

# Surgical outcomes and quality of life between laparoscopic and open approach for hepatic hemangioma

## A propensity score matching analysis

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### Abstract

The main objective of the study was to compare the surgical outcomes and quality of life (QOL) of patients with hepatic hemangioma either by laparoscopic or open surgery using a propensity score analysis.

We retrospectively reviewed patients with hepatic hemangioma undergoing laparoscopic liver surgery (LLS) or open liver surgery (OLS) between January 2016 and December 2017. Intraoperative and postoperative characteristics, and quality of life, according to Short Form-36 Healthy Survey (SF-36) questionnaire, were compared between groups. We performed 1:1 propensity score matching (PSM) between the LLS and OLS groups.

A total of 205 patients who involved in the analysis (80 LLS vs 125 OLS) were matched (1:1) by age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, previous upper abdominal surgery, comorbidities, operation method, type of resection, tumor localization, size, and number. After PSM, 73 well-matched patients in each group were obtained. LLS was associated with significantly less blood loss, shorter postoperative hospital stay and fewer complications. The QOL scores weren't significantly different between the 2 groups, though the LLS group tended to be superior to the OLS group in terms of bodily pain (BP) and mental health (MH) at 3 months after surgery.

In comparison with the conventional open approach, laparoscopic liver surgery for hepatic hemangioma appears to have improved short-term surgical outcomes and comparable QOL in selected patients.

**Abbreviations:** ASA = American society of anesthesiologists, BMI = body mass index, BP = bodily pain, COPD = chronic obstructive pulmonary disease, GH = general health, LLS = laparoscopic liver surgery, MH = mental health, OLS = open liver surgery, PF = physical functioning, PSM = propensity score matching, QOL = quality of life, RCTs = randomized controlled trials, RE = role-emotional, RP = role-physical, SF = social functioning, SF-36 = short Form-36 healthy survey, VT = vitality.

**Keywords:** hepatic hemangioma, laparoscopy, propensity score matching, quality of life

## 1. Introduction

Hepatic hemangiomas are the most common benign liver tumors with an estimated prevalence of 0.4% to 20% in the general population.<sup>[1]</sup> The majority of patients with hepatic hemangioma are discovered incidentally with increasing use of abdominal imaging techniques for abdominal complaints

or routine physical examination. Traditionally, hepatic hemangiomas are generally asymptomatic and require no further clinical intervention.<sup>[2,3]</sup> However, one-half of hepatic hemangiomas grow during long-term follow-up and abdominal symptoms may be present.<sup>[2]</sup> Surgical treatment is indicated if hepatic hemangioma is symptomatic or of progressive size.

Over the past decades, laparoscopic liver approach has gained widespread acceptance and is recognized as a safe approach for the management of various benign and malignant liver lesions. This technique has the advantages over open surgery with reported decreased postoperative complications, shorter postoperative stays, and better postoperative cosmetic satisfaction than conventional open surgery.<sup>[4–8]</sup> However, the current evidence was based on retrospective studies.

So far, no randomized controlled trials (RCTs) on laparoscopic approach versus open approach had been completed. According to the Second International Consensus Conference for Laparoscopic Liver Resection, pain and quality of life in laparoscopic liver resections were still unknown with low quality of evidence.<sup>[9]</sup> And the superiority of LLS in terms of health related QOL has not been evaluated. Therefore, this study was introduced and aimed to assess surgical outcomes and QOL in patients with hepatic hemangiomas through an open or laparoscopic approach.

Editor: Goran Augustin.

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The authors declare no conflict of interest.

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Medicine (2019) 98:6(e14485)

Received: 4 July 2018 / Received in final form: 6 January 2019 / Accepted: 18 January 2019

<http://dx.doi.org/10.1097/MD.0000000000014485>

## 2. Materials and methods

### 2.1. Patient

From January 2016 to December 2017, 205 patients who had been operated for hepatic hemangioma with either an open or a laparoscopic approach in West China Hospital were included in the study. Of these patients, laparoscopic procedures were performed in 80 patients and 125 patients underwent open surgery. The patients who underwent laparoscopic converted to open surgery were included in the LLS group. Surgical indications for these patients were giant hemangiomas larger than 5.0 cm in combination with the presence of abdominal symptoms or complications.<sup>[3,10–12]</sup> The following patients were excluded: failed to be followed up for QOL assessment and severe dysfunction of the heart, lung, kidney, or other organs. Intraoperative liver ultrasound was performed in all cases to confirm the location, number and size of the lesions. Patients' medical records were reviewed for demographic data, operative method, tumor characteristics, surgical data, postoperative outcomes as well as the QOL according to the SF-36 questionnaire (version 2.0).<sup>[13]</sup> The study was approved by the Committee of Ethics in West China Hospital of Sichuan University.

### 2.2. Surgical approach

Our detailed techniques for laparoscopic liver surgery had been previously described.<sup>[14,15]</sup> Briefly, the patients under general anesthesia were put in the left lateral position with the operator standing on the right side of the patients. Five abdominal ports were inserted (two 5-mm trocars and three 12 mm-trocars) and the pneumoperitoneum was established with intra-abdominal pressure maintaining at approximately 13 mmHg. A low central venous pressure (<5 mmHg) was maintained during liver resection. Intraoperative ultrasonography was performed to confirm the tumor location and its relationship with adjacent hepatic vasculature. The intermittent Pringle maneuver was adopted to control hepatic inflow if necessary. The liver parenchyma was transected with harmonic scalpel (Ethicon Endo-Surgery, USA) or electrocautery (Medtronic, USA). Hepatic resection was carried out with an incision margin of 0.5 to 1.0 cm. For hepatic enucleation, hemangioma was separated from the border of normal hepatic parenchyma by meticulous dissection of the surgical plane. After surgery, the specimen was then placed into a protective bag and extracted through an enlarged port in the upper abdomen or the suprapubic transverse incision. Abdominal drains were routinely placed on the cut surface. In the open approach, a laparotomy was performed via a right subcostal incision with the patients placed in supine position. The surgical techniques were similar to LLS.

### 2.3. Propensity score matching (PSM)

The PSM analysis is gaining increasing consensus in non-randomized and observational studies, which can minimize treatment selection bias.<sup>[16,17]</sup> In our study, the 2 operative techniques were compared using a PSM analysis to minimize patient selection bias and confounding differences between LLS and OLS group. The following variables associated with undergoing either LLS or OLS were enrolled into the PSM model: age, sex, BMI, ASA grade, comorbidities, operative method, type of resection, previous abdominal surgery, lesion location, size, and number. A propensity score was calculated by

logistic regression with the imbalanced variables for each patient. Then a 1:1 match between the 2 groups was applied through the nearest available neighbor matching.

### 2.4. Surgical outcomes

The following variables were analyzed: operative time, blood loss, Pringle time, intraoperative transfusion, bowel function recovery, postoperative hospital stay, and postoperative complications according to Clavien–Dindo grade.<sup>[18]</sup> Symptomatic pleural effusion was diagnosed by chest radiography and/or color ultrasonic examination and lead to respiratory dysfunction requiring thoracocentesis. Postoperative hemorrhage was defined as a drop in hemoglobin level >3 g/dL postoperatively compared with the postoperative baseline level and/or any postoperative transfusion for a falling hemoglobin.<sup>[19]</sup> Ascites was identified by the postoperative daily drainage >10 mL/Kg of preoperative body weight.<sup>[20]</sup>

### 2.5. QOL assessment

Quality of life (QOL) is the patient's subjective perceptions associated with physical, mental, and social domains, which has recently become important outcome parameter for defining surgical performance. Among various QOL assessment tools, the Short Form-36 Health Survey is a well-recognized questionnaire that evaluates QOL.<sup>[21,22]</sup> The questionnaire evaluates 8 different health quality domains: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE) and mental health (MH). SF-36 questionnaire consists of 36 items, with each domain varying from 2 to 10 items. Each domain is Scored range from 0 to 100 (worst to best possible health status).<sup>[23]</sup> SF-36 questionnaire was administered to patients by outpatient, telephone or e-mail before surgery and at 1 and 3 months after surgery.

### 2.6. Statistical analysis

Continuous data were expressed as mean with standard deviation or median with interquartile range and categorical variables were presented as number with percentage. Statistical analyses were performed using Mann–Whitney U test or Wilcoxon rank test for continuous data and Chi-square test or Fisher exact test for categorical variables. Two-sides  $P < .050$  was considered statistically significant. Statistical analyses and PSM were performed with SPSS version 22.0 (IBM SPSS, Inc., Chicago, IL).

## 3. Results

### 3.1. Baseline characteristics

A total of 205 patients meeting the study criteria were enrolled in this study. Of these, 80 were in the LLS group and 125 were in the OLS group. Baseline characteristics of all patients are outlined in Table 1. Age, sex, BMI, ASA grade, previous abdominal surgery, comorbidities and type of resection were similar between the 2 groups. The LLS and OLS groups differed before propensity score matching in terms of operative method ( $P = .030$ ), tumor location ( $P = .005$ ), largest tumor size ( $P = .002$ ) and tumor number ( $P = .008$ ). After PSM, the 73 LLS patients were matched with 73 OLS patients and the baseline demographics were well balanced.

**Table 1****Baseline characteristics before and after propensity score matching.**

|                            | Before matching |               | P    | After matching |               | P     |
|----------------------------|-----------------|---------------|------|----------------|---------------|-------|
|                            | LLR (n=80)      | OLR (n=125)   |      | LLR (n=73)     | OLR (n=73)    |       |
| Age, years                 | 47.3 (8.6)      | 48.3 (8.5)    | .396 | 48.0 (8.2)     | 49.4 (8.9)    | .321  |
| Sex (Male:Female)          | 25:55           | 49:76         | .248 | 22:51          | 28:45         | .295  |
| BMI, Kg/m <sup>2</sup>     | 23.8 (2.9)      | 23.4 (3.1)    | .333 | 23.8 (2.8)     | 23.1 (3.0)    | .152  |
| ASA grade                  |                 |               | .828 |                |               | 1.000 |
| I                          | 7               | 9             |      | 6              | 7             |       |
| II                         | 70              | 111           |      | 64             | 63            |       |
| III                        | 3               | 5             |      | 3              | 3             |       |
| Previous abdominal surgery | 9 (11.3%)       | 21 (16.8%)    | .273 | 9 (13.3%)      | 10 (13.7%)    | .806  |
| Comorbidities              |                 |               | .654 |                |               | .188  |
| COPD                       | 2 (2.5%)        | 3 (2.4%)      |      | 2 (2.7%)       | 2 (2.7%)      |       |
| Hypertention               | 4 (5.0%)        | 8 (6.3%)      |      | 3 (4.1%)       | 5 (6.8%)      |       |
| Diabetes mellitus          | 2 (2.5%)        | 3 (2.4%)      |      | 1 (1.4%)       | 2 (2.7%)      |       |
| Autoimmune disorder        | 0 (0.0%)        | 1 (0.8%)      |      | 0 (0.0%)       | 0 (0.0%)      |       |
| Operative method           |                 |               | .030 |                |               | .493  |
| Hepatic enucleation        | 48              | 93            |      | 48             | 44            |       |
| Hepatic resection          | 32              | 32            |      | 25             | 29            |       |
| Type of resection          |                 |               | .720 |                |               | .553  |
| Major resection            | 15              | 21            |      | 15             | 18            |       |
| Minor resection            | 65              | 104           |      | 58             | 55            |       |
| Tumor location             |                 |               | .005 |                |               | .552  |
| Caudate lobe (I)           | 2               | 4             |      | 2              | 3             |       |
| Left lobe (II, III, IV)    | 43              | 36            |      | 36             | 28            |       |
| Right lobe                 |                 |               |      |                |               |       |
| Anterior sector (V, VIII)  | 13              | 30            |      | 13             | 18            |       |
| Posterior sector (VI, VII) | 22              | 55            |      | 22             | 24            |       |
| Largest tumor size, cm     | 5.9 (5.5–7.8)   | 7.6 (5.9–9.2) | .002 | 6.5 (5.5–8.0)  | 7.2 (5.7–9.0) | .270  |
| Tumor number (solitary)    | 47 (61.8%)      | 53 (42.4%)    | .008 | 43 (58.9%)     | 35 (47.9%)    | .184  |

ASA=American Society of Anesthesiologists, BMI=body mass index, COPD=chronic obstructive pulmonary disease, LLS=laparoscopic liver surgery, OLR=open liver surgery.

**3.2. Perioperative outcomes**

After PSM, the short-term results are summarized in Table 2. There was no difference in operative time, Pringle time and intraoperative transfusion between the OLS and LLS groups. Similarly, no difference was found in bowel function recovery between the 2 groups, with 3.0 days in the OLS group and 2.0 days in the LLS group ( $P = 1.48$ ). The blood loss in the LLS group was significantly less than that in OLS group (200 vs 300 mL,  $P = .044$ ), respectively. In addition, the LLS group was associated with significantly shorter median postoperative hospital stay compared to the OLS group (4.0 vs 6.0 days;  $P < .001$ ). Overall complications were significantly lower in the LLS than in the OLS group (3 vs 14 cases;  $P = .005$ ).

The proportion of overall complication in terms of pleural effusion, ascites, hemorrhage, pneumonia, intestinal obstruction, obstructive jaundice, and deep vein thrombosis was lower in the LLS group when compared to the OLS group (4.1% vs 19.2%,  $P = .005$ ). According to Clavien–Dindo grade, grade I complication was 1 in the LLS group, and 5 in the OLS group ( $P = 1.000$ ). Grade II complication was 1 in the LLS group, and 4 in the OLS group ( $P = .364$ ). In addition, 5 patients in the OLS group had grade III complication: 1 patient suffering from intestinal obstruction received relaparotomy, 3 patients with pleural effusion treated by thoracentesis and continuous drainage, and 1 patient with obstructive jaundice received percutaneous transhepatic cholangiography and drainage. No mortality was observed during the study in the 2 groups.

**3.3. QOL outcomes**

Descriptive statistics for SF-36 scores comparing the laparoscopic versus open techniques before surgery and at 1 and 3 months

**Table 2****Intraoperative data and postoperative outcomes.**

|                                   | LLR (n=73)          | OLR (n=73)          | P     |
|-----------------------------------|---------------------|---------------------|-------|
| Surgical data                     |                     |                     |       |
| Operative time, min               | 185.0 (140.0–250.0) | 176.5 (135.0–235.0) | .856  |
| Blood loss, mL                    | 200.0 (100.0–300.0) | 300.0 (120.0–400.0) | .044  |
| Pringle time, min                 | 40.0 (20.0–60.0)    | 40.0 (29.0–50.0)    | .637  |
| intraoperative transfusion        | 14 (19.2%)          | 23 (31.5%)          | .087  |
| Postoperative outcomes            |                     |                     |       |
| Bowel function recovery, days     | 2.0 (1.0–4.0)       | 3.0 (2.0–4.0)       | .148  |
| Postoperative hospital stay, days | 4.0 (4.0–5.0)       | 6.0 (5.0–7.0)       | <.001 |
| Overall complications             | 3 (4.1%)            | 14 (19.2%)          | .005  |
| Type of complication              |                     |                     |       |
| Pleural effusion                  | 1 (1.4%)            | 5 (6.8%)            | .211  |
| Ascites                           | 0 (0.0%)            | 2 (2.7%)            | .476  |
| Hemorrhage                        | 0 (0.0%)            | 0 (0.0%)            | 1.000 |
| Pneumonia                         | 2 (2.7%)            | 5 (6.8%)            | .438  |
| Intestinal obstruction            | 0 (0.0%)            | 1 (1.4%)            | 1.000 |
| Obstructive jaundice              | 0 (0.0%)            | 1 (1.4%)            | 1.000 |
| Deep vein thrombosis              | 0 (0.0%)            | 1 (1.4%)            | 1.000 |
| Clavien–Dindo grade               |                     |                     |       |
| I                                 | 1 (1.4%)            | 2 (2.7%)            | 1.000 |
| II                                | 1 (1.4%)            | 4 (5.5%)            | .364  |
| IIIa                              | 0 (0.0%)            | 3 (4.1%)            | .243  |
| IIIb                              | 0 (0.0%)            | 2 (2.7%)            | .476  |
| mortality                         | 0 (0.0%)            | 0 (0.0%)            | 1.000 |

LLS=laparoscopic liver surgery, OLR=open liver surgery.

**Table 3**  
**Comparison of SF-36 scores between LLS group and OLS group after PSM.**

| SF-36 items          | Preoperative |             |      | Postoperative |             |      |             |             |      |
|----------------------|--------------|-------------|------|---------------|-------------|------|-------------|-------------|------|
|                      | LLS group    | OLS group   | P    | 1 months      |             | P    | 3months     |             |      |
|                      |              |             |      | LLS group     | OLS group   |      | LLS group   | OLS group   | P    |
| Physical functioning | 62.5 (14.5)  | 58.8 (16.6) | .449 | 69.4 (19.6)   | 68.5 (21.1) | .912 | 89.4 (12.3) | 84.5 (15.0) | .383 |
| Role-physical        | 50.3 (10.1)  | 52.2 (12.3) | .731 | 65.4 (13.7)   | 59.7 (15.8) | .264 | 85.1 (10.8) | 82.1 (13.1) | .512 |
| Bodily pain          | 55.9 (16.8)  | 53.5 (19.2) | .701 | 51.5 (18.7)   | 42.5 (21.6) | .181 | 88.2 (16.2) | 74.0 (17.6) | .033 |
| General health       | 60.3 (18.5)  | 62.5 (15.8) | .671 | 68.2 (23.6)   | 70.1 (20.5) | .731 | 85.9 (20.7) | 87.1 (18.3) | .886 |
| Vitality             | 57.3 (18.8)  | 54.3 (17.1) | .512 | 64.7 (24.1)   | 59.3 (21.5) | .312 | 82.3 (20.2) | 78.2 (17.7) | .413 |
| Social functioning   | 55.2 (16.3)  | 55.5 (17.0) | .992 | 69.1 (18.4)   | 66.2 (18.7) | .532 | 85.4 (15.1) | 80.2 (16.2) | .331 |
| Role-emotional       | 50.4 (22.9)  | 52.1 (25.1) | .851 | 68.2 (26.2)   | 62.6 (28.0) | .294 | 87.6 (13.8) | 76.6 (26.1) | .047 |
| Mental health        | 51.4 (16.8)  | 49.6 (13.2) | .823 | 61.5 (20.2)   | 55.1 (16.2) | .125 | 75.4 (16.0) | 71.2 (11.2) | .392 |

LLS=laparoscopic liver surgery, OLR=open liver surgery, PSM=propensity score matching, SF-36=short form-36 healthy survey.

after surgery were reported in Table 3. In terms of QOL using the SF-36, there was no difference between the 2 groups in the preoperative scores. One-month results showed no statistical difference for SF-36 scores between the 2 groups. At 3 month, no differences were noted for PF, RP, GH, VT, SF, RE. But the LLS group had statistically significant higher scores for BP and MH postoperatively than the OLS group ( $P=.033$  and  $P=.047$ ) at 3 month. There is no difference in QoL between the 2 surgical approaches, even though the LLS group had better QOL BP and MH scales at 3 months after surgery.

#### 4. Discussion

With improvements of surgical techniques and experience in laparoscopic surgery, the laparoscopic approach has gained popularity worldwide with favorable operative outcomes. Nevertheless, to the best of our knowledge, no randomized controlled trial has been completed and health related QOL is limited in current literature. Thus, this retrospective study was designed to compare the short-term perioperative outcomes and QOL between LLS and OLS for hepatic hemangioma. Differing from the previous studies, our study only focused on patients with hepatic hemangioma and used PSM to minimize the potential confounders to increase the comparability between the 2 groups.

Our research showed incomparable baseline clinical characteristics between the groups with significant differences in terms of operative methods, tumor location, largest tumor size and tumor number, which would influence patients' selection for surgical procedures. The surgeons tended to select relatively simple lesions and easy case for laparoscopic approach. Therefore, we performed the PSM method to overcome selection bias in the study and build matched groups for comparison of short-term outcomes. Although we only considered 4 independent variables in the model, other potential confounders including age, sex, BMI, ASA grade, previous abdominal surgery, comorbidities, and type of resection were also included to efficiently control for confounding effects. Thus, we evaluated the surgical and QOL outcomes of LLS after propensity score model adjustment.

In this study, a comparison of perioperative outcomes showed less blood loss, decreased overall operative complications and reduced postoperative hospital stay in the LLS group, which compared well with the literature.<sup>[24,25]</sup> In general, much attention has been paid to hemorrhage during liver surgery. Keeping the central vein pressure below 5 cm H<sub>2</sub>O during the liver parenchyma dissection and confirming important vascular

with the help of Intraoperative ultrasonography contributed to less blood loss.<sup>[26,27]</sup> The laparoscopic magnification provided a clear visual field to allow precise manipulation. What is more, laparoscopic pneumoperitoneum and intermittent Pringle maneuver limited intraoperative bleeding. Consistent with reported literature,<sup>[28]</sup> we found that the overall postoperative complications were lower in the LLS group, but the Clavien grade III did not differ between the 2 groups. In our study, the differences between the 2 groups are mainly Clavien grade I and II, such as pleural effusion and pneumonia, and the invasive treatment is not needed. With reduced tissue handling and less environmental exposure of the bowel, patients who underwent laparoscopic surgery suffered fewer adhesion-related complications and reoperations compared with open surgery.<sup>[27,29–30]</sup> The present study showed that the LLS group got obvious advantages of smaller abdominal incision and dissection area, and was associated with less blood loss, less postoperative pain and faster postoperative recovery. Thus, these may lead to earlier breathing exercises and earlier ambulation, which improved pulmonary function recovery and a lower incidence of postoperative symptomatic pleural effusion.<sup>[31]</sup> In our study, the postoperative hospital stay was significantly shorter in the LLS group compared to the OLS group. The decrease in the quantity and severity of complications could explain the significant reduction in postoperative hospital stay.

For hepatic hemangioma patients enrolled in this study, no difference was observed in QOL for the 2 groups in the short term after surgery. Although, we found a significant improvement in BP and MH of QOL following laparoscopy at 3 months after surgery. To date, there is not much evidence on liver surgery with regards to QOL outcomes. Kamphues et al<sup>[32]</sup> found that cancer-related QOL scores in 31 patients operated for symptomatic liver cyst improved after surgery without comparing laparoscopic and open approaches. Giuliani et al<sup>[33]</sup> compared quality of life outcomes between laparoscopy and open technique for benign liver lesions and reported an advantage of the laparoscopic approach at 1-year follow-up, but he didn't control selection bias. Thus, our study is not comparable to the one of the present studies. The short-term QOL observed in the 2 groups was similar in our study. While the BP and MH scores were slightly higher after laparoscopic surgery may be related to multiple factors. Overall, the minimally invasive approaches were associated with less postoperative pain, faster postoperative recovery, lower complication rates and shorter postoperative hospital stay. The possible explanation is that LLS decreased tissue trauma with four or 5 trocars placed in the upper abdomen. Whether better cosmetic effect, reduced abdominal wall

damage, less postoperative adhesions, or faster gastrointestinal recovery<sup>[33,34]</sup> can be responsible for an earlier return to normal activity. All these benefits attributed to the improved QOL scores in BP and MH for patients undergoing laparoscopic approach. However, further studies with long-term QOL are definitely warranted.

There are several limitations in the study that must be noted. The present study is a retrospective analysis, not a randomized trial. Thus, the PSM method was employed to reduce the bias due to confounding between the 2 groups. However, PSM itself has limitations that cannot eliminate the bias. In addition, the study is limited to small sample size and lack data about long-term QOL outcomes. And another limitation that must be mentioned is that we only used the SF-36 scale to assess the postoperative QOL instead of disease specific QOL tools.<sup>[35]</sup> Further well-designed and prospective investigations are warranted.

In conclusion, the present study showed that laparoscopic approach was associated with less blood loss, shorter postoperative hospital stay and lower complication rates compared with open approach. But short-term QOL outcomes were not different between the 2 surgical approaches. Laparoscopic approach for hepatic hemangioma is a feasible and safe procedure with good short-term outcomes, but further studies are needed to confirm these results.

## Author contributions

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