Comparison of efficacy and safety of laparoscopic and open enucleation for liver hemangioma in the right hemi liver: a retrospective cohort study

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Background: Open enucleation (OE) is often performed for giant liver hemangioma (LH) because of its advantage in maximum preservation of functional liver parenchyma. Laparoscopic enucleation (LE) has been applied to LHs more frequently for its potential advantages in postoperative recovery and blood loss. However, to date, LE is still a difficult and complex surgical technique especially when the hemangioma is located in the right hemi liver. The aim of this study was to analyze whether LE is superior to OE for LH in the right hemi liver.

Methods: Demographics and perioperative data of patients who underwent LE or OE for LH in the right hemi liver between May 2013 and July 2020 were collected. To decrease the selection bias, patients who underwent OE in first 2 years and those underwent LE in next 5 years by a same operation team were included. The data of sex, age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, largest tumor size, and removed tumor number were enrolled in the propensity score matching (PSM) method to compensate for differences in the baseline characteristics between LE and OE groups. The perioperative outcomes were compared between 2 matched groups after PSM method.

Results: A total of 110 patients (36 LE *vs.* 74 OE) were matched by age, sex, BMI, ASA grade score, largest tumor size, removed tumor number and tumor location. Finally, 34 patients in each group were retained after PSM. There were no significant differences in operative time, estimated blood loss, amount of autologous transfusion, morbidity grade and the levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) on postoperative day 1 or 3 or 5. LE was associated with a significantly higher rate of use of the Pringle maneuver (P<0.001), shorter time to oral feeding (P<0.001) and shorter postoperative length of stay (P<0.001).

Conclusions: For LHs in the right hemi liver, the perioperative safety of LE is not inferior to OE, and LE seems to achieves a faster recovery from surgery compared with OE.

Keywords: Enucleation; laparoscopic hepatectomy; liver hemangioma (LH)

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Introduction

Hemangiomas are the most common benign liver tumors, with an estimated prevalence of 0.4–20% (1-3). They are usually asymptomatic and need no intervention, but symptoms may present when a hemangioma is >5 cm and treatment then needs to be considered (4). Surgical management is indicated if the hemangioma is symptomatic or grows rapidly and comprises liver resection, enucleation and even liver transplantation (5-7). Of these, resection and enucleation are applied more frequently as effective therapeutic modalities (8-10), and enucleation may be the preferred method because it has fewer overall complications, less blood loss and shorter postoperative length of stay (8,11-14). Moreover, enucleation is selected more frequently when the hemangioma is located in the right hemi liver because of its advantage in maximum preservation of functional liver parenchyma (13,15).

Over the past decades, laparoscopic liver surgery has gained broad acceptance for its smaller incisions and faster postoperative recovery (16-19). With the development of laparoscopic techniques, laparoscopic enucleation has been applied to liver hemangiomas (LHs) more frequently as a minimally invasive procedure for its potential advantages in postoperative recovery and blood loss (20). laparoscopic enucleation (LE) is frequently applied for left LHs (21), and even for giant right LHs >20 cm (22). The location of the tumor may be a risk factor of perioperative safety but not a strict contraindication for LE (23). To date, LE is still a more difficult and complex surgical technique compared with open enucleation (OE) when the hemangioma is located in the right hemi liver. However, the perioperative efficacy and safety of LE for LHs located in right hemi liver have not been verified compared with OE. Therefore, the aim of this study was to analyze whether LE is a safe and effective approach for right hepatic hemangioma and provide a referential basis for clinical application of LE. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3074/rc).

Methods

Patients

The departmental database was searched for patients who had been surgically treated for LH between May 2013 and July 2020 in an experienced tertiary hospital. In the first 2 years, we preferred to choose OE based our initial technical experience in LHs located in right hemi liver and attempted to perform LE in selected cases. Since 2015, LE have been performed in all LHs cases after we crossed the Learning curve. To decrease the selection bias, patients who underwent OE May 2013 to May 2015 and those underwent LE from June 2015 to July 2020 were included in our study (patients underwent LE in first 2 years were excluded). In total, 110 patients who underwent LE or OE for the main lesion located in the right liver (segments V–VIII) were included.

The diagnosis of LH was confirmed by contrast-enhanced computed tomography (CT) or magnetic resonance imaging. The indications for surgery were LH (≥5 cm) with symptoms (abdominal distention, abdominal pain, or others), Kasabach-Merritt syndrome, or hemangioma >10 cm that increased rapidly over at least 3 years of follow-up. The operation was not determined by tumor size alone. If a patient's symptoms did not match the size or location of the LH, upper gastrointestinal endoscopy and/or colonoscopy were implemented for further decision making.

We collected the following data of each patient: demographics, location and number of hemangioma(s), symptoms, operative time, blood transfusion requirement, amount of autologous transfusion, use of Pringle maneuver, occlusion time, duration of postoperative stay, time of postoperative oral feeding, morbidity, mortality and the levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) on postoperative day 1 or 3 or 5. According to surgical method, patients were classified as the LE or OE group and compared for demographic characteristics, surgical procedure and perioperative variables.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Institutional Ethical Review Board of the China-Japan Friendship Hospital. Informed consent was given by all patients.

Surgical procedure

Enucleation is considered to remove the LH with no loss of normal hepatic parenchyma. The surgical procedure was chosen by an experienced surgical team who had performed >300 operations for LH, considering the following factors: the size and location of the LH, its relationship to major vascular and biliary structures, and the remnant volume of the liver parenchyma. All operations were performed by the same team of surgeons and all patients received the same

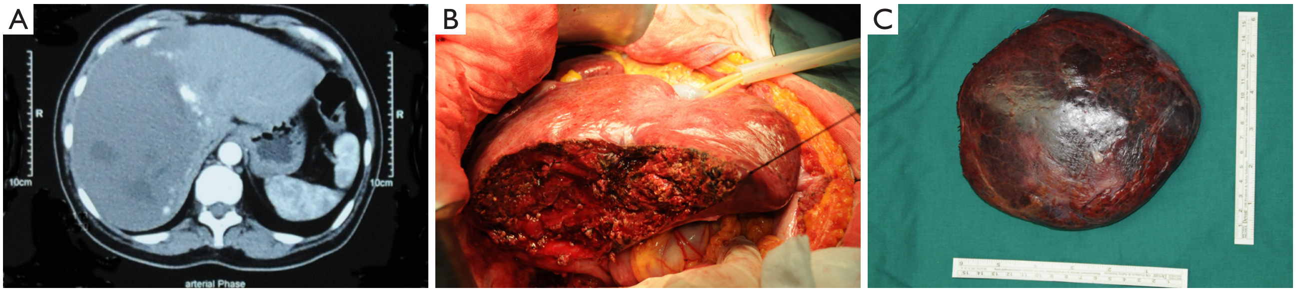

Figure 1 Procedure of open enucleation. (A) CT images show a large mass (>15 cm) in the right liver. (B) Wound surface of remnant liver after open enucleation of the hemangioma. (C) Gross specimen shows a brown, cavernous mass. CT, computed tomography.

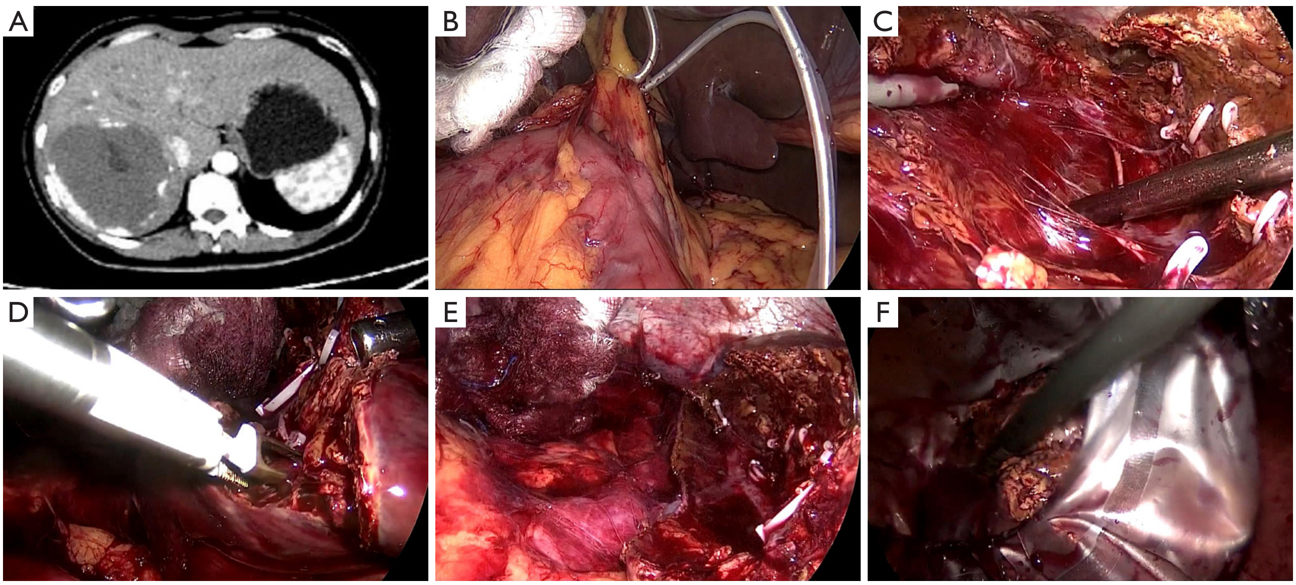

Figure 2 Procedure of laparoscopic enucleation. (A) CT images show the mass (~10 cm) in the right liver. (B) Pringle maneuver using a plastic pipe in the laparoscopic approach. (C) Blunt dissection to separate the mass and the remnant normal liver. (D) Hemostasis of wound surface using bipolar forceps. (E) Wound surface of remnant liver after laparoscopic enucleation of the hemangioma. (F) Removal of specimen using a retrieval bag. CT, computed tomography.

perioperative management.

The open procedure (*Figure 1*) was conducted through a right or bilateral subcostal incision with the patient in the supine position. To reduce bleeding during enucleation, the Pringle maneuver was conducted during parenchymal transection in cycles of 30/5 min of clamp/unclamp time when it was appropriate. The enucleation of the LH was performed with a Cavitron Ultrasonic Surgical Aspirator (SonoCA300; Soring Inc., Quickborn, Germany). The surrounding bile ducts and vessels were preserved as much as possible and bleeding control was performed by clips or ligation.

In the laparoscopic procedure (*Figure 2*), a supine position was required with the head elevated higher than the feet and the legs apart and tilted 30° to the left. Four or five abdominal incisions were made routinely (two 12-mm trocars and two 5-mm trocars), but another 1 to 2 ports were inserted according to the location and number of tumors. Pneumoperitoneum was maintained at approximately 14 mmHg. Intraoperative ultrasonography (ProSound A-10; Aloka Inc., Tokyo, Japan) was used to guide the operation. The Pringle maneuver was routinely performed. The surrounding bile ducts and vessels were dissected by transonic scalpel and suction implement; smalldiameter vessels were coagulated using bipolar forceps and larger vessels were clip or hem-o-lock ligated. Generally, the surgical technique was similar to the open procedure.

The Cell Saver system (Electa; Sorin Group Inc., Mirandola, Italy) for autologous transfusion was prepared for each case. For patients with multiple LHs, the largest lesion and those close to the surface of liver and >5 cm were removed. After investigating the amount of remnant liver, the location of the LH, blood loss, and operative time, the decision on removing any deeper LHs (<5 cm) was made and in most cases they were not resected. All resected specimens were verified by histopathologic examination.

Parenteral nutrition and early enteral nutrition support were given to all patients during the early postoperative period and when bowel activity returned, respectively. All postoperative complications were classified (Clavien-Dindo classification) and recorded (24).

Propensity score matching (PSM)

To minimize the influence of potential confounders and selection bias, PSM was conducted to compensate for differences in the baseline characteristics between LE and OE groups. The following variables were enrolled in the PSM model: sex, age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, largest tumor size, and removed tumor number. A propensity score was generated by logistic regression with the imbalanced variables for each patient. Matched patients were chosen by 1:1 nearest neighbor matching of the propensity score.

Statistical analysis

Categorical variables are presented as the number of patients or ratios, and continuous variables following normal distributions are presented as the mean ± standard deviation. Continuous variables with abnormal distributions are presented as medians with interquartile range. Categorical variables were compared using the Chi-square test or Fisher's exact test. Student's *t*-test was applied for continuous variables with a normal distribution. The Mann-Whitney U test was applied for nonparametric variables. The statistical significance threshold was set to 5% for two-tailed tests and corrected P values <0.05 were considered statistically significant. The statistical analysis was conducted with SPSS software (version 24.0, IBM Corp, Armonk, NY, USA).

Results

Baseline characteristics

A total of 110 patients with LHs located in the right hemi liver (36 underwent LE, 74 underwent OE) were enrolled in this study. There was no significant difference in the largest tumor size between the LE and OE groups (11.2±5.7 *vs.* 10.0±3.3 cm). Also, age, sex, BMI, ASA grade and tumor location were comparable between groups, but the groups differed significantly before PSM in terms of removed tumor number (P=0.002). After PSM, 34 patients who underwent LE and 34 patients who underwent OE were matched in a case-control approach (*Table 1*).

Perioperative outcomes

The perioperative outcomes of the groups are presented in *Table 2*. There were no significant differences in operative time, estimated blood loss, autologous transfusion, and blood transfusion rate between the LE and OE groups. Although the LE group had a higher rate of use of the Pringle maneuver (P<0.001), there was no differences in occlusion time between the LE group and patients undergoing the Pringle maneuver in the OE group. Both groups had similar Clavien-Dindo grades of postoperative complications and no deaths were reported during the study. In addition, the levels of ALT and AST after surgery (postoperative day 1 or 3 or 5) in the LE group were similar to those in the OE group. However, there were differences of statistical significance between the groups in the postoperative timing of oral feeding (3 *vs.* 5 days, P<0.001) and the length of stay (7 *vs.* 9 days, P<0.001).

Discussion

With the development of techniques and operator experience, laparoscopic liver surgery has similar safety and improved short-term outcomes to open liver surgery when performed in selected patients and by trained surgeons (25). For resection of liver tumors located in the left hemi liver, laparoscopic left-lateral sectionectomy and hemihepatectomy have become the standard of care (26). However, for tumors located in the right hemi liver, especially deep-seated tumors close to the bare area of the liver and the inferior vena cava, laparoscopic surgery is still a challenging procedure and remains controversial because of its difficult exposure and high risk of bleeding (27).

Enucleation and liver resection are the two main

Table 1 Comparison of baseline characteristics of the LE and OE groups

Variables	Before matching			After matching		
	LE (N=36)	OE (N=74)	P value	LE (N=34)	OE (N=34)	P value
Sex (male: female)	11:25	17:57	0.392	10:24	7:27	0.401
Age (years)	42.0±9.1	44.1±9.3	0.257	42.5±9.1	42.4±9.4	0.937
BMI (kg/m^2)	22.9±3.1	23.0±2.7	0.652	23.0±3.1	23.3±2.8	0.516
ASA grade			0.079			0.774
1	6	6		3	3	
2	29	61		23	22	
3	1	7		1	2	
Largest tumor size (cm)	10.0 (8.3–10.0)	10.0 (8.0–12.0)	0.363	10.0 (8.0–10.3)	10.0 (8.0–10.3)	0.504
Removed tumor number (single: multiple)	30:6	39:35	0.002	28:6	26:8	0.549
Tumor location			0.679			0.457
Segment V/VI	16	36		15	12	
Segment VII/VIII	20	38		19	22	

Values are presented as mean ± SD, medians with interquartile range, or numbers. LE, laparoscopic enucleation; OE, open enucleation; BMI, body mass index (kg/m^2); ASA, American Society of Anesthesiologists.

Table 2 Comparison of perioperative outcomes of the LE and OE groups

Variables	LE (N=34)	OE (N=34)	P value
Operative time (min)	200 [157–240]	213 [179–270]	0.193
Use of Pringle maneuver, n (%)	34 (100.0)	23 (67.6)	<0.001
Rate of conversion to open surgery, n (%)	7 (20.6)	N/A	–
Occlusion time[a] (min)	30.5 [15.0–45.3]	30.0 [20.0–45.0]	0.844
Estimated blood loss (mL)	500 [200–975]	500 [300–925]	0.844
Autologous transfusion (mL)	150 [0–600]	225 [0–313]	0.847
Blood transfusion rate, n (%)	6 (17.6)	9 (26.5)	0.380
Morbidity[b], n (%)			1.000
Grade 1	2 (5.9)	3 (8.8)	
Grade 2	1 (2.9)	2 (5.9)	
≥ Grade 3	0	0	
Mortality	0	0	1.000
ALT (day 1) (IU/L)	356 [197–569]	250 [210–357]	0.144
ALT (day 3) (IU/L)	200 [105–329]	161 [116–251]	0.367
ALT (day 5) (IU/L)	81 [52–137]	71 [53–91]	0.320
AST (day 1) (IU/L)	270 [187–468]	212 [134–347]	0.225
AST (day 3) (IU/L)	65 [44–149]	91 [71–136]	0.096
AST (day 5) (IU/L)	33 [22–57]	44 [31–51]	0.249
Time of oral feeding (day)	3.0 [2.0–4.0]	5.0 [4.0–6.0]	<0.001
Length of stay (day)	7.0 [6.0–8.0]	9.0 [9.0–11.3]	<0.001

Values are presented as medians with interquartile range or n (percentage). [a], to calculate occlusion time, only patients who underwent the Pringle maneuver during operation were included; [b], Clavien-Dindo classification. LE, laparoscopic enucleation; OE, open enucleation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; IU, international units.

surgical procedures for LHs. Recent studies have shown that, compared with liver resection, enucleation may be preferable for suitable LHs by preserving more hepatic parenchyma and reducing postoperative complications (28,29), and in our experience, enucleation is suitable for lesions in the right hemi liver (13,15). Although several studies had reported their experience with LE of LHs and advocated the laparoscopic approach for its safety and fast recovery (30-32), few studies have evaluated the outcome of LE for LHs in the right hemi liver. Thus, we designed this retrospective study to compare the surgical outcomes between LE and OE groups for LHs. Unlike the previous study, we only focused on patients who had LHs in the right hemi liver and underwent LE performed by the same team.

The results of our comparison of baseline characteristics showed that the removed tumor number of the OE group was significantly higher than that in the LE group, which may be explained by selection bias because the surgeons tended to perform laparoscopic surgery for selected patients with a single tumor. For multiple hemangiomas located in different lobes or hemi liver, OE was the preferred operative method. To minimize the potential selection bias and increase comparability, a PSM comparison was performed.

LHs have abundant blood supply and intraoperative bleeding is the main and serious risk. Hemangiomas in the right hemi liver have a higher rate of vessel compression (15), which can potentially result in severe intraoperative bleeding (33-35), and the Pringle maneuver is usually performed. In our study, the Pringle maneuver was routinely performed for all patients in the LE group to prevent surgical difficulties caused by unexpected hemorrhage. Even still, there were 7 cases (20.6%, 7/34) of conversion to open procedure in the LE group due to unmanageable hemorrhage.

However, the LE group had a similar occlusion time to patients who underwent the Pringle maneuver in the OE group and there were no differences in the levels of ALT and AST on postoperative day 1 or 3 or 5. These findings showed that each procedure did not affect the postoperative recovery of liver function. Moreover, there were no significant differences in operative time, estimated blood loss, autologous transfusion and blood transfusion rate, which suggested that hemorrhage control in the LE group was similar to that in OE group when blood inflow control and careful dissection are performed by an experienced surgical team. In our study, there were no surgery-related deaths in either group and no difference in morbidity between the LE and OE groups.

The LE group had the advantages of smaller abdominal incisions, less postoperative pain and faster postoperative recovery. Overall, the LE group had a similar operative time compared with the OE group. Because of the faster postoperative recovery, the median time to oral feeding after surgery was 3 days (*vs.* 5 days in the OE group, P<0.001) and the postoperative length of stay was 7 days (*vs.* 9 days in the OE group, P<0.001).

There are several limitations to this study. Firstly, we collected patients' data retrospectively. Surgical procedures were determined by the surgeon's experience and the features of the lesion. However, to minimize selection bias, the cases were selected from different periods into two groups, and in more complicated cases the laparoscopic approach was used with increasing operator experience. In addition, a 1:1 PSM comparison was performed due to unequal baseline patient characteristics between the two groups. Secondly, this study was a single institution's experience over a relatively short period (5 yeas) and it might not be comparable to other centers. However, the surgical techniques and indications for surgery were consistent, which helped to reduce performance and assessor bias. Lastly, additional external studies are required to validate our findings.

In conclusion, LE had comparable safety and efficacy to OE in cases of LHs located in the right hemi liver. LE may offer significant benefits over OE by decreasing the time to postoperative oral feeding and the length of stay. As far as we know, this is the first study to compare the surgical outcomes of LE *vs*. OE.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-3074/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-3074/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3074/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Institutional Ethical Review Board of the China-Japan Friendship Hospital. Informed consent was taken from all the patients.

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