 4-year rates of 94.4%, 87.2%, 70.6%, and 70.6%, respectively. The mean overall survival was 50.0 ± 2.30 months, with corresponding rates of 96.7%, 92.9%, 86.8%, and 86.8%. Preoperative AFP <400 ng/mL and resection margin >0.5 cm were favorable prognostic factors.

Conclusions: Laparoscopic hepatectomy is a safe and effective treatment option for hepatocellular carcinoma offering significant survival benefits.

Keywords: Laparoscopic hepatectomy, Difficulty Scoring System, Hepatocellular carcinoma.

Introduction

Hepatocellular carcinoma (HCC) makes the leading number in terms of incidence and deaths from cancer in Vietnam, with an estimated of

26,418 newly diagnosed patients and 25,272 deaths each year. [1] Currently, there are many radical treatment methods for HCC being applied, among which liver resection is still

considered a fundamental and effective treatment method. Laparoscopic liver resection has been increasingly adopted in the treatment of HCC worldwide, including in Vietnam, demonstrating the significance of minimally invasive techniques in achieving curative outcomes. However, laparoscopic liver resection (LLR) is still considered a difficult operation, requiring surgeon skills as well as the synchronous development of many supporting specialties and equipment. The article aims to evaluate the results of applying this technique in the treatment of patients with HCC at the Organ Transplantation Center - Viet Duc University Hospital in the period of 2019 - 2023.

Patients and methods

Study population.

Selection criteria: Patients diagnosed with HCC, treated with LLR at the Organ Transplantation Center - Viet Duc University Hospital from January 2019 to December 2023.

Exclusion criteria: Patients with incomplete medical records, final pathological results of mixed HCC-ICC.

Research methods

Research design: descriptive, retrospective and prospective data collection

Sample size: convenient sample size, with patients who met the selection criteria

Definitions and research data

Postoperative liver failure was determined according to the **Balzan-Belghiti criteria**: A prothrombin ratio below 50% and a serum bilirubin level greater than 50 $\mu\text{mol/L}$ on postoperative day 5. [2]

Postoperative complications were classified according to the **Clavien-Dindo classification**. [3]

The difficulty of each procedure was assessed according to the **Ban Daisuke (Iwate) scale** [5].

It was calculated by summing the scores applied to the extent of liver resection, tumor location, liver function, tumor size, and tumor invasion to major blood vessels. Difficulty indexes of 1 and 10 were

defined as the easiest and most difficult cases, respectively. Difficulty was classified into three levels: Low (1–3), Medium (4–6), and High (7–10).

Based on the surgical results, LLR was considered as successful: when the procedure was completed laparoscopically or with the assistance of a small incision. It was a deemed failure : when a large laparotomy had to be performed to complete the liver resection.

Patients in the study were evaluated for clinical factors, laboratory results, imaging, operative characteristics, and survival time.

Data processing: Data were statistically analyzed using Jamovi 2.3.28.0 software; survival analysis by survival module using packages: survival, survminer, finalfit

Results

Baseline and operative characteristics

During the 5-year period from 01/2019 - 12/2023 at the Organ Transplantation Center - Viet Duc University Hospital, there were 41 patients with HCC treated by LLR. The average age was 56.8 ± 12 y/o, mostly male (male/female ratio of 5.8). The patients had an average BMI of 22.4 ± 2.12 (19.3 - 29.1). The rate of hepatitis B infection was 78.0%. Preoperative liver function was mainly Child-Pugh A (97.6%) and ALBI grade 1 (80.5%). Total bilirubin concentration before surgery was 13.06 ± 5.22 $\mu\text{mol/L}$. 63.4% had AFP < 20ng/ml, 17% had AFP ≥ 400 ng/ml. 37 patients underwent successful laparoscopic liver resection, the conversion rate for open surgery was 9.8% due to intraoperative bleeding. Minor liver resection accounted for 78.0%. The intraoperative blood transfusion rate was 18.9%. The average surgical time was 192 ± 66.1 minutes.

The majority of patients in the study were classified as high level of difficulty according to the Ban Daisuke scale. All cases of failed LLR were in the high difficulty level. The failure rate in the high difficulty level was 15.4%. 62.2% of patients achieved a liver resection margin ≥ 0.5 cm, 83.8% had moderately differentiated tumors. The patients

were mostly in TNM stage IB and II (37.8% and 43.2%, respectively). Postoperative complications were mostly grade I, mainly minor pleural

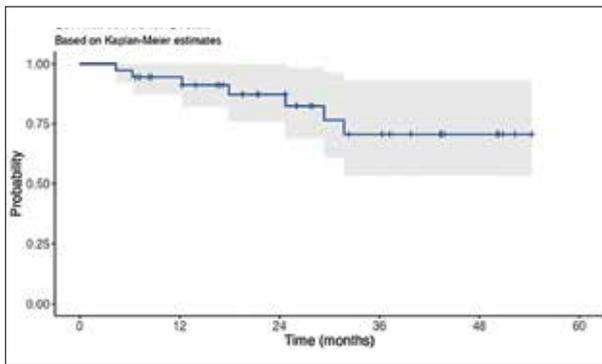
effusions. There were no patients with liver failure or postoperative death. The rate of complications above grade IIIA was 5.4%.

Table 1. Tumor characteristics in imaging

Variables		No. of patients	%
Number of tumors	Single	35	85.4%
	2 – 3	5	12.2%
	> 3	1	2.4%
	Mean	1.20 ± 0.56 (Min: 1 – Max: 4)	
Tumor size (cm)	≤ 2	4	9.8%
	≤ 5 cm	11	26.8%
	2 < x ≤ 3		
	> 5cm	10	24.4%
	3 < x ≤ 5	16	39.0%
Mean	4.02 ± 1.91 (Min: 1.3 – Max: 9.8)		
Type of liver resection			
<i>Minor resection (n=30)</i>			
1 segment	Tumorectomy	1	2.7%
	Segment 1	0	0%
	Segment 2	0	0%
	Segment 3	0	0%
	Segment 4b	1	2.7%
	Segment 5	3	8.1%
	Segment 6	7	18.9%
	Segment 7	0	0%
	Segment 8	1	2.7%
<i>Major resection (n=7)</i>			
2 segments	Posterior	7	18.9%
	Left lateral	6	16.2%
	Segment 5, 6	4	10.8%

3 segments	Left hepatectomy	4	10.8%
	Extended posterior hepatectomy	1	2.7%
>3 segments	Right hepatectomy	1	2.7%
	Extended left hepatectomy	1	2.7%
Difficulty level	Low	0	0%
	Intermediate	15	36.6%
	High	26	63.4%
Mean: 7.05 ± 1.80 points (4-11)			
Resection margin (cm)	< 0.5 cm	14	37.8%
	0.5 – 1 cm	11	29.7%
	>1 cm	12	32.4%
Tumor size (mean ± SD)		4.7 ± 2.5 cm	
Microvascular invasion	Yes	18	48.6%
	No	19	51.4%
Tumor differentiation	High	3	8.1%
	Intermediate	31	83.8%
	Low	3	8.1%
Tumor staging	IA	4	10.8%
	IB	14	37.8%
	II	16	43.2%
	IIIA	3	8.1%
	Above IIIB	0	0%
Complications grading (Clavien – Dindo classification)	Grade I	25	67.6%
	Grade II	2	5.4%
	Grade IIIA	1	2.7%
	Grade IIIB	1	2.7%

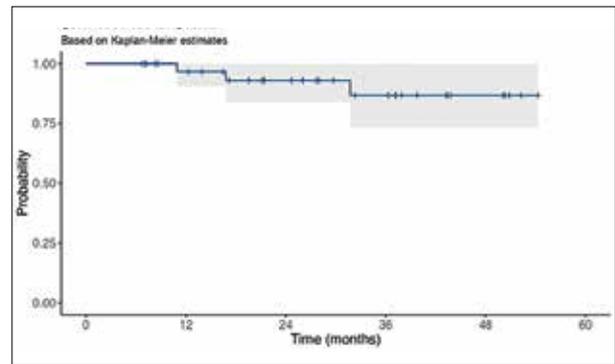
Long-term outcomes and prognostic factors



1A

The disease-free survival (DFS) time was 44.5 ± 3.19 months.

The DFS rates at 1, 2, 3, and 4 years were 94.4 %; 87.2 %; 70.6 %, and 70.6 %, respectively.



1B

The overall survival (OS) time was 50.0 ± 2.30 months.

The OS rates at 1, 2, 3, and 4 years were 96.7 %; 92.9 %; 86.8 %, and 86.8 %, respectively.

Figure 1. Disease-free survival (1A) and overall survival (1B)

Preoperative AFP concentration < 400 ng/mL and a resection margin > 0.5 cm were identified as favorable prognostic factors for better overall survival. Overall survival of patients in the moderate difficulty group

was longer than that of patients in the high difficulty group; tumor size ≤ 5 cm showed longer survival than that of patients with tumor size > 5 cm, however, the difference was not statistically significant.

Table 2. Prognostic factors of the survival outcomes

Characteristics		DFS (months)	p	OS (months)	P
Pre-operative AFP	< 400 ng/ml	45.9 ± 3.32	0.29	52.4 ± 1.80	0.024
	≥ 400 ng/ml	36.8 ± 9.37		38.1 ± 8.89	
Difficulty level	Intermediate	47.8 ± 4.00	0.37	54.3 ± 0.00	0.11
	High	42.3 ± 4.53		46.7 ± 3.93	
Tumor size	≤ 5 cm	44.0 ± 4.48	0.87	54.3 ± 0.00	0.068
	> 5 cm	45.1 ± 4.57		45.7 ± 4.38	
Resection margin	> 0.5 cm	47.6 ± 3.52	0.19	54.3 ± 0.00	0.018
	≤ 0.5 cm	38.9 ± 5.90		42.9 ± 5.45	

Discussion

Baseline characteristics

During the study period from January 2019 to December 2023, 41 patients underwent laparoscopic liver resection at the Organ Transplantation Center. The average age was 56.8 ± 12.9 , mostly males, similar to some domestic and international studies. [6–8] The patients in the study had an average body mass index of 22.4, which was favorable for laparoscopic surgery.

In our study group, the average tumor size based on pathological examination was 4.7 cm, larger than reported by some other authors such as Yoon (Korea, 2019) at 2.8 cm; Yamamoto (Japan, 2019) at 1.70 cm; Ghielmetti (Switzerland, 2021) at 2.56 cm. [8–10]

Difficulty of laparoscopic liver resection

Liver resection has been widely applied, however, it is still a difficult technique and many authors have proposed models to classify the difficulty through scales such as Halls, Hasegawa, Kawaguchi and Iwate. Andrea Ruzzenente argued that the difficulty grading scale is useful in predicting the possibility of intraoperative events and early postoperative outcomes. Most studies found that the modified IWATE scale is the most important factor in predicting the duration of surgery, blood loss and the need for conversion to open surgery, thereby ranking as the most important variable in predicting the overall surgical outcome. [11] In this study, we used the Ban Daisuke (IWATE) scale to evaluate the surgical difficulty due to its ease of use, convenience, and effectiveness. [5]

In our patient group, the surgical difficulty score had a high positive correlation with the intraoperative blood transfusion volume ($r(5) = 0.811$; $p = 0.027$) and total operative time ($r(35) = 0.623$; $p < 0.001$) and a moderate positive correlation with mortality ($r(34) = 0.365$; $p = 0.029$). There was no correlation between the surgical difficulty score and the rate of postoperative complications or tumor recurrence.

Surgical outcomes

Most of the surgeries were minor liver resections,

similar to other studies. [6], [8], [12] In our study, there was 1 patient who underwent LLR for segment VIII tumor and simultaneous right kidney resection. Postoperative pathology confirmed HCC in the liver and RCC in the kidney. During the latest follow-up, this patient had no recurrence.

Intraoperative blood loss, intraoperative and postoperative blood transfusions were factors associated with an increased rate of postoperative recurrence. There were 3 cases (8.1%) of intraoperative complications, all of which were bleeding-related complications. Our intraoperative complication rate was comparable to that of Tran Cong Duy Long (2016) at 5% and Tsai (Taiwan, 2019) at 9.8%. [6], [12] The intraoperative blood transfusion rate was 18.9%. The mean intraoperative blood transfusion volume was 735.7 ml. The nonspecific immunosuppressive effect caused by blood transfusion may explain the increased postoperative complication rate and recurrence rate after hepatectomy in HCC. [13]

Short-term outcomes and complications

Short-term outcomes

In our study, the average tumor size was 4.7 ± 2.5 cm. The average resection margin was 1.09 cm. Cheng et al. (Taiwan 2022) analysed 983 patients operated between 2003 to 2009, comparing group with resection margins ≤ 1 mm and > 1 mm, there was no difference in recurrence rates or survival rates between the two groups after adjusting for various factors. [14]

The rate of low differentiation in our study was 8.1%, comparable to Soubrane (2014) at 9%. [13] Low differentiation is a poor prognostic factor for recurrence and postoperative survival. [12], [14]

Complications

The rate of postoperative complications classified as grade III or higher was 5.4% in 2 patients. We had one patient with postoperative bleeding on the 3rd day (rate of 2.7%), but the patient only needed a blood transfusion and did not need to be reoperated. This patient was also the patient with the slowest bowel movement recovery (4 days). There was

1 patient (2.7%) with grade IIIB complications who required general anesthesia to close the abdominal wall due to a disrupted incision on the 6th day. This patient was a 73-year-old male with a history of open cholelithiasis surgery, who had undergone laparoscopic liver resection, and was the only patient who had a common bile duct drainage during surgery. The patient was discharged in stable condition after 14 days.

Long-term outcomes

The longest follow-up time was 54.3 months. During the study period, 7 patients had recurrence and 3 patients died. In our study, the disease-free survival time was better than that of other authors. [6], [12], [13] The survival rate at 1 year after surgery was quite similar, but it was higher over longer follow-up periods compared to several other authors. This may be due to careful patient selection criteria, suitable surgical strategy, close follow-up and timely intervention when recurrence occurred. Postoperative complications negatively affect the disease-free survival time. Factors affecting the overall survival time include: preoperative AFP concentration; surgical difficulty level (Ban Daisuke); tumor size > 5 cm and resection margin > 0.5 cm. There are many factors affecting the recurrence rate. Cheng et al. (Taiwan - 2022) concluded that intrahepatic recurrence was the most common type, and it related to the degree of portal hypertension and adverse biological factors of the tumor. [14] In our study, disease-free survival did not differ with respect to preoperative AFP concentration of 400 ng/ml, difficulty of surgery; resection margin of 0.5 cm; tumor size of 5 cm. However, in the assessment of overall survival, preoperative AFP concentration < 400 ng/ml and resection margin > 0.5 cm were associated with better overall survival (see Table 2). Soubrane's (2014) univariate analysis found that AFP concentration > 200 ng/ml, cirrhosis, multiple tumors, satellite nodules, vascular invasion, and low differentiation were poor prognostic factors for overall survival. [13] Cheng et al. (2022)

showed no difference in overall survival between the 2 groups with resection margins ≤ 0.1 cm and > 0.1 cm. The authors also concluded that although wider resection margins could be achieved, resection with narrow resection margins can still be an effective treatment strategy. [14]

Conclusion

Laparoscopic liver resection has been performed in many centers around the world. This study showed many advantages, feasibility and safety of the surgery with an average postoperative hospital stay of 6.95 days and a low complication rate. The success rate of laparoscopic liver resection was 90.2%. Overall survival was 50.0 months. The Ban Daisuke liver resection difficulty scale is a valuable tool in predicting surgical outcomes, helping to choose a surgical strategy that fits the surgeon's learning curve. Careful patient selection, close follow-up and timely intervention in case of recurrence are important factors determining the long-term survival benefits.

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