Laparoscopic versus open major liver resection for hepatocellular carcinoma: a case-matched analysis of short- and long-term outcomes

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Research

Keywords: Lapaproscopic, open, hepatocellular carcinoma, case-matched analysis, live resection

Posted Date: April 7th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-18533/v1

Version of Record: A version of this preprint was published at Open Medicine on January 1st, 2021. See the published version at https://doi.org/10.1515/med-2021-0308.

Abstract

Background: The feasibility and safety of laparoscopic major hepatectomy (LMH) is still uncertain. The purpose of the present study is to compare the short- and long-term outcomes of LMH with those of open major hepatectomy (OMH) for hepatocellular carcinoma (HCC).

Method: Between January 2012 and December 2018, a total of 26 patients received laparoscopic major hepatectomy in our center. To minimize any confounding factors, a 1:3 case-matched analysis was conducted based on the demographics and extent of liver resection. Data of demographics, perioperative outcomes and long-term oncologic outcomes were reviewed.

Results: Intraoperative blood loss (P=0.007) were significantly lower in LMH group. In addition, LMH group exhibited a lower overall complication rate (P=0.039) and shorter postoperative hospital stay (P=0.024). However, no statistically significant difference was found between LMH and OMH regarding operation time (P=0.215) and overall cost (P=0.024). Two laparoscopic cases were converted to open liver resection. In regard with long-term outcomes, there was no significant difference between LMH and OMH regarding disease-free survival (DFS) (P=0.079) and overall survival (OS) (P=0.172).

Conclusion: LMH can be an effective and safe alternative to OMH for selected patients with liver cancer in short- and long-term outcomes.

Introduction

Laparoscopic liver resection (LLR) has been increasingly utilized by surgeons, since the first introduction of LLR in 1992 [1]. With the continuous development in laparoscopic devices and approaches, laparoscopic minor resections have even become standard surgical procedures for treating solitary lesion located in liver segments 2–6 [2–4]. However, laparoscopic major hepatectomy (LMH) has been relatively slow, because of LMH often correlated with a high risk of uncontrollable intraoperative bleeding, difficult procedures and high rate of conversion. The second International Consensus Conference of Morioka recommended that LMH comprised innovative procedures in the exploration phase and could only be performed in those with experience of major open liver resections and advanced laparoscopic techniques [4]. With accumulating the development of new instruments, the introduction of novel techniques, the improvements in surgical skills and experience of LLR, some recent studies reported that LMH and OMH had similar oncologic outcomes in patients with hepatocellular carcinoma (HCC) [5–8]. However, just a few studies described the long-term oncologic outcomes of LMH for HCC. Therefore, the present study aimed to compare the short- and long-term outcomes between LMH and OMH in patients with hepatic disease, especially those with HCC.

Materials And Methods

Patients

Between January 2012 and December 2018, we retrospectively collected data of 26 patients who underwent laparoscopic major hepatectomy (LMH) for hepatocellular carcinoma (HCC) at The Second Affiliated Hospital of Nanchang University. In addition, a 1:3 case-matched patients (n=78) who underwent open major hepatectomy (OMH) was also collected based on the demographics and extent of liver resection. The study protocol was approved by the Institutional Review Board at the Second Affiliated Hospital of Nanchang University and the informed consents were taken from all patients. Data of the medical records including patient demographics, perioperative outcomes and long-term oncologic follow-up was retrieved. The patients were divided into two groups according to the type of procedure: LMH group (n=26) and OMH group (n=78).The study was conducted in accordance with the Helsinki Declaration of 1964 and all subsequent amendments, it was approved by the Ethics Committee of the Second Affiliated Hospital of Nanchang University in China, and all patients provided written informed consent.

Definitions

According to The Brisbane 2000 terminology, major hepatectomy (MH) was defined as resection of more than 3 liver segments [9,10]. Because of right posterior sectionectomy and right anterior sectionectomy were difficult to perform by open laparoscopic hepatectomy, these procedures were also considered as major hepatectomy [11]. Overall complication was defined as those occurred within 30 days after hepatectomy. The Claviene-Dindo classification was used to grade the severity of complications [12]. Postoperative mortality was defined as those death within 90 days after surgery.

Surgical procedures

The preferred type of liver resection was anatomical resection, if indicated. The selection for type of liver resection was based on the remaining liver function, the proximity of lesion to major vascular structure, the number of lesions and the depth of the lesion. If the hepatic reserve was expected to be enough for the deep-seated lesion, major liver resection was performed. The hepatic reserve was evaluated in terms of the computed tomographic volumetry and indocyanine green retention rate at 15 min (ICG-R15). The indication of LMH was similar to that of OMH including the terms of the hepatic reserve, type of hepatectomy, and postoperative care [13,14]. For these patients with central lesions in the suprahepatic junction adjacent to the major hepatic vein and tumors adjacent or invading to the main portal pedicle or inferior vena cava, however, laparoscopic hepatectomy was not usually considered.

It has been described in more detail elsewhere for the techniques of LMH and OMH performed at our institution [13,14]. For both anatomical right or left hepatectomy, intraoperative ultrasonography was used routinely in order to decide the type of hepatectomy and get the free resection margin (Fig. 1A and B). The Glissonean approach was used to control the liver inflow before mobilization of the hepatic lobe (Fig. 1C and D). For right posterior sectionectomy or hemihepatectomy, multiple small hepatic veins were divided and the liver was fully mobilized from the inferior vena cava as much as possible. For left hemihepatectomy, the round ligament was firstly divided. Then, the left triangular ligaments and left falciform were dissected until the left hepatic vein was exposed. The left portal vein and hepatic artery were isolated and divided by Hem-o-lock clips and or Endo-GIA device, after fully mobilizing the left liver (Fig. 1E and F).

Postoperative care and follow-up

The same postoperative monitoring and care were used to all patients, which included routine liver function tests and blood examinations. The abdominal drainage was removed in the absence of bile leakage or peritonitis. Assessment of serum AFP levels, ultrasonography, CT and liver function tests were required bimonthly during the first postoperative year of follow-up. Then, the above tests should be required quarterly if no recurrence was detected. Recurrence was defined as HCC-characterisitc findings on follow up CT or MRI.

Statistical analysis

SPSS 17.0 software program (IMB Inc., Chicago, IL, USA) was used to process all data. Categorical variables were compared using χ^2 test or Fisher's exact test as appropriate, and continuous parameters using Student's t test. Kaplan-Meier estimates for DFS and OS were compared between the LMH group and the OMH group using the log-rank test. $P < 0.05$ was regarded as statistically significant.

Results

During the study period, a total of 456 consecutive patients were treated by hepatectomy. Of these patients, 26 patients underwent LMH, and a 1:3 case-matched patients (n=78) who underwent open major hepatectomy (OMH) was also collected based on the demographics and extent of liver resection.

Patients' characteristics

Patients' characteristics of both groups were listed in Table 1. No significant differences were found between both groups in preoperative demographic characteristics, including gender, age, Child–Pugh classification, histologic cirrhosis, tumor size, and number of tumors.

Surgical results

The surgical results of both groups were listed in Table 2, and no mortality during surgery were observed. Two patients (7.7%) in the laparoscopic group were converted to open procedure because of uncontrollable bleeding during parenchymal transection. A total 55 patients (70.5%) were treated by portal triad clamping during hepatectomy in the OMH group, and 15 patients (57.7%) was used in the LMH group (P=0.227). Significantly less intraoperative blood loss was found in the LMH group than OMH group (340.8±225.2 ml vs. 601.4±509.4 ml, P=0.007); however, no significant difference between LMH group and OMH group was found in intraoperative transfusion (26.9% vs. 29.5%, P=0.803). In addition, the operation time did not differ significantly between both groups (264.2±14.1 min vs. 255.4±36.3 min, P=0.215).

A total 18 patients (69.2%) were performed by right hepatectomy in the LMH group and 54 patients (69.2%) in the OMH. Pathologic examination of free resection margin was similar between both group (96.2% vs. 91.0%, P=0.671).

Postoperative outcomes and cost

Postoperative results of both groups were listed in Table 2. There were one laparoscopy patient (3.8%) and five (6.4%) patients undergoing open surgery with hepatectomy related complications after surgery (P=1.000). Overall complications were significantly lower in the LMH group comparing with OMH group (15.4% vs. 37.2%, P=0.039). There was no perioperative mortality between both groups. Although no significant difference was found in recovery of bowel movement (1.5 ± 0.5 days vs. 3.1 ± 0.6 days, P=0.083) between both groups, the time of off-bed activities (2.8 ± 0.6 days vs. 4.9 ± 1.1 days, P=0.003) and postoperative hospital stay (11.0 ± 2.9 days vs. 15.5 ± 5.2 days, P=0.024) were significantly shorter in LMH group comparing with OMH group. Both the surgical and overall costs were collected. Interesting, we found that although no significant difference was found in surgical cost between both groups (4850.0±1041.8 RMB vs. 4790.3±904.3 RMB, P=0.860), the overall cost of LMH group was significantly lower than OMH group (56306.4±9477.5 RMB vs. 59251.9±16075.6 RMB, P=0.024).

Long-term survival outcomes

The median follow-up was (33.3±15.6) months in the LMH group and (31.4±15.7) months in the OLH group, and no significant difference was found between both groups (P=0.752). Median DFS of LMH and OMH groups was 63.0 months [95% confidence interval (CI) 31.8-94.1 months] and 36.0 months (95% CI 29.7-42.3 months), respectively (Fig. 2A). Median OS of LMH and OMH groups was 60.0 months (95% CI 50.3-69.7 months) and 60.0 months (95% CI 47.6-72.4 months) (Fig. 2B). No significant difference in DFS (P=0.079) and OS (P=0.172) was found between both groups.

Discussion

With the continuous development in laparoscopic devices and approaches, laparoscopic minor liver resections have even become standard surgical procedures for treating solitary lesion located in liver segments 2-6 [2-4]. Due to the long learning curve for laparoscopic liver resection, it is necessity to consider the expertise of the surgeon for safe laparoscopic minor resection [15,16]. Recently, in some highly specialized centers, LMH can be performed as effectively and safely as OMH [3]. LMH even was not inferior to OMH in terms of resection margin, postoperative complications, operative mortality and long-term outcomes stated by the Second International Consensus Conference held in Morioka; in addition, LLR was superior in terms of shorter hospital stay [4].

As showed in table 3, we have summarized all comparative studies of major LLR vs. major OLR [4-8,17-23]. The negative margins and oncologic integrity of the procedure should be obtained, when major laparoscopic liver resection is performed for cancer. No difference in the resection margin was found in the comparative studies of major LLR vs. major OLR, although tumor size of major LLR was large than major OLR in the studies of Goumard [8], Guro [17], Komatsu [18] and Tarantino [20]. In the present case-matched study, the negative margin of major LLR was similar to major OLR. In addition, the R0 resection

rate of LMH group was 96.2%. Recently, some meta-analyses of retrospective studies also observed that no significant difference was found between major LLR and major OLR in the resection margin for HCC patients [24,25]. In order to better learn major LLR for HCC patients, long-term survival rate should also be obtained. As showed in table 3, there were three studies provided data of five-year over survival (OS) and disease-free survival (DFS) including the data of our study. Although laparoscopic group has a longer OS comparing with open group, no significant difference was found between both groups in regarding with OS and DFS. Therefore, we can conclude that major LLR may be as oncological safety as major OLR. Due to the above data come from observational clinical studies (OCS), however, additional randomized controlled trials (RCTs) studies are required to provide convincing evidence in the future.

With regard to the data on perioperative outcomes, major LLR was associated with favorable intraoperative blood loss, total postoperative complications and postoperative hospital stay in the summarized comparative studies. However, the operation time of major LLR was significantly longer than major OLR in most of the retrospective studies [4-8,17-19,21,22]. Recently, the Japanese National Clinical Database showed that major LLR was associated with less blood loss, a lower complication rate and shorter hospital stay comparing with major OLR [26]. Regarding short-term outcomes in the present study, the average operation time of major LLR group was longer than OLR group. However, major LLR group has a significantly lower intraoperative blood loss and postoperative complication rate and shorter postoperative hospital stay. This indicates that although major LLR is technically more difficult than OLR, major LLR is similar to major OLR in short-term outcomes. Furthermore, owing to its minimal invasiveness, major LLR facilitates earlier patient recovery. Interesting, our results showed that although no significant difference was found in surgical cost between both groups, the overall cost of LMH group was significantly lower than OMH group which might be related with fast recovering.

To the best of our knowledge, the present report was the first study summarized the long-term survival rate of major LLR in patients with HCC. However, several limitations should be care in our study. First, this was a retrospective study, which may introduce bias. Second, although there was no difference in the resection margin between the two groups, we preferred major OLR in patients with HCC close to the major Glisson pedicle or the inferior vena cava. In conclusion, major LLR of HCC is feasible and safe with favorable short- and long-term outcomes, when performed in experienced centers.

Declarations

Acknowledgments

Not applicable

Funding

The present study was supported by grants from the Department of Education Project of Jiangxi Province,China(Grant No. GJJ180079 and No. CJJ180083),the Key Research and Development Project of Science and Technology Department of Jiangxi

Province,China.(Grant No. 20181BBG70025).

Availability of data and materials

The data sets used or analyzed in this study are available from the corresponding author on reasonable request.All patients provided written informed consent.

Authors’contributions

Aoxiao He,Yong Li,Long Peng and Linquan Wu conceived and designed the study; collected, assembled, analyzed, and interpreted the data; wrote the manuscript; and approved the final manuscript.Jiakun Wang,Qian Feng and Wenjun Liao collected, assembled, analyzed, and interpreted the data; wrote the manuscript; and approved the final manuscript.Zhihao Huang,Zhouqing Xiao and Junjun WU conceived and designed the study, helped perform the analysis with constructive discussions, and approved the final manuscript.

Ethics approval and consent to participate

The study was conducted in accordance with the Helsinki Declaration of 1964 and all subsequent amendments, it was approved by the Ethics Committee of the Second Affiliated Hospital of Nanchang University in China.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 patients' characteristics and perioperative outcomes

	LMH (n = 26)	OMH (n = 78)	*p* value
Gender (M:F)	11:15	33:45	1.000
Age (years)	56.1 ± 10.6	52.0 ± 12.2	0.698
Child–Pugh class, no. (%)			
A	23 (88.5%)	70 (89.7%)	1.000
B	3 (11.5%)	8 (10.3%)	
Histologic cirrhosis, no. (%)	16 (61.5%)	45 (57.7%)	0.730
Tumor size (mm)	75.0±35.1	75.5±38.8	0.378
Number of tumors	1.3±0.6	1.4±0.7	0.381

LMH laparoscopic major hepatectomy, OMH open major hepatectomy, M male, F female.

Table 2 Operative outcomes

	LMH (n = 26)	OMH (n = 78)	*P* value
Operation time (min)	264.2±14.1	255.4±36.3	0.215
Intraoperative blood loss (ml)	340.8±225.2	601.4±509.4	**0.007**
Intraoperative transfusion no. (%)	7 (26.9%)	23 (29.5%)	0.803
Total complication, no. (%)	4 (15.4%)	29 (37.2%)	**0.039**
Wound infection	2 (7.7%)	6 (7.7%)	1.000
Bile leakage	1 (3.8%)	5 (6.4%)	1.000
Intraabdominal fluid collection	1 (3.8%)	10 (12.8%)	0.357
Bleeding	0	1 (1.3%)	1.000
Pulmonary infection	0	5 (6.4%)	0.427
Abdominal incisional hernia	0	2 (2.6%)	1.000
Recovery of bowel movement, days	1.5 ± 0.5	3.1 ± 0.6	0.083
Time of off-bed activities, days	2.8 ± 0.6	4.9 ± 1.1	**0.003**
Postoperative hospital stay, days	11.0 ± 2.9	15.5 ± 5.2	**0.024**
pR1, no. (%)	1 (3.8%)	7 (9.0%)	0.671
pRM (mm)	7.5 ± 35.1	7.1 ± 36.4	0.895
Operative cost (RMB)	4850.0±1041.8	4790.3±904.3	0.860
Overall cost (RMB)	56306.4±9477.5	59251.9±16075.6	**0.024**

LMH laparoscopic major hepatectomy, OMH open major hepatectomy, pR1 positive surgical resection margin, pRM pathological resection margin.

Table 3 Main characteristics of the comparative studies of of major LLR vs. major OLR.

Authors	Type of Surgery	No. of patients	Tumor size (mm)	Number of tumors	Resection margins (mm)	Operation time (min)	Intraoperative blood loss (mL)	No. transfusions	Total complications	Postoperative hospital stay (days)
Chen et al [5]	LMH	126	64 (14-130)	112/14	NA	**240 (75-590)**	**200 (20-2500)**	**6 (4.8%)**	28 (22.2%)	**6 (3-21)**
	OMH	133	67 (16-240)	110/23	NA	**230 (100-495)**	**400 (50-2000)**	**22 (16.5%)**	36 (27.1%)	**8 (4-46)**
Cho et al [6]	LRPS	24	37 ± 18	NA	3.0 ± 5.8	**567.4 ± 212.4**	NA	NA	2 (8.3%)	10.6 ± 4.8
	ORPS	19	48 ± 25	NA	7.0 ± 5.0	**316.1 ± 63.0**	NA	NA	4 (21.1%)	11.1 ± 3.2
Cho et al [7]	LCH	20	26 (6-140)	NA	7 (0.1-40)	**388 (246-661)**	350 (100-1300)	2 (10%)	6 (30%)	8 (5-24)
	OCH	20	27 (10-82)	NA	6.5 (0.1-23)	**268 (98-412)**	400 (50-3300)	1 (5%)	4 (20%)	10 (5-24)
Goumard et al [8]	LRH	16	**39 (2-85)**	1.5 (1-3)	13.5 (0-50)	**360 (240-450)**	150 (100-700)	1 (6.3%)	4 (25%)	**7 (5–11)**
	ORH	16	**62 (0-250)**	1.5 (1-3)	6.5 (0-60)	**300 (240-390)**	100 (100-800)	0 (0%)	8 (50%)	**12 (7–25)**
Guro et al [17]	LMH	67	**41 ± 24**	NA	2 (2.4%)	**416.6 ± 166.9**	1543.3 ± 2641.8	29 (34.9%)	**17 (20.5%)**	**11.3 ± 8.3**
	OMH	110	**63 ± 38**	NA	6 (5.4%)	**332.5 ± 105.4**	1248.1 ± 1402.8	45 (40.5%)	**43 (38.7%)**	**18 ± 21.4**
Komatsu et al [18]	LMH	38	**47.5 (23-180)**	19/19	6 (15.8%)	**365 (180-600)**	100 (20-900)	2 (5.2%)	**12 (31.6%)**	7.5 (3-51)
	OMH	38	**85.0 (20-180)**	16/22	6 (15.8%)	**300 (210-425)**	80 (20-800)	1 (2.6%)	**23 (60.5%)**	10.0 (5-53)
Rhu et al [19]	LRPS	53	31 ± 18	47/6	13 ± 10	**381 ± 149**	NA	7 (13.2)	5 (9.4%)	8.9 ± 3.6
	ORPS	97	31 ± 17	89/8	12 ± 9	**220 ± 91**	NA	2 (2.1)	8 (8.3%)	10.2 ± 3.6
Tarantino et al [20]	LRPS	13	**27 ± 9**	1.0 ± 0.2	10 ± 3	234 ± 57	125 ± 80	NA	**2 (15.3%)**	**5.7 ± 3**
	ORPS	51	**37 ± 23**	1.0 ± 0.2	10 ± 2	216 ± 73	208 ± 263	NA	**27 (52.9%)**	**10.7 ± 5**
Yoon et al [21]	LRH	33	33.1 ±16.5	1.1 ±0.2	26 ±21	**297 ± 113**	125.5 ±229	0 (0)	1(3.03%)	**9.97 ±3.02**
	ORH	33	29.6 ±15	1.1 ±0.2	20 ±15	**176 ± 60**	132 ±178	0 (0)	7 (21.21%)	**13.94 ±3.37**
Zhang et al [22]	LRH	35	67±42	NA	35/0	**309± 108**	**293± 82.5**	NA	**0**	**9±2**
	ORH	42	59±30	NA	42/0	**223± 110**	**433± 105.5**	NA	**21(50%)**	**15±3**
Zhang et al [23]	LLH	20	67±42	NA	20/0	143±35.6	**180±20.5**	NA	**0**	**7±1**
	OLH	25	59±30	NA	25/0	137±29.8	**350±45.3**	NA	**10(40%)**	**12±2**
Our results	LMH	26	75±35	1.3±0.6	7.5 ± 35.1	264.2±14.1	**340.8±225.2**	7 (26.9%)	**4 (15.4%)**	**11.0±2.9**
	OMH	78	76±39	1.4±0.7	7.1 ± 36.4	255.4±36.3	**601.4±509.4**	23 (29.5%)	**29 (37.2%)**	**15.5±5.2**

LCH, laparoscopic central hepatectomy; LRPS, laparoscopic right posterior sectionectomy; LRH, laparoscopic right hepatectomy; LLH, l
hemihepatectomy

Statistically significant results are shown in bold.

Figures

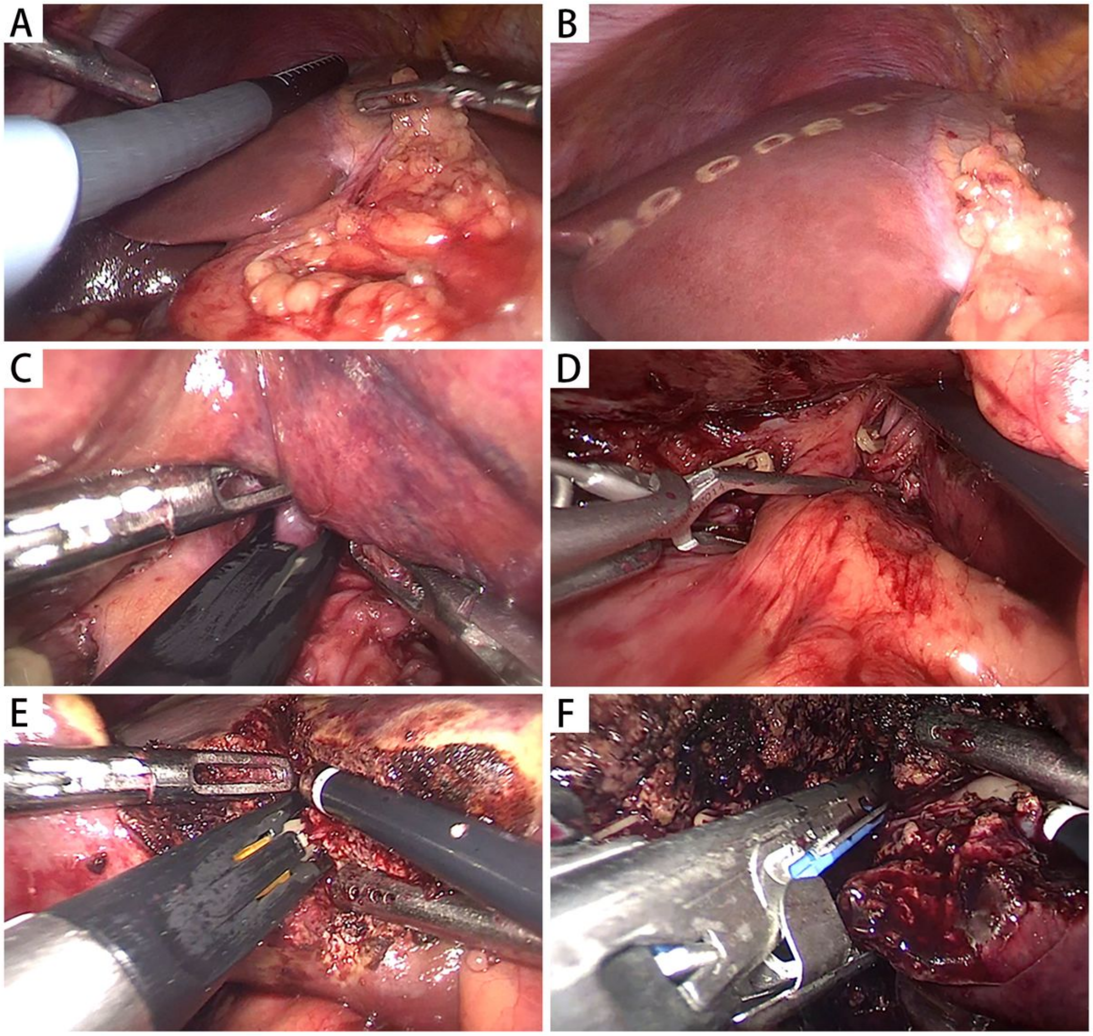

Figure 1

Surgical techniques for LMH. (A) and (B) intraoperative ultrasonography is used routinely and the hepatic transection line was marked. (C) and (D) The Glissonean approach is used to control the liver inflow. (E) and (F) The left portal vein and hepatic artery are isolated and divided by Hem-o-lock clips and/or Endo-GIA device.

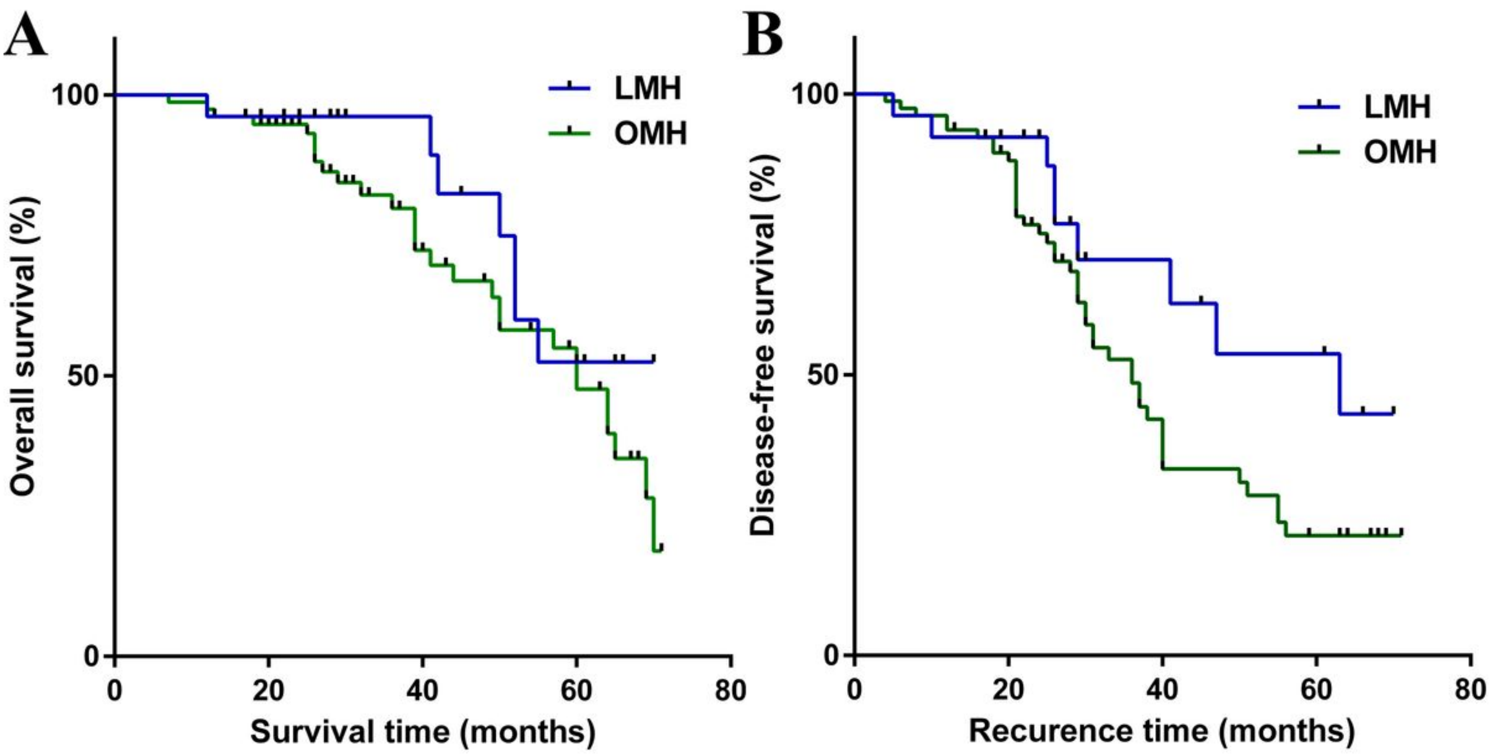

Figure 2

Weighted Kaplan–Meier plot for DFS and OS for LMH versus OMH. (A) Median DFS of LMH and OMH groups is 63.0 and 36.0 months (P=0.079). (B) Median OS of LMH and OMH groups was 60.0 and 60.0 months (P=0.172).