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Original Article

Laparoscopic versus open hepatectomy for hepatocellular carcinoma: short- and long-term outcomes comparison

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Abstract: Despite the theoretical advantages of laparoscopic hepatectomy, it is still not considered the standard treatment for hepatocellular carcinoma patients because of criticism concerning oncologic stability. This study aimed at examining the short- and long-term follow-up results of laparoscopic hepatectomy versus open hepatectomy for hepatocellular carcinoma and at investigating clinical outcomes, oncologic safety, and any potential advantages of laparoscopic hepatectomy for hepatocellular carcinoma. A series of 53 patients who underwent laparoscopic hepatectomy (Lap group) for hepatocellular carcinoma were matched with 53 patients who underwent open hepatectomy during the same time period (Open group). The short- and long-term outcomes were compared between the two groups of patients. The patients who underwent the laparoscopic procedure showed a significantly faster recovery and less blood loss compared with patients who underwent open surgery. No differences were found in 5-year overall and disease-free survival rates. Our results suggested that the laparoscopic approach was as safe as the open alternative. Laparoscopic hepatectomy has been shown to be a favorable surgical option with better short-term outcomes and similar long-term oncological control compared with open hepatectomy.

Keywords: Hepatocellular carcinoma, hepatectomy, minimally invasive surgery, survival

Introduction

Hepatocellular carcinoma represents one of the leading cause of death worldwide, and the indications for laparoscopic surgery have expanded gradually [1-8]. Indeed, laparoscopic hepatectomy has been shown to have more benefits for postoperative recovery, such as blood blood, postsurgical pain and hospital stay, leading to a general acceptance of laparoscopic surgery as an alternative to conventional open surgery for hepatocellular carcinoma [5-10]. However, despite the theoretical advantages of laparoscopic hepatectomy, it is still not considered the standard treatment for hepatocellular carcinoma patients because of criticism concerning oncologic stability. Potential risks regard port-site recurrence after curative resection of tumor and positive surgical margin. In fact, given the technical difficulty of laparoscopic hepatectomy for hepatocellular carcinoma, laparoscopic liver resection is often limited by the need for experienced surgeons [11-13]. Thus, from a public health perspective, there are controversies regarding the cost-effective value of this treatment, taking into account such issues and the greater economic costs compared with conventional open hepatectomy for hepatocellular carcinoma.

This study aimed at examining the short- and long-term outcomes of laparoscopic hepatectomy versus open hepatectomy for hepatocellular carcinoma over a period of 7 years in our institution and at investigating clinical outcomes, oncologic safety, and any potential advantages of laparoscopic liver resection for hepatocellular carcinoma.

Patients and methods

This study complied with the Declaration of Helsinki. This retrospective research was approved by our local ethics committees. The

Table 1. The demographic parameters

	Lap group (*n* = 53)	Open group (*n* = 53)	*P* value
Age (years)	49 (36-72)	51 (38-68)	0.760
Sex			0. 529
Male	38	35	
Female	15	18	
ASA score			0.552
I	33	36	
II	19	16	
III	1	1	
ICG retention at 15 min (%)	29 (13-34)	27 (11-35)	0.658
Underlying liver disease			0.624
Hepatitis B virus	41	38	
Hepatitis C virus	8	8	
Alcoholic hepatitis	4	7	
Type of resection			0.433
Left lateral sectionectomy	21	25	
Subsectionectomy	32	28	

Table 2. Pathological data

	Lap group (*n* = 53)	Open group (*n* = 53)	*P* value
Histology			0.927
Well differentiated	24	23	
Moderately	15	17	
Differentiated	11	9	
Poorly differentiated	3	4	
Undifferentiated			
Tumor size (cm)	3 (2-5)	3 (1-6)	0.581
Margin status (R0/R1/R2)	53/0/0	53/0/0	1.000
Pathological TNM stage			0.506
I	41	38	
II	12	15	

Table 3. Surgical outcomes

	Lap group (*n* = 53)	Open group (*n* = 53)	*P* value
Operative time (min)	180 (150-380)	150 (120-280)	0.025
Blood loss (ml)	210 (190-450)	290 (210-540)	0.012
Length of hospital stay (d)	10 (7-25)	12 (8-35)	0.015
Need of analgesic injection	2 (1-4)	3 (2-6)	0.030

need for informed consent from patients was waived because of its retrospective nature.

This matched case-control study investigated a series of 53 patients (Lap group) who received laparoscopic hepatectomy between January 2008 and January 2015. For the analysis, the patients who required conversion to an open procedure were excluded, and the patients who underwent resection without radical intent or R2 resection were also excluded from this group. The control group (Open group) included an equal number of patients (*n* = 53) from a cohort that underwent conventional open hepatectomy for hepatocellular carcinoma during the same period. The Open group was identified from this cohort by random matching with the Lap group for age, gender, liver function, underlying liver disease, type of surgery, and American Society of Anesthesiologists (ASA) class. The matching was performed using a computer-generated program. Patients with Child-Pugh class A cirrhosis, tumor size smaller than 5 cm, tumor located in the peripheral segments, tumors resectable by limited segments and without previous upper abdominal surgery were considered for laparoscopic hepatectomy with radical intent.

Liver function, serum alpha fetoprotein (AFP), abdomen computed tomographic scan or magnetic resonance imaging was performed for all the patients [14-17]. Positron emission tomography-computerized tomography (PET-CT) was performed in selected cases. Types of liver resection were based on the Brisbane 2000 classification [18]. Anatomical resections were preferred over non-anatomical hepatectomy when an indocyanine green test showed that the liver function could tolerate anatomical resection. Non-anatomic resections were performed for small peripheral lesions. Details of laparoscopic and open hepatectomy have been reported in previous literatures [13]. The resected specimens were subjected to histologic examination as described by previous literatures.

Table 4. Postoperative adverse events

	Lap group (n = 53)	Open group (n = 53)	P value
Overall complications	16	19	0.536
Major complications			-
Intraabdominal bleeding	1	0	
Intra-abdominal abscess	0	0	
Bile leakage	1	2	
Liver failure	1	2	
Minor complications			-
Ileus	3	5	
Pneumonia	2	4	
Postoperative ascites	3	3	
Bile leakage	5	3	

Table 5. Tumor recurrence data

Outcomes	Laparoscopy (n = 59)	Open (n = 59)	P
Tumor recurrence	20	24	0.430
Recurrence stie			
Locoregional	9	12	
Intrahepatic	8	10	
Local lymph nodes	1	2	
Distant	10	11	
Brain	2	3	
Lung	5	4	
Distant lymph nodes	1	2	
Bone	1	1	
Adrenal gland	1	1	
Mixed	1	1	
Time to recurrence (median)	21	18	0.079

The outcomes measured for comparison between the Lap and Open groups included blood loss, duration of hepatectomy, postoperative hospital stay, status of surgical margin, intra- and postoperative complications. The stage of hepatocellular carcinoma was based on the 7th edition of the TNM classification of hepatocellular carcinoma which was proposed by Union Internationale Contre le Cancer (UICC) and American Joint Committee on Cancer (AJCC) [19-22]. For those of the patients operated before 2010, their staging was recalculated to match the 7th TNM classification proposed by UICC and AJCC. Postoperative complications, morbidity occurring within 30 postoperative days, were classified using Clavien-Dindo classification, which simplified the definition of postoperative complications and graded the severity of these events. The definition of Clavien-Dindo system was as follows: Grade 1: oral medication or bedside medical care required; Grade 2: intravenous medical therapy required; Grade 3: radiologic, endoscopic, or operative intervention required; Grade 4: chronic deficit or disability associated with the event; and Grade 5: death related to surgical complication. Major complications were defined as grades 3, 4 and 5. Major complications were defined as grades 3, 4 and 5. Minor complications were classified as 1 and 2 [23].

Follow-up data were reviewed from follow up database. Patients follow-up were scheduled to perform liver function, serum AFP, abdomen computed tomographic scan or magnetic resonance imaging every 3-4 months after hepatectomy. The overall survival was assessed from the date of hepatectomy until the last follow up or death of any cause. The disease-free survival was calculated from the date of hepatectomy until the date of cancer recurrence or death from any cause. The last follow up was July 2015.

For statistical analysis, data were presented as mean and standard deviations for variables following normal distribution and were analyzed by t test. For variables following non-normal distribution, results were expressed as median and range and were compared by nonparametric test. Differences of semiquantitative results were analyzed by Mann-Whitney U-test. Differences of qualitative results were analyzed by chi-square tests or Fisher exact test as appropriate. Survival rates were analyzed using the Kaplan-Meier method; differences between the two groups were analyzed with the log-rank test. $P < 0.05$ was considered statistically significant using SPSS 14.0 for windows (SPSS Inc., Chicago, IL, USA).

Results

No statistically significant difference was found in the demographic parameters between the two patient populations (**Table 1**).

Resection margins were similar in both groups, and none of them was found to be positive.

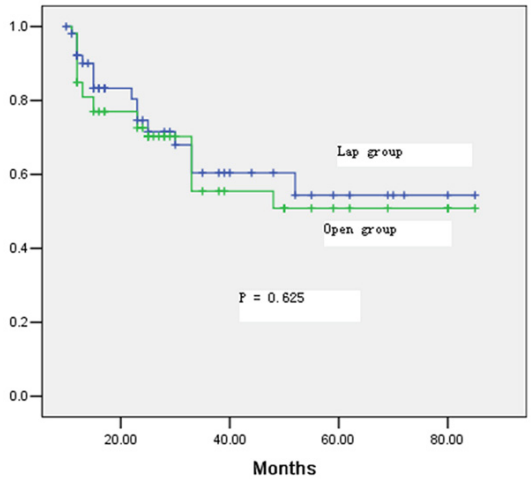

Figure 1. Kaplan-Meier curves for comparison of overall survival between laparoscopic hepatectomy and open hepatectomy.

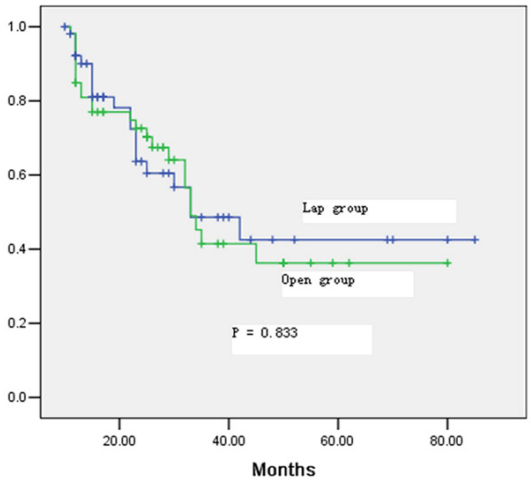

Figure 2. Kaplan-Meier curves for comparison of disease-free survival between laparoscopic hepatectomy and open hepatectomy.

There were no significant differences in TNM staging (**Table 2**).

A significant difference in the operative time between the two groups was observed (P = 0.025) (**Table 3**). Moreover, significantly lower blood loss during laparoscopic surgery compared with open surgery was found (P = 0.012). Compared with patients who underwent open surgery, laparoscopic colorectal surgery obviously caused less pain for patients leading to lower need of analgesic (P = 0.030) and less hospital recovery time (P = 0.015).

No significant difference was found in the number of postoperative 30-day adverse events during the operation procedures between the laparoscopy and open surgery groups (**Table 4**). Most of the complications were minor in both groups.

The mean follow-up times were 35 and 37 months in the laparoscopic and open surgically treated groups, respectively. No significant difference in the rate and site of cancer recurrence between the two groups was found (**Table 5**). According to the results of Kaplan-Meier analysis, laparoscopic and open surgery groups did not have significant differences in overall survival trend (**Figure 1**) and disease-free survival (**Figure 2**).

Discussion

Laparoscopic surgery has evolved rapidly and gained worldwide acceptance as a viable alternative for open surgical procedures. Laparoscopic coloectomy and distal gastrectomy have already started replacing their open surgery counterparts; however, laparoscopic hepatectomy is slow to gain such acceptance. The main reason is the difficultly of the technique [24].

Nonetheless, numerous studies have demonstrated increased skills with laparoscopic hepatectomy to be able to consider it as a replacement for open hepatectomy, or at least adding it to their armament of procedures [11-13, 25-27]. A summary of our results shows that open hepatectomy for hepatocellular carcinoma had a shorter operative time than laparoscopic hepatectomy; however, laparoscopic hepatectomy had less blood loss, transfusion requirement, less morphine requirement and shorter length of postoperative hospital stay. Furthermore, laparoscopic hepatectomy and open hepatectomy had no difference in postoperative parameter, such as postoperative 30-day adverse events and short-term oncological outcomes. More importantly, no difference was found between the two groups regarding survival outcomes or tumor recurrence.

Similarly variable operative and postoperative findings were echoed by the comparative studies with larger patient cohorts. Hadrien Tranchart and his hospital colleagues reported that the patients undergoing laparoscopic hepatectomy for hepatocellular carcinoma had significantly less blood loss, transfusion rate,

postoperative stay and early recovery. Hyeyoung Kim and his hospital colleagues [11] found that only postoperative stay was less for the laparoscopic hepatectomy group, otherwise no difference was found. Tan To Cheung and his hospital colleagues [13] reported that the laparoscopic hepatectomy group had comparable longer operative time and less blood loss and hospital stay. Jonghun J. Lee [25] and his hospital colleagues found a significant difference with the severity of complications favoring the laparoscopic hepatectomy group. Keun Soo Ahn and his hospital colleagues [26] also reported that the laparoscopic hepatectomy needed a shorter hospital length of stay.

Hence thus far, from the reported literatures, it is evident that laparoscopic hepatectomy is at least as safe and efficient as open hepatectomy, with the only parameter favoring open hepatectomy that stands out is the operative time. Nonetheless, the survival and tumor recurrence rate are vital to truly determine if laparoscopic hepatectomy can replace open hepatectomy.

The long-term outcomes of laparoscopic hepatectomy for hepatocellular carcinoma from literatures have not yet been determined. In the present study, the follow-up data, including rates of local recurrence, distant metastasis, overall survival and disease-free survival, were assessed, and the median follow-up time was about 35 months for each group. With regard to the cancer recurrence rate, patients who underwent laparoscopic hepatectomy displayed rates comparable to those who underwent open hepatectomy. The study revealed that the recurrence rate for patients with hepatocellular carcinoma was similar with literatures. The number of patients with recurrent hepatocellular carcinoma was similar in the laparoscopy and open hepatectomy groups of these studies, and these results were comparable to the present study. Similar overall and disease-free survival rates in the two groups confirmed the long-term oncological safety of the laparoscopic hepatectomy compared with open hepatectomy. With regard to the 5-year overall survival rate, a certain degree of controversy has been found among different studies (data ranging between 40% and 92%) due to the difference in surgical indication and follow-up period [11-13, 25-34]. The present results were consistent with those findings in which laparoscopic hepatectomy appeared to be equivalent to the open method.

The present study was limited in that the patients were not assigned randomly into the two treatment arms. However, as there were no differences in demographic data, we suggest that this bias had a negligible affect on the results. In addition, the mean follow-up time was not very long (median 35 months), which may cause deletions of the long-term follow-up results; thus, we cannot provide a more reliable basis with regard to the long-term outcomes.

In conclusion, comparing laparoscopic hepatectomy to open hepatectomy, laparoscopic hepatectomy has less blood loss, less blood transfusion requirement, less morphine requirement, and less length of hospital stay. However, laparoscopic hepatectomy seems to have longer operative times. No difference was found between the two groups regarding Clavien-Dindo classification of postoperative 30-day complication rates or pathological findings. Furthermore, there was no difference between the laparoscopic hepatectomy and open hepatectomy groups regarding 5-year overall and recurrence-free survival rates. However, further randomized studies are required to verify the results.

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Disclosure of conflict of interest

None.

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