Laparoscopic hepatectomy versus open hepatectomy for hepatocellular carcinoma in 158 patients: A prospective cohort study

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Abstract

Background

Hepatocellular carcinoma (HCC) ranks as the fourth most common cancer and the third leading cause of cancer-related mortality worldwide. With the development of minimally invasive surgical techniques, laparoscopic hepatectomy is becoming more prevalent in liver surgery. There are multiple reports to evaluate the safety and feasibility of laparoscopic liver resection. Unfortunately, the jury is still out on whether laparoscopic hepatectomy is better than open hepatectomy. The aim of this study is to compare the perioperative and postoperative long-term outcomes of open hepatectomy and laparoscopic hepatectomy for hepatocellular carcinoma, and to evaluate the safety and efficacy of the two surgical methods for hepatocellular carcinoma.

Methods

A prospective cohort study of patients who underwent major hepatectomy for hepatocellular carcinoma between October 2017 and September 2018 was performed. And these patients were followed for 24 months after surgery. There are 158 patients involved in the present study and they were randomly divided into two groups, LH group (n=60), and OH group (n=98). And all of 158 patients underwent hepatectomy. Continuous data were compared by one-way ANOVA, and categorical data were compared by Fisher's exact test or the c2 test. Survival curves were calculated by the Kaplan–Meier method and compared using the log-rank test. The study was approved by the ethics committee of Union Hospital. (No. WHUH2018S002) and registered in the International Clinical Trial Registry (No. NCT03585166). Informed consent was signed by all patients.

Results

Incision lengths of LH (5.14±3.11cm) were shorter than OH (20.92±6.44cm), P<0.001. Operating time of LH (398.53±170.51 minutes) were longer than OH (257.74±91.31 minutes), P=0.003. Hospital stay of LH (17.72±5.82 days) were shorter than OH (21.42±8.44 days), P<0.001. The average hospitalization costs of LH group (82741.18±26128.81) were significantly less than OH group (94998.75±30499.64), p=0.011<0.05. The incidence of total complications was also lower in LH group than in OH group (P=0.001). Postoperatively, the leukocyte was significantly lower at 1st day in LH group (9.79±2.92 G/L) than in OH group (12.6±4.85 G/L), p<0.001. The aspartate aminotransferase (AST) was significantly lower at 7th day in LH group (39.25±16.63 U/L) than in OH group (62.49±67.77 U/L), p=0.01<0.05. The albumin was significantly higher at 3rd day in LH group (34.21±3.94 g/L) than in OH group (31.24±5.23 g/L), p<0.001. The albumin was significantly higher at 7th day in LH group (35.26±3.73 g/L) than in OH group (33.31±4.51 g/L), p=0.006<0.05. Direct bilirubin was significantly higher at 1st day in LH group (10.28±10.70 µmol/L) than in OH group (315.03±15.71 µmol/L), p=0.04<0.05. The follow-up time after surgery was 24 months (1-24). The mean follow-up time after surgery was 17.94±9.132. Log rank test was performed to compare overall survival rates between the two groups. There were no statistically
significant differences with 2-year survival rate between LH and OH group for liver cancer patients, nor was disease-free survival.

Conclusions

Laparoscopic hepatectomy surgery supplied a lower incision lengths, hospital stay and incidence of total complications. Laparoscopic hepatectomy was cheaper the open hepatectomy.

There were no statistically significant differences with 2-year survival rate between the two group for liver cancer patients, nor was disease-free survival.

Background

Hepatocellular carcinoma (HCC) ranks as the fourth most common cancer and the third leading cause of cancer-related mortality worldwide \(^{[1\sim2]}\). Although there are many choices for the treatment of HCC, including hepatectomy, liver transplantation, interventional therapy, chemoradiotherapy, targeted therapy, and immunotherapies. Surgical resection is still the most effective treatment for patients with early HCC. There are two surgical methods for primary liver cancer, which are open hepatectomy (OH) and laparoscopic hepatectomy (LH) \(^{[3]}\). With the development of minimally invasive surgical techniques, laparoscopic hepatectomy is becoming more prevalent in liver surgery. It is considered to have less bleeding, shorter hospital stay, and fewer complications, as compared with open hepatectomy. Whether laparoscopic surgery has a significant therapeutic advantage over open surgery in certain segments of the liver or tumors of a certain size has not been determined.

There are multiple reports to evaluate the safety and feasibility of laparoscopic liver resection. Unfortunately, the jury is still out on whether laparoscopic hepatectomy is better than open hepatectomy \(^{[4]}\). This study is a follow-up report of our previous study. The aim of this study is to compare the perioperative and postoperative long-term outcomes of open hepatectomy and laparoscopic hepatectomy for hepatocellular carcinoma.

Methods

Patient selection

The hepatocellular carcinoma patients admitted to the Department of Hepatobiliary Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, from October 2017 to September 2018. This is a prospective cohort study. Patients meeting the following criteria were included in the study: (1) regardless of gender and age; (2) normal vital organ function; (3) meeting the requirements of general anesthesia; (4) a tumor diameter of < 10 cm on imaging; (5) no tumor thrombus in the portal vein, bile duct or inferior vena cava; (6) Child-Pugh grade A or B; (7) no extrahepatic metastasis; (8) no active hepatitis. Patients who were excluded with a severe organic disease or hepatic cirrhosis, or a conversion from a laparoscopic to an open surgery \(^{[5]}\).
There are 158 patients involved in the present study and they were randomly divided into two groups, LH group (n = 60), and OH group (n = 98). All patients were followed up until August 2020, by clinic visits every 3 months in the first year after surgery, every 4 months during the second year after surgery and every 6 months thereafter. The study was approved by the ethics committee of Union Hospital. (No. WHUH2018S002) and registered in the International Clinical Trial Registry (No. NCT03585166). Informed consent was signed by all patients.

Surgical Procedures

Surgery for LH

This operation was performed in accordance with the consensus of Chinese experts on laparoscopic hepatectomy\(^6\). Specifically \(^5, 7\), The patient was placed in the left semi-recumbent position with total venous anesthesia. Intra-abdominal pressure was maintained at 13–15 mmHg (1 mmHg = 0.133 kPa). Four 10-mm trocars are commonly used for liver anatomy, and one 10 mm trocar is inserted above the umbilicus for camera. The vessel and parenchyma tissue were dissected by harmonic scalpel (Ethicon Endo-Surgery, USA) and laparoscopic cavitation ultrasonic surgical aspirator (Valleylab, USA). Hem-o-lock clips (Weck Surgical Instruments, USA) were used for vessels of \(\geq 5\) mm in diameter. Intraoperative ultrasound examination (Toshiba, Japan) was used to determine the location of the main catheter in the liver and the size of the tumor, including their relationships, and to look for any metastatic sites or tumor clots\(^8\).

Surgery for OH

The same anesthesia with LH was performed, patients were placed in supine position and the laparotomy was performed through right subcostal incision. The vascular and parenchymal tissues were separated by ultrasonic sputum aspirator. During the operation, bipolar electrocoagulation was used to stop the blood\(^5\).

Postoperative hospitalization and follow-up

Postoperatively, all patients were taken off by the same care and monitoring. Liver function tests and routine blood tests were conducted at 1, 3, and 7 days. When the drainage fluid was serous and in the absence of bile leakage, the abdominal drainage tube was removed. Also, an ultrasound imaging was usually performed before discharge.

After discharge, all these patients were followed at 1 months, 3 months, 6 months, 12 months, and 24 months. The follow-up indexes included adverse reactions such as nausea, diarrhea, liver pain and fever, complications such as biliary leakage, bleeding, infection, ascites pleural effusion, number and size of recurrent tumors, and death.

Statistical Analysis
Continuous variables were indicated by means and standard deviations, and categorical variables were indicated by number and percentages. Continuous data were compared by one-way ANOVA, and categorical data were compared by Fisher’s exact test or the χ² test. Overall survival was defined as the interval between the initial surgery and death or the date of the last or most recent follow-up visit. Disease-free survival was defined as the interval between the initial surgery and the date when recurrence was detected by radiological examination [3]. Survival curves were calculated by the Kaplan–Meier method and compared using the log-rank test. All analysis were performed using SPSS 23. P < 0.05 was considered statistically significant.

Results

Patient Characteristics

The clinico-pathological characteristics of the 158 patients are shown in Table I, which include age, gender, education, income, health insurance, body mass index (BMI), tumor size(cm), hospitalization cost, hepatitis B positive rate, alpha fetoprotein positive and Child-Pugh grade. There were no significant differences between the two groups with these clinicopathological parameters.
| Characteristic                      | LH group        | OH group        | F/χ² | P    |
|------------------------------------|-----------------|-----------------|------|------|
| Age(year)                          | 53.10 ± 9.756   | 53.99 ± 10.703  | 0.275| 0.601|
| Gender(%)                          |                 |                 |      |      |
| Female                             | 52(86.67)       | 78(79.59)       | 1.278| 0.258|
| Male                               | 8(13.33)        | 20(20.41)       |      |      |
| Education                          |                 |                 |      |      |
| Primary schools and below          | 16(26.67)       | 30(30.61)       | 7.717| 0.103|
| junior high school                 | 17(28.33)       | 39(39.80)       |      |      |
| High school                        | 17(28.33)       | 15(15.31)       |      |      |
| College degree or above            | 10(16.67)       | 14(14.29)       |      |      |
| Income                             |                 |                 | 0.73 | 0.393|
| 0-5000                             | 39(65.00)       | 57(58.16)       |      |      |
| 5000-                              | 21(35.00)       | 41(41.84)       |      |      |
| Health insurance                   |                 |                 |      |      |
| Health insurance in cities and towns| 5(8.33)        | 9(9.18)         | 7.613| 0.107|
| Commercial insurance               | 1(1.67)         | 3(3.06)         |      |      |
| Provincial health insurance        | 42(70.00)       | 61(62.24)       |      |      |
| New rural cooperative medical insurance| 5(8.33)     | 21(21.43)       |      |      |
| Self-paying                        | 7(11.67)        | 4(4.08)         |      |      |
| BMI                                | 23.55 ± 2.75    | 23.62 ± 2.59    | 0.029| 0.865|
| Tumor size(cm)                     | 5.15 ± 2.80     | 5.65 ± 2.58     | 0.922| 0.634|
| tumor type                         |                 |                 |      |      |
| Single                             | 39(65)          | 60(61.22)       | 0.227| 0.634|
| Multiple                           | 21(35)          | 38(38.78)       |      |      |
| HBsAg                              |                 |                 |      |      |
| Positive                           | 46(76.67)       | 76(77.55)       | 0.017| 0.898|
| Negative                           | 14(23.33)       | 22(22.45)       |      |      |
| Characteristic                     | LH group | OH group | F/χ²  | P   |
|----------------------------------|----------|----------|-------|-----|
| AFP                              |          |          |       |     |
| Positive                         | 29(48.33)| 61(62.24)| 2.938 | 0.087|
| Negative                         | 31(51.67)| 37(37.76)|       |     |
| Child-Pugh grade                 |          |          |       |     |
| A                                | 53(88.33)| 84(85.71)| 0.222 | 0.638|
| B                                | 7(11.67) | 14(14.29)|       |     |

Perioperative outcomes of the patients who underwent LH and OH

Perioperative outcomes of the patients who underwent LH and OH were shown in table 2. Incision lengths of LH were shorter than OH. The average incision lengths of LH group was 5.14 ± 3.11 cm, and the OH group was 20.92 ± 6.44 cm, P < 0.001. Operating time of LH were longer than OH. The mean operating time of LH group was 398.53 ± 170.51 minutes, and the OH group was 257.74 ± 91.31 minutes, P < 0.001. Hospital stay of LH were shorter than OH. The mean hospital stay of LH group was 17.72 ± 5.82 days, and the OH group was 21.42 ± 8.44 days, P = 0.003. The average hospitalization costs of LH group (82741.18 ± 26128.81) were significantly less than OH group (94998.75 ± 30499.64), p = 0.011 < 0.05. Significant difference was found in the Intra-operative blood transfusion, eating time, exhaust time, defecation time, use of analgesia, ambulation time, abdominal drainage, post-operative albumin transfusion between two groups, p < 0.05.
Table 2
Comparison of perioperative outcomes between the patients who underwent LH and OH

| Parameter                              | LH group    | OH group    | F/χ²  | P       |
|----------------------------------------|-------------|-------------|-------|---------|
| Incision length(cm)                    | 5.14 ± 3.11 | 20.92 ± 6.44 | 315.079 | < 0.001 |
| Number of patients with intra-operative bleeding(%) |             |             | 0.282 | 0.595   |
| Yes                                    | 28(46.67)   | 50(51.02)   |       |         |
| No                                     | 32(53.33)   | 48(48.98)   |       |         |
| Intra-operative bleeding(ml)           | 632.81 ± 591.28 | 739.8 ± 859.63 | 0.989 | 0.487   |
| Number of patients with intra-operative blood transfusion(%) |             |             |       |         |
| Yes                                    | 48(80.00)   | 61(62.24)   | 5.484 | 0.019   |
| No                                     | 12(20.00)   | 37(37.76)   |       |         |
| Intra-operative blood transfusion (ml) | 787.50 ± 363.15 | 855.41 ± 837.31 | 0.378 | 0.540   |
| Operating time(min)                    | 398.53 ± 170.51 | 257.74 ± 91.31 | 45.597 | < 0.001 |
| Eating time (days)                     | 1.47 ± 0.75  | 1.91 ± 0.76  | 12.700 | < 0.001 |
| Exhaust time (days)                    | 2.35 ± 0.66  | 2.87 ± 0.64  | 23.933 | < 0.001 |
| Defecation time (days)                 | 3.08 ± 0.93  | 3.54 ± 0.63  | 13.665 | < 0.001 |
| Use of analgesia (days)                | 3.85 ± 1.63  | 6.59 ± 2.76  | 48.638 | < 0.001 |
| Ambulation time (days)                 | 3.93 ± 0.82  | 5.04 ± 1.28  | 36.041 | < 0.001 |
| Hospital stay (days)                   | 17.72 ± 5.82 | 21.42 ± 8.44 | 8.938  | 0.003   |
| Hospitalization cost($)                | 82741.18 ± 26128.81 | 94998.75 ± 30499.64 | 6.683  | 0.011   |
| Abdominal drainage (days)              | 8.02 ± 3.5   | 11.77 ± 7.11 | 14.520 | < 0.001 |
| Number of patients with post-operative blood transfusion (%) |             |             |       |         |
| Yes                                    | 2(3.33)      | 20(20.41)    | 9.053  | 0.003   |
| No                                     | 58(96.67)    | 78(79.59)    |       |         |
| Post-operative blood transfusion (mL)  | 1450 ± 1060.66 | 2767.5 ± 2217.29 | 0.668  | 0.423   |
**Parameter** | **LH group** | **OH group** | \( F/\chi^2 \) | \( P \)
--- | --- | --- | --- | ---
Post-operative blood transfusion time (days) | 3 ± 2.83 | 3.55 ± 2.91 | 0.065 | 0.801

Number of patients with post-operative albumin transfusion (%)

|   | LH group | OH group | \( \chi^2 \) | \( P \) |
|---|---|---|---|---|
| Yes | 20(33.33) | 68(69.39) | 19.605 | < 0.001 |
| No | 40(66.67) | 30(30.61) | 0.001 | 0.989 |

Postoperative outcomes of the patients who underwent LH and OH

Postoperative outcomes of the patients who underwent LH and OH were shown in table 3. The incidence of total complications was also lower in LH group than in OH group (\( P < 0.001 \)). The ascites(\( P = 0.001 \)), incision infection (\( P < 0.001 \)), bleeding(\( P = 0.003 \)) in LH group were significantly lower than those in OH group.

| Parameter | LH group | OH group | \( \chi^2 \) | \( P \) |
|---|---|---|---|---|
| Ascites | 4 | 27 | 10.092 | < 0.001 |
| Pleural effusion | 7 | 18 | 1.255 | 0.263 |
| Venous thrombosis of the lower extremities | 2 | 1 | 1.069 | 0.301 |
| Incision infection | 1 | 21 | 12.126 | < 0.001 |
| Bile leakage | 0 | 1 | 1* | |
| Bleeding | 2 | 20 | 9.053 | 0.003 |
| Intestinal fistula | 0 | 1 | 0.616 | 1* |
| Total | 12 | 55 | 19.883 | < 0.001 |

* Fisher’s exact test.

**Comparison of liver function between LH group and OH group**

Liver function of the patients who underwent LH and OH were shown in table 4. Preoperatively, there was no significant difference between LH group and OH group in liver function. Postoperatively, the leukocyte was significantly lower at 1st day in LH group (9.79 ± 2.92G/L) than in OH group (12.6 ± 4.85 G/L), \( p < \)
The aspartate aminotransferase (AST) was significantly lower at 7th day in LH group (39.25 ± 16.63 U/L) than in OH group (62.49 ± 67.77 U/L), p = 0.01 < 0.05. The albumin was significantly higher at 3rd day in LH group (34.21 ± 3.94 g/L) than in OH group (31.24 ± 5.23 g/L), p < 0.001. The albumin was significantly higher at 7th day in LH group (35.26 ± 3.73 g/L) than in OH group (33.31 ± 4.51 g/L), p = 0.006 < 0.05. Direct bilirubin was significantly higher at 1st day in LH group (10.28 ± 10.70 µmol /L) than in OH group (315.03 ± 15.71 µmol /L), p = 0.04 < 0.05.
Table 4  
Comparison of liver function between LH group and OH group

| Parameter      | LH group        | OH group        | F     | P     |
|----------------|-----------------|-----------------|-------|-------|
| Leukocyte (G/L) |                 |                 |       |       |
| Pre-operation  | 5.52 ± 1.88     | 5.56 ± 2.29     | 0.014 | 0.907 |
| Post-operation |                 |                 |       |       |
| 1st day        | 9.79 ± 2.92     | 12.6 ± 4.85     | 16.399| < 0.001|
| 3rd day        | 9.4 ± 2.51      | 9.37 ± 3.59     | 0.006 | 0.941 |
| 7th day        | 7.28 ± 2.06     | 7.98 ± 3.41     | 2.057 | 0.153 |
| (U/L)          |                 |                 |       |       |
| Pre-operation  | 51.68 ± 115.35  | 42.76 ± 49.3    | 0.453 | 0.502 |
| Post-operation |                 |                 |       |       |
| 1st day        | 356.52 ± 542.96 | 338.3 ± 262.81  | 0.080 | 0.778 |
| 3rd day        | 341.3 ± 398.69  | 315.36 ± 252.99 | 0.251 | 0.617 |
| 7th day        | 104.6 ± 111.8   | 110.24 ± 82.73  | 0.132 | 0.717 |
| AST (U/L)      |                 |                 |       |       |
| Pre-operation  | 43.97 ± 74.08   | 37.20 ± 18.30   | 0.745 | 0.389 |
| Post-operation |                 |                 |       |       |
| 1st day        | 342.5 ± 322.63  | 423.65 ± 334.22 | 2.252 | 0.135 |
| 3rd day        | 158 ± 182.94    | 192.94 ± 173.03 | 1.453 | 0.230 |
| 7th day        | 39.25 ± 16.63   | 62.49 ± 67.77   | 6.789 | 0.010 |
| Albumin (g/L)  |                 |                 |       |       |
| Pre-operation  | 40.35 ± 4.67    | 38.88 ± 5.33    | 3.093 | 0.081 |
| Post-operation |                 |                 |       |       |
| 1st day        | 31.8 ± 5.38     | 30.54 ± 6.21    | 1.680 | 0.197 |
| 3rd day        | 34.21 ± 3.94    | 31.24 ± 5.23    | 14.402| < 0.001|
| 7th day        | 35.26 ± 3.73    | 33.31 ± 4.51    | 7.903 | 0.006 |
| Globulin (g/L) |                 |                 |       |       |
| Pre-operation  | 25.55 ± 4.7     | 26.06 ± 5.18    | 0.387 | 0.535 |
| Post-operation |                 |                 |       |       |
| Parameter                                    | LH group      | OH group      | F       | P       |
|----------------------------------------------|---------------|---------------|---------|---------|
| 1st day                                      | 21.35 ± 3.77  | 21.87 ± 4.95  | 0.485   | 0.487   |
| 3rd day                                      | 21.67 ± 3.8   | 21.82 ± 4.71  | 0.047   | 0.828   |
| 7th day                                      | 24.21 ± 4.24  | 24.23 ± 4.75  | 0.001   | 0.984   |
| Albumin and globulin ratio                   |               |               |         |         |
| Pre-operation                                | 1.64 ± 0.34   | 1.55 ± 0.35   | 2.393   | 0.124   |
| Post-operation                               |               |               |         |         |
| 1st day                                      | 1.54 ± 0.37   | 1.46 ± 0.42   | 1.412   | 0.236   |
| 3rd day                                      | 1.62 ± 0.34   | 1.49 ± 0.41   | 3.909   | 0.050   |
| 7th day                                      | 1.5 ± 0.29    | 1.43 ± 0.35   | 1.658   | 0.200   |
| Total bilirubin (µmol/L)                     |               |               |         |         |
| Pre-operation                                | 17.52 ± 20.82 | 17.61 ± 20.70 | 0.001   | 0.979   |
| Post-operation                               |               |               |         |         |
| 1st day                                      | 24.96 ± 17.62 | 31 ± 25.48    | 2.608   | 0.108   |
| 3rd day                                      | 24.62 ± 16.48 | 28.88 ± 27.22 | 1.199   | 0.275   |
| 7th day                                      | 18.83 ± 10.04 | 22.04 ± 18.77 | 1.486   | 0.225   |
| Direct bilirubin (µmol/L)                    |               |               |         |         |
| Pre-operation                                | 7.24 ± 15.46  | 7.61 ± 14.28  | 0.024   | 0.878   |
| Post-operation                               |               |               |         |         |
| 1st day                                      | 10.28 ± 10.7  | 15.03 ± 15.71 | 4.279   | 0.040   |
| 3rd day                                      | 10.49 ± 7.8   | 14.38 ± 16.28 | 3.005   | 0.085   |
| 7th day                                      | 8.32 ± 5.63   | 11.29 ± 11.86 | 3.320   | 0.070   |

**Overall Survival Between LH Group And OH Group**

The follow-up time after surgery was 24 months (1–24). The mean follow-up time after surgery was 17.94 ± 9.132. In LH group, the median follow-up time after surgery was 24 months (1–24), and the mean follow-up time after surgery was 17.52 ± 9.253. In OH group, the median follow-up time after surgery was 24 months (1–24), and the mean follow-up time after surgery was 18.19 ± 9.096, P = 0.625. Log rank test was performed to compare overall survival rates between the two groups. The 6,12 and 24-month overall survival rates were 97.96%, 84.22%, 84.22% in LH group. The 6,12 and 24-month overall survival rates
were 92.39%, 82.13%, 80.92% in OH group, \( \chi^2 = 0.398, P = 0.528 \), indicating that there were no statistically significant differences with 2-year survival rate between LH and OH group for liver cancer patients (Fig. 1).

During the follow-up period, recurrence was observed in 14 of the 158 patients in two groups. The 2-year disease-free survival rate was 90.01% after laparoscopic hepatectomy and 88.24% after open hepatectomy, \( \chi^2 = 0.126, P = 0.722 \). There were no statistically significant differences with 2-year disease-free survival rate between LH group and OH group. (Fig. 2).

The factors associated with overall survival rate were shown in table 5. The univariate analysis shown that Child-Pugh grade (RR = 0.362, 95%CI 0.139–0.944) was the risk factor of overall survival rate. And Child-Pugh grade A was the protective factor of overall survival rate. But other factors such as surgical methods, sex, age, tumor size, HBsAg, AFP were not the risk influence factors of overall survival rate. The factors associated with disease-free survival rate were shown in table 6. The univariate analysis shown that none of these were risk factors of disease-free survival rate.

### Table 5

| Parameter                        | B    | p     | RR   | 95%CI       |
|----------------------------------|------|-------|------|-------------|
| LH (vs. OH)                      | -0.166 | 0.709 | 0.847 | 0.354–2.027 |
| Male (vs. female)                | -0.188 | 0.726 | 0.829 | 0.290–2.370 |
| Age < 65 (vs. ≥ 65)              | -0.247 | 0.635 | 0.781 | 0.281–2.169 |
| Tumor size < 5 cm (vs. ≥ 5 cm)   | -0.698 | 0.115 | 0.497 | 0.209–1.186 |
| HBsAg positive (vs. negative)    | -0.358 | 0.488 | 0.699 | 0.255–1.919 |
| AFP positive (vs. negative)      | -0.016 | 0.971 | 0.984 | 0.404–2.397 |
| Child-Pugh grade A (vs. B)       | -1.017 | 0.038 | 0.362 | 0.139–0.944 |
Table 6
Analyses of factors associated with disease-free survival rate

| Parameter                        | B   | p     | RR  | 95%CI        |
|----------------------------------|-----|-------|-----|--------------|
| Surgical methods                 | 0.166 | 0.771 | 1.181 | 0.386–3.614  |
| Male (vs. female)                | -0.493 | 0.488 | 0.611 | 0.151–2.464  |
| Age < 65 (vs. ≥ 65)              | 13.088 | 0.977 | 482949.424 |            |
| Tumor size < 5 cm (vs. ≥ 5 cm)   | -0.837 | 0.155 | 0.433 | 0.137–1.373  |
| HBsAg positive (vs. negative)    | 1.357 | 0.225 | 3.885 | 0.434–34.793 |
| AFP positive (vs. negative)      | -0.212 | 0.740 | 0.809 | 0.231–2.833  |
| Child-Pugh grade A (vs. B)       | -0.309 | 0.693 | 0.734 | 0.158–3.411  |

Discussion

It was not until 1991 that laparoscopic hepatectomy was first reported, open hepatectomy was the only choice for surgical method to treatment the liver cancer\[4\]. The first International Concensus Conference on Laparoscopic Hepatectomy, in Louisville, Kentucky, US, set the standard laparoscopic hepatectomy practice, which was laparoscopic left lateral sectionectomy in 2008\[9\]. Acceptable diameter indications of laparoscopic hepatectomy was less than or equal to 5 cm. The first Asia-Pacific consensus meeting on hepatocellular carcinoma in Hong Kong defined the role of laparoscopic hepatectomy in hepatocellular carcinoma management and developed guidelines in 2016\[10\]. And laparoscopic hepatectomy was regard as less blood loss the open hepatectomy. The First European Guidelines meeting on Laparoscopic Liver Surgery was held in Southampton in 2017\[11\]. This meeting presented and developed the guidelines of laparoscopic liver surgery.

Over the past 20 years, laparoscopic liver surgery indications were depended on tumor size, location, and time, initially, but recently the indications have been expanded. With the developed of minimally invasive technology, due to this surgical method could reduce the incision size, decrease complications and shorten hospital length of stay, laparoscopic liver surgery has been widely used all over the world. And hepatectomy has become a preferred method to treatment the liver cancer\[12\].

Both laparoscopic hepatectomy and open hepatectomy, have strict access criteria and indications. We performed these two surgical method by strict criteria and indications. In this study, before surgery, there was no statistical difference between the two groups in demographic characteristics and disease characteristics (Table 1).

According to this study results, the incision length of laparoscopic hepatectomy was significantly shorter than open hepatectomy. As all we known, laparoscopic liver surgery is a noninvasive procedure. This is also consistent with the aesthetic requirements of the body, which is one of the reasons for the increasing
popularity of laparoscopy. A shorter hospitalization stay was observed in laparoscopic hepatectomy. This result is in line with Meidai Kasai et al\textsuperscript{13}. Laparoscopic hepatectomy is always considered to have shorter hospitalization stay, which probably due to a smaller incision under laparoscopic liver surgery, making it easier for patients to heal and recover more quickly. Compared to open liver surgery, laparoscopic liver surgery was cheaper. The cost of hospitalization is related to the type of surgery, payment method, length of stay, type of medical insurance, and drug use.

The operating time of laparoscopic hepatectomy was significantly longer than open hepatectomy. Many studies\textsuperscript{[13–14]} also thought a longer operating time in the laparoscopic hepatectomy. Because laparoscopic hepatectomy is more complicated, and it depends on surgeon experience and skill level. Eating time, exhaust time, defecation time, use of analgesia time and ambulation time of laparoscopic hepatectomy were shorter than open hepatectomy. The earlier patients eating, the more nutrients can be provided to patients, and it can promote recovery. At the same time, it can reduce the input of nutritional supplements, reduce the pain of patients, reduce the cost of hospitalization. Laparoscopic liver surgery is always considered to have less bleeding, less blood transfusion, comparing with open liver surgery\textsuperscript{[3]}. However in the present study, there were no statistically significance between the two group\textsuperscript{[15]}.

The rate of patients with intra-operative blood transfusion of laparoscopic hepatectomy was more than open hepatectomy. This finding is consistent with Macacari et al\textsuperscript{[15]}. The proportion of patients with post-operative albumin transfusion was less than open hepatectomy. Komorowski A L et al\textsuperscript{[16]} result shown that the laparoscopy hepatectomy had lower intra-operative blood loss and also required less blood transfusion.

The incidence of total complications was also lower in LH group than in OH group. This finding is consistent with our earlier findings\textsuperscript{[5]}. The ascites, incision infection, and bleeding in LH group were significantly lower than those in OH group. Komorowski A L et al found that ascites was similar in both groups\textsuperscript{[17]}. Laparoscopy hepatectomy could reduce the rate of ascites especially in patients who had cirrhotic liver\textsuperscript{[18]}. The smaller the incision, the lower the infection rate. A lot of research demonstrated that less bleeding in laparoscopy hepatectomy, comparing with open hepatectomy.

Nonsignificant difference were found in the two groups for 2-year overall survival and for 2-year disease-free survival. Kandil et al\textsuperscript{[16]}found that the 3-year overall survival rate was 100% in the laparoscopic group, but which was 71.4%in the open group. It was different from overall survival (p = 0.03) but not different from disease-frees survival (p = 0.2). This indicates that the long-term efficacy of laparoscopic hepatectomy is basically equivalent to that of open hepatectomy, which is basically consistent with the conclusions of other scholars\textsuperscript{[19–21]}.

**Conclusion**

Combined with recent experience, indications and use of laparoscopic hepatectomy have improved with the development of laparoscopic instruments widening\textsuperscript{[22]}. Laparoscopic hepatectomy surgery supplied a
lower incision lengths, hospital stay and incidence of total complications. Laparoscopic hepatectomy was cheaper the open hepatectomy. There were no statistically significant differences with 2-year survival rate between LH and OH group for liver cancer patients, nor was disease-free survival. The result of this study indicated that laparoscopic hepatectomy surgery was as safe as open hepatectomy surgery. Laparoscopic hepatectomy surgery supplied a lower rate of mobidity and postoperative recovery and outcomes. The results of this study shown that laparoscopic hepatectomy surgery was as efficacy as open hepatectomy surgery.

There are some deficiencies in this study. Lacking of long-term follow-up data, the short follow-up time in this study could not fully reflect the long-term postoperative survival rate and disease-free survival rate of the patients. And this is not a strictly random. We need to follow up these patients for a long period, such as 5 years, 10 years or even longer, to further compare and analyze the similarities and differences between laparoscopic hepatectomy and open hepatectomy, so as to further improve the safety and effectiveness of laparoscopic hepatectomy surgery, reduce complications, prolong survival time and improve the quality of life.

**Abbreviations**

HCC: Hepatocellular carcinoma; LH:Laparoscopic hepatectomy; OH:open hepatectomy; ALT:alanine aminotransferase; AFP:Alpha-feto-protein; AST:aspartate aminotransferase; HBsAg:hepatitis B surface antigen

**Declarations**

**Availability of data and materials**

The datesets generated and analyzed during the current study are available from the corresponding author.

**Consent for publication**

Not applicable.

**Conflict of Interest Statement**

The authors of this study declare no conflict of interest.
This study was reviewed and approved by the institutional Ethical Board of Union hospital, Tongji Medical College, Huazhong University of Science and Technology. The informed consent of the patients was obtained for data collection and follow-up.

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**Authors’ contributions**

JY performed design, statistical analysis, interpretation and drafted the manuscript. LZ, MT, SSC, HYY performed collection, analysis and assembly of data; SLY, LY conducted the study and managed the database, revised the article and given guidance. All authors read and approved the final manuscript.

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Figures
Figure 1
Cumulative overall survival of the LH and OH groups

Figure 2
Cumulative disease-free survival of the LH and OH groups