Laparoscopic Hepatectomy as a Feasible and Safe Choice for Primary Hepatocellular Carcinoma Located at Favorable Location during the development period in a tertiary hospital: A case-control study

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Research Article

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Abstract

Background

Laparoscopic hepatectomy (LH) for hepatocellular carcinoma (HCC) has been well-known for its advantages in the past 10 years, but little is known regarding its oncologic outcomes while the technique is being developed at an institution. This study aimed to evaluate the safety and effectiveness of LH for patients with primary HCC at favorable locations, focusing on postoperative short-, and long-term outcomes during the development period.

Methods

We retrospectively reviewed patients diagnosed with primary HCC that underwent hepatectomy between January 2013 and December 2019 at Hualien Tzu Chi Hospital. Patients with HCC at favorable locations (anterolateral segments) were collected and divided into laparoscopic and open hepatectomy (OH) groups. The primary end point was long-term oncologic outcomes, including overall, and disease-free survival, whereas the secondary end point was postoperative short-term outcomes.

Results

The review included 159 patients, and among which 42, and 44 patients with HCC in favorable locations were underwent open and laparoscopic hepatectomies. There were no significant differences in intraoperative blood loss (200 vs. 300 mL, p = 0.072), overall complication rate (57.2% vs. 36.4%, p = 0.083), major complication rate (11.9% vs. 2.3%, p = 0.080), and 90-day mortality rate (7.1% vs. 0.0%, p = 0.071) between the two groups. The laparoscopic group had a lower transfusion rate (14.3% vs. 2.3%, p = 0.042), shorter postoperative hospital stay (10 days vs. 7 days, p < 0.001), and lower 90-day readmission rate (14.3% vs. 2.3%, p = 0.042). There were no significant differences in 12-, 36,- and 60-month overall survival and disease-free survival.

Conclusions

LH for favorably located HCC is the preferred surgical approach compared to OH due to the decreased transfusion rate, shorter postoperative hospital stay, and lower 90-day readmission rate. LH did not compromise the 90-day mortality rate with sustained long-term overall and disease-free survival. LH for favorably located HCC is a safe and effective surgical approach even during the development period.

Background

Hepatocellular carcinoma (HCC) was the sixth most common neoplasm and the third leading cause of cancer death worldwide in 2020, with 905,677 diagnosed cases and 830,180 deaths[1]. The Barcelona Clinic Liver Cancer strategy identifies hepatectomy as one of the treatment options for HCC[2]. Since the first laparoscopic hepatectomy (LH) described in 1991[3], it has gradually been developed as a surgical option. After the first feasibility study of LH published in 2000[4], plenty of studies were merged to confirm the safety of the laparoscopic approach for hepatectomy under different conditions, such as tumor size[5], previous abdominal surgery[6], cirrhotic patients[7], and elder patients[8]. Furthermore, the benefit of LH included many advantages, including a smaller incision size, shorter operation time, lower transfusion rate, lower major complication rate, shorter hospital stay, and would not compromise similar overall survival and disease-free survival compared with OH[9–12].

A variety of difficulties, including liver mobilization, hemorrhage control, loss of manual palpation, deeper surgical field, and intraoperative hazards, makes it difficult for institutions to develop aptitude for LH[13, 14]. Recent studies on the feasibility and safety of LH were mostly conducted by well-developed centers and lacked data from developing centers or from their development period. Furthermore, the impact of location in LH has not been clearly elucidated.
The aim of this study was to evaluate the safety and effectiveness of our initial experience of LH for HCC located at favorable location and focus on the short-term and long-term outcomes during the development period.

**Methods**

**Patient characteristics**

We retrospectively analyzed the data of consecutive cases of newly diagnosed HCC who underwent hepatectomy between January 2013 and December 2019 in Hualien Tzu Chi General Hospital, a tertiary referral center in eastern Taiwan. The preoperative diagnosis of HCC was made based on the results of two sets of noninvasive dynamic imaging in high-risk groups with chronic hepatitis B, chronic hepatitis C, or cirrhosis with or without elevated alpha-fetoprotein (AFP). Postoperative HCC was confirmed by pathological examination of resected specimens in all patients. Patients with a diagnosis of recurrent HCC, prior HCC treatment, or synchronous malignancy were excluded. The patients were divided into the LH and OH groups. Those with tumors at favorable locations were placed into the favorable location group. In the favorable location group, patients were also divided into an open group (F-OH) and laparoscopic group (F-LH). The criteria for inclusion of patients into the open or laparoscopic group depended on the surgeon's preference, including patient age, liver function, and tumor size, location, and distance to major vessels. This preference adjusts when the surgeon is more adept in laparoscopic interventions. Volumetric evaluation of the tumor was not routinely performed because it was not covered by the National Health Insurance of Taiwan, and most patients could not afford this evaluation. The Makuuchi criteria were used to determine the resection volume[15]. Medical records were retrospectively reviewed for demographic characteristics, perioperative variables, and follow-up outcomes. The primary endpoint was long-term oncologic outcomes, including overall, and disease-free survival. The secondary endpoint was perioperative outcomes. The overall median follow-up duration was 48 months.

**Definitions and surgical technique**

Definitions were adopted from the Brisbane 2000 Guidelines for liver anatomy[16]. Resection of $\geq$3 segments was defined as major resection. The Clavien–Dindo classification was used to grade postoperative complications[17]. Major complications were defined as $\geq$3 complications. The definition of bile leakage and post-hepatectomy liver failure was adopted from the International Study Group of Liver Surgery[18, 19]. The favorable tumor locations were defined as segments S2, S3, S4b, S5, and S6 and the unfavorable tumor locations were defined as segments S1, S4a, S7, and S8. The surgical technique of OH and LH was mentioned in our previous study[9].

**Statistical analysis**

The chi-square test used to analyze categorical variables, presented as numbers, and percentages. The Kolmogorov–Smirnov test was used to check the normality of continuous variables. Normally distributed continuous variables are presented as means with standard deviations and were analyzed with student’s t-test. Non-normally distributed continuous variables are presented as medians with interquartile ranges and were analyzed using the Mann–Whitney U-test. The Kaplan–Meier curve with the log-rank test was used for the survival analysis. SPSS for MAC ver. 26 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Statistical significance was set at a p-value of <0.05.

**Ethic declaration**

Ethical approval for this study (Research Ethics Committee, REC No. IRB 109-074-B) was provided by the Research Ethics Committee of Hualien Tzu Chi Hospital, the Buddhist Tzu Chi Medical Foundation, on April 16, 2020. Informed written consent was waived because the study was a retrospective data analysis.

**Results**
Figures 1 and 2 illustrate the trend of development of LH during 2013 to 2019. During the development period, the ratio of LH (Fig. 1) increased gradually to more than 50% after 2017. The proportion of F-LH (Fig. 2) also increased to more than 50% after 2017, which was compatible with the trend of development of LH.

**Baseline characteristics**

The baseline characteristics of the patients are shown in Table 1. A total of 159 patients were included, with 86 (54.1%) having favorable tumor locations. There were 96 patients (60.3%) in the OH group and 63 patients (39.6%) in the LH group. Male patients are dominant in both groups, and the presence of comorbidities (e.g., diabetes mellitus, hypertension, and coronary artery disease), was not significantly different between the OH and LH groups. More patients in the LH group versus the OH group were Child–Pugh class A (98.4% vs. 88.9%, p = 0.026), but the Model for End-stage Liver Disease-Na (MELD-Na) score was similar in both groups (8 vs. 7, p = 0.229). The preoperative 15-minute retention rate for indocyanine green was 13.3% and 9.1% in the LH and OH groups, respectively (p = 0.748).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Whole cohort (n = 159)</th>
<th>OH (n = 96)</th>
<th>LH (n = 63)</th>
<th>p-value</th>
<th>Favorable location subgroup (n = 86)</th>
<th>F-OH (n = 42)</th>
<th>LH (n = 44)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong> *</td>
<td>65 ± 10</td>
<td>64 ± 11</td>
<td>67 ± 9</td>
<td>0.156</td>
<td>65 ± 10</td>
<td>64 ± 11</td>
<td>66 ± 9</td>
<td>0.148</td>
</tr>
<tr>
<td><strong>Sex, male (%)</strong></td>
<td>75.5 (120/159)</td>
<td>72.9 (70/96)</td>
<td>79.4 (50/63)</td>
<td>0.452</td>
<td>75.6 (65/86)</td>
<td>78.6 (33/42)</td>
<td>72.7 (32/44)</td>
<td>0.619</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong> *</td>
<td>25.2 ± 3.6</td>
<td>25.0 ± 3.7</td>
<td>25.7 ± 3.6</td>
<td>0.687</td>
<td>25.6 ± 3.7</td>
<td>25.7 ± 4.0</td>
<td>25.5 ± 3.4</td>
<td>0.379</td>
</tr>
<tr>
<td><strong>Comorbidity (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>35.8 (57/159)</td>
<td>29.2 (28/96)</td>
<td>46.3 (29/63)</td>
<td>0.042</td>
<td>36.0 (21/86)</td>
<td>23.8 (10/42)</td>
<td>47.7 (21/44)</td>
<td>0.026</td>
</tr>
<tr>
<td>HTN</td>
<td>45.3 (72/159)</td>
<td>41.7 (40/96)</td>
<td>51.0 (32/63)</td>
<td>0.329</td>
<td>48.8 (42/86)</td>
<td>50.0 (21/42)</td>
<td>47.7 (21/44)</td>
<td>1.00</td>
</tr>
<tr>
<td>CAD</td>
<td>6.3 (10/159)</td>
<td>6.2 (6/96)</td>
<td>6.3 (4/63)</td>
<td>0.98</td>
<td>7.0 (6/86)</td>
<td>7.1 (3/42)</td>
<td>6.8 (3/44)</td>
<td>0.953</td>
</tr>
<tr>
<td>FEV1/FVC§</td>
<td>79.3 (72.4,83.5)</td>
<td>78.8 (70.3,82.7)</td>
<td>77.9 (73.2,83.0)</td>
<td>0.244</td>
<td>78.7 (72.0,82.6)</td>
<td>79.1 (71.1,84.1)</td>
<td>77.8 (74.1,82.4)</td>
<td>0.554</td>
</tr>
<tr>
<td>LVEF (%)§</td>
<td>75.3 (69.3,79.8)</td>
<td>73.9 (66.1,77.8)</td>
<td>75.4 (69.8,79.7)</td>
<td>0.047</td>
<td>75.4 (67.0,80.3)</td>
<td>74.5 (66.1,78.5)</td>
<td>76.0 (69.1,83.1)</td>
<td>0.345</td>
</tr>
<tr>
<td>Child–Pugh classification stage A (%)</td>
<td>92.8 (141/152)</td>
<td>88.9 (80/90)</td>
<td>98.4 (61/62)</td>
<td>0.026</td>
<td>95.1 (78/82)</td>
<td>89.7 (35/39)</td>
<td>100.0 (43/43)</td>
<td>0.031</td>
</tr>
<tr>
<td>MELD-Na score§</td>
<td>8 (7.9)</td>
<td>7 (7.8)</td>
<td>8 (10.11)</td>
<td>0.229</td>
<td>7 (7.9)</td>
<td>7 (7.10)</td>
<td>8 (7.9)</td>
<td>0.604</td>
</tr>
<tr>
<td>ICG-15 (%)§</td>
<td>10.6 (5.2,20.1)</td>
<td>9.1 (4.4,16.3)</td>
<td>13.3 (8.1,16.0)</td>
<td>0.748</td>
<td>10.7 (4.2,22.9)</td>
<td>10.6 (4.5,22.9)</td>
<td>12.2 (3.8,24.9)</td>
<td>0.871</td>
</tr>
<tr>
<td>Viral hepatitis (%)</td>
<td>87.4 (139/159)</td>
<td>89.6 (86/96)</td>
<td>84.1 (53/63)</td>
<td>0.273</td>
<td>88.4 (76/86)</td>
<td>90.5 (38/42)</td>
<td>86.4 (38/44)</td>
<td>0.602</td>
</tr>
</tbody>
</table>
In the subgroup analysis for the favorable location group, 42 patients (48.8%) were in the F-OH group, while 44 (51.2%) were in the F-LH group. Significantly more patients in the F-LH group versus the F-OH group were Child–Pugh class A (100% vs. 89.7%, p = 0.031), but the MELD-Na score was still similar in both groups (7 vs. 8, p = 0.604). The preoperative 15-minute retention rate of indocyanine green was 10.6% and 12.2% in the F-OH and F-LH groups, respectively (p = 0.871). The risk factor for HCC in both groups of patients is viral hepatitis (90.5% in the F-OH group and 86.4% in the F-LH group, p = 0.602).

**Perioperative outcomes and histopathology**

When comparing the OH versus LH groups, the rate of major hepatectomy was higher in the OH group versus the LH group (38.5% vs. 11.1%, p < 0.001) (Table 2). On the other hand, the LH group, compared to the OH group, had significantly shorter median operation time (208 vs. 255 min, p = 0.025) and intraoperative blood loss (250.0 vs. 355.0 mL, p = 0.005). In the favorable location subgroup analysis, more patients in the F-OH group underwent major hepatectomy compared to the F-LH group (38.1% vs. 4.5%, p < 0.001). The median operation time and the intraoperative blood loss were similar in both groups. The intraoperative transfusion rate was significantly lower in F-LH group (2.3% vs. 14.3%, p = 0.042).
Table 2
Perioperative outcomes and pathology findings

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Whole cohort (n = 159)</th>
<th>OH (n = 96)</th>
<th>LH (n = 63)</th>
<th>p-value</th>
<th>Favorable location subgroup (n = 86)</th>
<th>F-OH (n = 42)</th>
<th>F-LH (n = 44)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IWATE score</td>
<td>7 (5, 10)</td>
<td>9 (6, 10)</td>
<td>5 (3, 7)</td>
<td>&lt; 0.001</td>
<td>3 (6, 7)</td>
<td>7 (6, 8)</td>
<td>4 (3, 6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Major resection (%)</td>
<td>27.7 (44/159)</td>
<td>38.5 (37/96)</td>
<td>11.1 (7/63)</td>
<td>&lt; 0.001</td>
<td>20.9 (18/86)</td>
<td>38.1 (16/42)</td>
<td>4.5 (2/44)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Operative time (min)§</td>
<td>248 (181, 340)</td>
<td>255 (195,348)</td>
<td>208 (167,372)</td>
<td>0.025</td>
<td>229 (170,296)</td>
<td>242 (175,307)</td>
<td>198 (159,267)</td>
<td>0.101</td>
</tr>
<tr>
<td>Pringle maneuver (%)</td>
<td>76.7 (122/159)</td>
<td>81.3 (78/96)</td>
<td>69.8 (44/63)</td>
<td>0.125</td>
<td>68.6 (59/86)</td>
<td>76.2 (32/42)</td>
<td>61.4 (27/44)</td>
<td>0.167</td>
</tr>
<tr>
<td>Pringle duration (min)§</td>
<td>72.0 (44.8, 101.0)</td>
<td>72.9 (55.0, 100)</td>
<td>59.0 (31.3, 93.5)</td>
<td>0.021</td>
<td>60.0 (35.0,85.0)</td>
<td>65.0 (49.2,82.5)</td>
<td>55.0 (27.0,88.0)</td>
<td>0.322</td>
</tr>
<tr>
<td>Blood loss (mL)§</td>
<td>300 (100, 900)</td>
<td>355 (150,730)</td>
<td>250 (125,815)</td>
<td>0.005</td>
<td>200 (100,448)</td>
<td>300 (138,700)</td>
<td>150 (50,388)</td>
<td>0.072</td>
</tr>
<tr>
<td>Intraoperative transfusion (%)</td>
<td>9.4 (15/159)</td>
<td>10.4 (10/96)</td>
<td>7.9 (5/63)</td>
<td>0.783</td>
<td>8.1 (7/86)</td>
<td>14.3 (6/42)</td>
<td>2.3 (1/44)</td>
<td>0.042</td>
</tr>
<tr>
<td>Solitary tumors (%)</td>
<td>81.8 (130/159)</td>
<td>76.0 (73/96)</td>
<td>90.5 (57/63)</td>
<td>0.022</td>
<td>87.2 (75/86)</td>
<td>85.7 (36/42)</td>
<td>88.6 (39/44)</td>
<td>0.755</td>
</tr>
<tr>
<td>Size (cm)§</td>
<td>3.5 (2.5, 5.5)</td>
<td>4.0 (3.0, 7.5)</td>
<td>3.0 (2.5, 4.2)</td>
<td>0.001</td>
<td>3.2 (2.5,5.0)</td>
<td>4.3 (2.7,6.1)</td>
<td>3.0 (2.3,8)</td>
<td>0.005</td>
</tr>
<tr>
<td>Margin (cm)§</td>
<td>0.7 (0.2, 1.2)</td>
<td>1.0 (0.2, 1.5)</td>
<td>0.5 (0.2, 0.9)</td>
<td>0.049</td>
<td>0.8 (0.2,1.2)</td>
<td>1.0 (0.2,1.4)</td>
<td>0.7 (0.2, 1.2)</td>
<td>0.640</td>
</tr>
<tr>
<td>Ishak score§</td>
<td>4 (1, 6)</td>
<td>3 (0, 6)</td>
<td>5 (3, 5)</td>
<td>0.436</td>
<td>4 (2.6)</td>
<td>4 (0.6)</td>
<td>4 (2.6)</td>
<td>0.346</td>
</tr>
</tbody>
</table>

* normal distribution; § non-normal distribution; OH, open hepatectomy; LH, laparoscopic hepatectomy; F-OH, open hepatectomy in favorable location group; F-LH, laparoscopic hepatectomy in favorable location group; IRQ, interquartile range.

The LH group, compared to the OH group, had more patients with solitary HCC (90.5% vs. 76.0%, p = 0.022) and smaller median tumor diameter (3.0 vs. 4.0 cm, p = 0.001) (Table 2). In the favorable location subgroup analysis, majority of patients in both groups underwent hepatectomy for solitary tumors (85.7% in F-OH group vs. 88.6% in F-LH group, p = 0.755). The median tumor diameter was smaller in the F-LH group versus the F-OH group (3.0 vs. 4.3 cm, p = 0.005). The resection margin status and Ishak score were not significantly different between the two groups.

**Postoperative short-term outcomes**

The overall complication rate was lower in the LH group than in the OH group (33.3% vs. 50.0%, p = 0.050) (Table 3). In the favorable location subgroup analysis, the F-LH group had a lower rate of major complications rate than the F-OH group (12.0% vs. 2.3%, p = 0.080). In the F-OH group, two patients experienced grade IIIa complications (both had pleural effusion); one patient experienced a grade IIIb complication (grade C bile leakage); one patient experienced a grade IVa complication (post-hepatectomy liver failure); and one patient experienced a grade IVb complications (acute kidney injury...
and post-hepatectomy liver failure). In the F-LH group, one patient experienced a grade IIIa complication (superficial surgical site infection). No grade V complications developed in either group.

The postoperative hospital stay was significantly shorter in the LH group than in the OH group (7 vs. 11 days, \( p < 0.001 \)) (Table 3). The 90-day readmission rate was significantly less in the LH group than in the OH group (3.2% vs. 12.5%, \( p = 0.048 \)) (Table 3), but there was no significant difference in 90-day mortality between both groups (1.6% vs. 5.2%, \( p = 0.241 \)). In the favorable location subgroup analysis, the F-LH group, when compared to the F-OH group, had shorter postoperative hospital stay (7 vs. 10 days, \( p < 0.001 \)) and a significantly lower 90-day readmission rate (2.3% vs. 14.3%, \( p = 0.042 \)), but no significant difference in 90-day mortality rate (0.0% vs. 7.1%, \( p = 0.071 \)).

![Table 3](image)

**Postoperative outcomes**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Whole cohort (n = 159)</th>
<th>OH (n = 96)</th>
<th>LH (n = 63)</th>
<th>P-value</th>
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<th>F-OH (n = 42)</th>
<th>F-LH (n = 44)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications (%)</td>
<td>43.4 (69/159)</td>
<td>50.0 (48/96)</td>
<td>33.3 (21/63)</td>
<td>0.050</td>
<td>46.6 (40/86)</td>
<td>57.2 (24/42)</td>
<td>36.4 (16/44)</td>
<td>0.083</td>
</tr>
<tr>
<td>Major complications (%)</td>
<td>7.5 (12/159)</td>
<td>9.4 (9/16)</td>
<td>4.8 (3/63)</td>
<td>0.281</td>
<td>7.0 (6/86)</td>
<td>11.9 (5/42)</td>
<td>2.3 (1/44)</td>
<td>0.080</td>
</tr>
<tr>
<td>Minor complications (%)</td>
<td>35.8 (57/159)</td>
<td>40.7 (39/96)</td>
<td>28.5 (18/63)</td>
<td>0.132</td>
<td>39.5 (34/86)</td>
<td>45.2 (19/42)</td>
<td>34.1 (15/44)</td>
<td>0.378</td>
</tr>
<tr>
<td>Postoperative hospital stay (days)</td>
<td>8 (7, 12)</td>
<td>11 (9, 14)</td>
<td>7 (6, 10)</td>
<td>&lt; 0.001</td>
<td>8 (6,10)</td>
<td>10 (8,17)</td>
<td>7 (6,8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>90-day readmission rate (%)</td>
<td>8.8 (14/159)</td>
<td>12.5 (12/96)</td>
<td>3.2 (2/63)</td>
<td>0.048</td>
<td>8.1 (7/86)</td>
<td>14.3 (6/42)</td>
<td>2.3 (1/44)</td>
<td>0.042</td>
</tr>
<tr>
<td>90-day mortality rate (%)</td>
<td>3.8 (6/159)</td>
<td>5.2(5/96)</td>
<td>1.6 (1/63)</td>
<td>0.241</td>
<td>3.5 (3/86)</td>
<td>7.1 (3/42)</td>
<td>0.0 (0/44)</td>
<td>0.071</td>
</tr>
</tbody>
</table>

* normal distribution; § non-normal distribution; OH, open hepatectomy; LH, laparoscopic hepatectomy; F-OH, open hepatectomy in favorable location group; F-LH, laparoscopic hepatectomy in favorable location group; IRQ, interquartile range.

### Long-term outcomes

Between the LH and OH groups, no significant difference was found in 12-, 36-, and 60-month overall survival (respectively, 88.5%, 82.9%, and 71.8% vs. 83.7%, 74.3%, and 67.6%, \( p = 0.257 \)) and disease-free survival (respectively, 77.2%, 53.3%, and 48.3% vs. 71.5%, 52.8%, and 39.7%, \( p = 0.509 \)) (Fig. 3A, B). In the favorable location subgroup analysis, the F-LH and F-OH groups demonstrated no significant difference in 12-, 36-, and 60-month overall survival (respectively, 90.7%, 88.1%, and 75.4% vs. 79.5%, 76.6%, and 70.4%, \( p = 0.184 \)) and disease-free survival (respectively, 79.2%, 52.9%, and 49.1% vs. 73.9%, 54.7%, and 39.5%, \( p = 0.683 \)) (Fig. 3C, D).

### Discussion

The first feasibility study for LH in 2000 concluded that LH was feasible and safe in patients with left- and right-sided peripheral lesions who required limited resection in 2000[4]. Since then, a variety of feasibility studies for LH have been published for the different circumstances, such tumor size[5], previous abdominal surgery[6], cirrhotic patients[7], and elderly patients[8], revealing that LH does not compromise perioperative outcomes, short-term outcomes, and long-term
survival. During this period, the indications for LH have evolved from the Louisville statement in 2008[20], which indicated the specific indications of LH, to the Morioka consensus in 2014[21], which found no definite indications for LH. Accordingly, our center started LH with smaller tumors and performed minor resections before performing major resections during the development period. We also followed the Louisville statement to resect the tumor located at peripheral segments, which means segments 2 to 6, which indicates favorable location.

Several retrospective studies have evaluated the feasibility and safety of LH in patients with HCC[22–24]. In these studies, LH was associated with significantly less postoperative ascites (0.0% vs. 17.2%, p = 0.025), shorter hospital stay (7.69 ± 2.94 vs. 13.38 ± 7.37 days, p < 0.001) without compromised long-term survival (12-, 36-, and 60-month survival rates of 100%, 100%, and 92.2%, respectively). The 12-, 36-, and 60-month disease-free survival rates were 81.7%, 61.7% and 54.0%, respectively in the study by Kim et al.[22]. There was also significantly shorter operative time (80 vs. 140 min, p = 0.02), shorter hospital stay (7 vs. 12 days, p < 0.0001), and lower morbidity rates (20% vs. 4%, p = 0.01) without compromised long-term survival rate (1-, 5-, and 10-year rates of 88%, 59%, and 12%, respectively) in a study by Memeo et al.[23]. A study by Lee et al. revealed significantly shorter postoperative hospital stay (8 vs. 10 days, p = 0.003) without compromised 12-, 36-, and 60-month overall survival rates (96.6%, 92.8%, and 73.3%, respectively) disease-free survival rates (84.4%, 64.0%, and 60.2%, respectively)[24]. Regarding tumor location, most papers on the feasibility of LH focused on those in unfavorable locations. When comparing posterior superior versus anterolateral tumors, Kwon et al. reported that tumors in unfavorable locations would have similar median blood loss (500 vs. 400 mL, p = 0.214), rate of intraoperative transfusion (39% vs. 19%, p = 0.061), median postoperative hospital stay (10 vs. 8 days, p = 0.166), and complication rate (21% vs. 11%, p = 0.148)[25]. The INSTALL-2 study reported that tumors located at S7 and S8 had a median operative time of 315 min, postoperative hospital stay of 7 days, and a major complicated rate of 11.9%[26].

Nevertheless, the aforementioned studies were conducted by a well-developed and well-experienced center. The studies focused on tumor location only provided evidence that LH would be feasible in unfavorable locations when done in a high-quality center. Unfortunately, there is no adequate evidence for centers that are eager to start the development of LH. The present study analyzed cases of favorably located HCC that underwent LH during the development period. According to the indications of LH in the Louisville statement, LH was started at the parts of the tumor in the favorable location and those that were of a smaller size; minor resection was done before performing the more difficult resection during the development period at our institution. This can explain why the ratio of major resection was significantly greater in the F-OH group than in F-LH group. During the development period in our study, the ratio of laparoscopic intervention gradually increased and eventually became the major intervention in the series as the technique was developed. During the development period, the short-term outcomes (e.g., intraoperative blood loss, major complication rate, postoperative hospital stay, 90-day readmission rate, and 90-day mortality rate) were not compromised under the laparoscopic approach. The long-term outcomes, including the overall, and disease-free survival rates, were not influenced by use of the laparoscopic method, either. This study provided evidence that centers starting to develop LH, even those that are not high-volume centers (less than 20–50 liver resections per year), may be benefit from using this technique on favorably located tumors without significantly affecting short- and long-term outcomes, even not in the high-volume center[27].

Only a few studies have focused on the experience of developing LH using cases of favorably located tumors. We were able to demonstrate the feasibility and safety when the technique is being developed in a single center. These findings can hopefully encourage institutions who want to start developing this procedure. However, this study still has some limitations that should be discussed. First, this was a retrospective, and non-randomized study, which may have led to observation bias. Second, there was no short-, or long-term data on the quality of life, such as the presence of incisional abdominal wall hernia and pain scale assessments. Third, the study had a relatively small sample size and was conducted in a single center. After the technique becomes more mature, we will gradually start to apply LH in more difficult cases, and the results will be presented in the following studies.
Conclusions

LH can be an alternative to OH for primary HCC with favorably located tumors due to the decreased intraoperative transfusion rate, shorter postoperative hospital stay, and lower 90-day readmission rate. LH will not compromise intraoperative blood loss, complication rate, morbidity, 90-day mortality rate, or long-term overall, and disease-free survival. LH appears to be a feasible and safe choice for primary HCC located at favorable location during the development period. Our findings can provide the evidence and confidence for institutions who want to start developing LH.

Abbreviations

HCC  
Hepatocellular carcinoma

ISGLS  
International Study Group of Liver Surgery

LH  
Laparoscopic hepatectomy

OH  
Open hepatectomy

MELD-Na  
Model for End-stage Liver Disease-Na

Declarations

Ethics approval and consent to participate

Ethical approval for this study (Research Ethics Committee, REC No. IRB 109-074-B) was provided by the Research Ethics Committee of Hualien Tzu Chi Hospital, the Buddhist Tzu Chi Medical Foundation, on April 16, 2020. Informed written consent was waived because the study was a retrospective data analysis by Research Ethics Committee of Hualien Tzu Chi Hospital, the Buddhist Tzu Chi Medical Foundation.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors’ contributions

YHL and YCC proposed the concept and designed the study protocol. YHL and TLK collected the data. YHL, YTH, TLK, and YCC performed the statistical analysis and interpretation. YHL and YTH wrote the manuscript. MCL and YCC critically revised the manuscript. All the authors read and approved the final manuscript.
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References


### Figures

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Figure 1

Distribution of hepatectomy. LH, laparoscopic hepatectomy; OH, open hepatectomy

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Figure 2

Distribution of hepatectomy of favorable location by year. F-OH, open hepatectomy in the favorable location group; F-LH, laparoscopic hepatectomy in the favorable location group.
Figure 3

Kaplan–Meier curve of the overall survival and disease-free survival in the LH, OH, F-LH, and F-OH groups. (A) The 12-, 36-, and 60-month overall survival rates, respectively, were 88.5%, 82.9%, and 71.8% in the LH group and 83.7%, 74.3%, and 67.6% in the OH group. Log-rank test, p = 0.257. (B) The 12-, 36-, and 60-month disease-free survival rates, respectively, were 77.2%, 53.3%, and 48.3% in the LH group and 71.5%, 52.8%, and 39.7% in the OH group. Log-rank test, p = 0.509. (C) The 12-, 36-, and 60-month overall survival rates, respectively, were 90.7%, 88.1%, and 75.4% in the F-LH group and 79.5%, 76.6%, and 70.4% in the F-OH group. Log-rank test, p = 0.184. (D) The 12-, 36-, and 60-month disease-free survival rates, respectively, were 79.2%, 52.9%, and 49.1% in the F-LH group and 73.9%, 54.7%, and 39.5% in the F-OH group. Log-rank test, p = 0.683. LH, laparoscopic hepatectomy; OH, open hepatectomy; F-OH, open hepatectomy in the favorable location group; F-LH, laparoscopic hepatectomy in the favorable location group.