Original Article

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A new strategy of laparoscopic anatomical right hemihepatectomy *via* a hepatic parenchymal transection-first approach guided by the middle hepatic vein

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SUMMARY: Laparoscopic anatomical right hemihepatectomy (LARH) is a highly challenging procedure due to the lack of an appropriate surgical approach. This study aimed to investigate the safety and efficacy of LARH *via* a hepatic parenchymal transection-first approach (HPF) guided by the middle hepatic vein (MHV) (HPFM) to treat hepatocellular carcinoma (HCC) by comparison with the extrahepatic Glissonian approach (EG). Between January 2017 and December 2019, a total of 105 HCC patients who underwent LARH, of whom 48 underwent HPFM, were included in this study. After a 1:1 propensity score matching, 41 LARH-HPFM were compared to 41 LARH-EG. We have analyzed perioperative and oncologic outcomes of the two different operative approaches for HCC treatments. Quality of two operative approaches was defined by textbook outcome (TO). The LARH-HPF group was associated with shorter mean operative time (P = 0.029) and less blood loss (P = 0.023). The LARH-HPFM did not increase the postoperative overall complication rates (P = 0.248) when compared with the LARH-EG. The results of univariable and multivariable analyses indicated that LARH-HPFM provided a clinical benefit for operative time and blood loss. In addition, patients who received LARH-HPFM cumulated more TO criteria (P = 0.017), and achieved higher rate of TO (46.3% *vs*. 24.4%; 2.68, 95% CI 1.05 - 6.86, P = 0.040) compared with those who received LARH-EG. These findings indicate LARH-HPFM is safe and feasible for HCC with certain advantages over LARH-EG, but there are still many problems worth further exploration.

Keywords: laparoscopic liver resection, anatomical, right hemihepatectomy, parenchymal transection-first, middle hepatic vein

1. Introduction

Laparoscopic liver surgery, a widely considered safe and feasible surgical practice without compromising oncological outcome, has expanded from initial local hepatectomy to anatomical hepatectomy (*1*). Nowadays, with increasing experience and developments in surgical techniques and instruments, an increasing number of reports have confirmed the feasibility and safety of laparoscopic anatomical right hemihepatectomy (LARH) in selected patients (*2-4*). However, due to the unique anatomical structure, complexity in identifying the boundary of right hemihepatectomy, surgical complication, LARH can be very challenging and technically demanding procedure (*5*). There are many technical tips for LARH, and the core technical tip is how to choose an appropriate laparoscopic approach, which is a main determinant of surgical success (*6*). To date, the approaches for LARH roughly include Glissonian approach (which can be divided into three types: the extrahepatic, intrahepatic, and transfissural approaches) (*7*), hilar dissection approach (HD) (*8*). However, all these approaches have certain drawbacks. Through continuous learning and exploration, we have carried out laparoscopic anatomical liver resection *via* a hepatic parenchymal transection-first approach (HPF) guided by the middle hepatic vein (MHV) (LARH-HPFM) (*9,10*) and applied it to LARH. LARH-HPFM is a feasible and effective technique. The specific strategy described here may help laparoscopic surgeons safely perform this challenging procedure. Therefore, the study aims to provide our initial experience using the HPF and compare the surgical outcomes with the extrahepatic Glissonian approach (EG).

2. Materials and Methods

2.1. Patients and data

The data of patients who underwent laparoscopic liver resection in the Second Affiliated Hospital, Third Military Medical University (Army Medical University) between January 2017 and December 2019 were retrospectively collected. The selection criteria for patients in this study included (1) male or female patients aged 18–75 years, (2) liver function classified as Child–Pugh class A or B; (3) histologically confirmed hepatocellular carcinoma (HCC) and (4) patients underwent LARH with lesions localized in the right liver. The following patients were excluded: (1) the presence of severe dysfunction of organs, (2) LARH combined with the resection of other parts of the liver and/or other organs except for cholecystectomy. To standardize HCC management, our institution formed a multidisciplinary tumor board where all new cases were presented for joint decision-making. Patients with hepatitis B virus (HBV) received the whole course of antiviral treatment. The prophylactic antibiotic therapy was intravenously administered 30 min before the surgery and maintained until the second postoperative day. Post-operative management included hemostasis, hepatic function protection, analgesia, rehydration and other symptomatic and supportive care. This study was conducted in accordance with the Declaration of Helsinki and relevant ethical guidelines. It was approved by the Ethics Committee of the Second Affiliated Hospital of the Third Military Medical University (Army Medical University) and registered in the Chinese Clinical Trial Registry prior to the enrollment of the first subject (Registration ID: ChiCTR2400086625).

2.2. Methods

The patient was placed in a reversed Trendelenburg and left semilateral position with head up 30° and leg splitting (Figure 1A). The surgeon stood on the right side of the patient, the camera assistant stood between the spread legs, and the assistant and monitor were on the left side of the patient, facing the surgeon (Figure 1B). The trocars were inserted according to the 5-port-method (Figure 1C). To prepare for extracorporeal Pringle's maneuver, a 3-mm length incision was made between left two ports through which a self-designed tube (Figure 2) would be inserted for holding a cotton tape around the hepatoduodenal ligament. Central venous pressure (CVP) was kept lower than 5 cmH_2O.

In the LARH-HPFM group, operation began with division of liver ligaments and right liver mobilization. Intraoperative laparoscopic ultrasonography (IOUS) was performed on the liver surface to determine the courses of main trunk of the MHV. Parenchymal dissection proceeded from the caudal to cranial side along the markings of the MHV (right of the vein), exposing the MHV on the cutting plane of the liver remnant. The caudate process was cut from the back side. Short

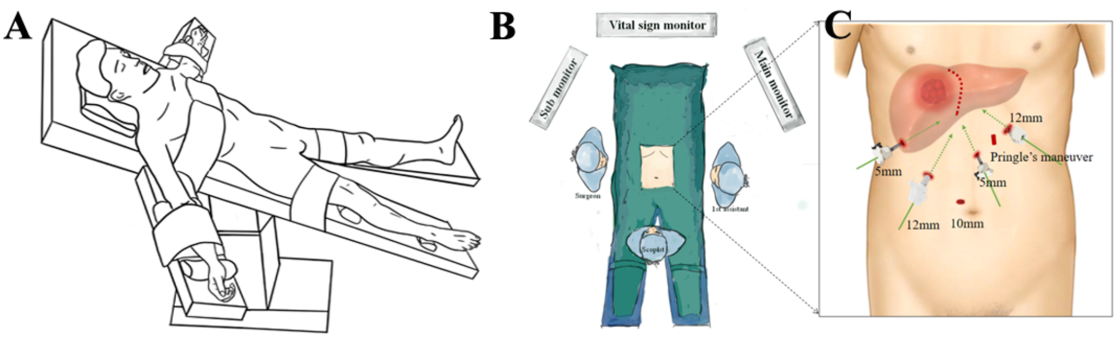

Figure 1. (A) Patient position. (B) The position of operators and instruments. (C) Diagrams of trocar placement for LARH-HPFM. Two 12-mm trocars, two 5-mm trocars and one 10-mm trocar are used. The incision was made 3 mm in length for insertion of extracorporeal Pringle's maneuver. *Abbreviation*: LARH-HPFM, laparoscopic anatomical right hemihepatectomy *via* a hepatic parenchymal transection-first approach guided by the middle hepatic vein.

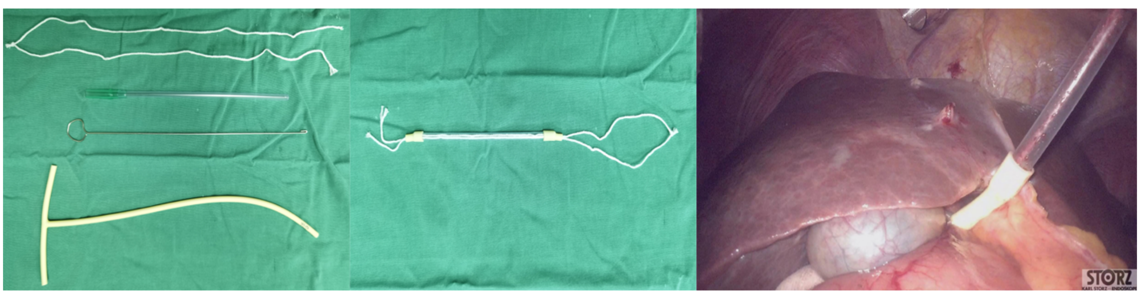

Figure 2. An illustration and image of the laparoscopic first hepatic hilum blood flow occlusion device.

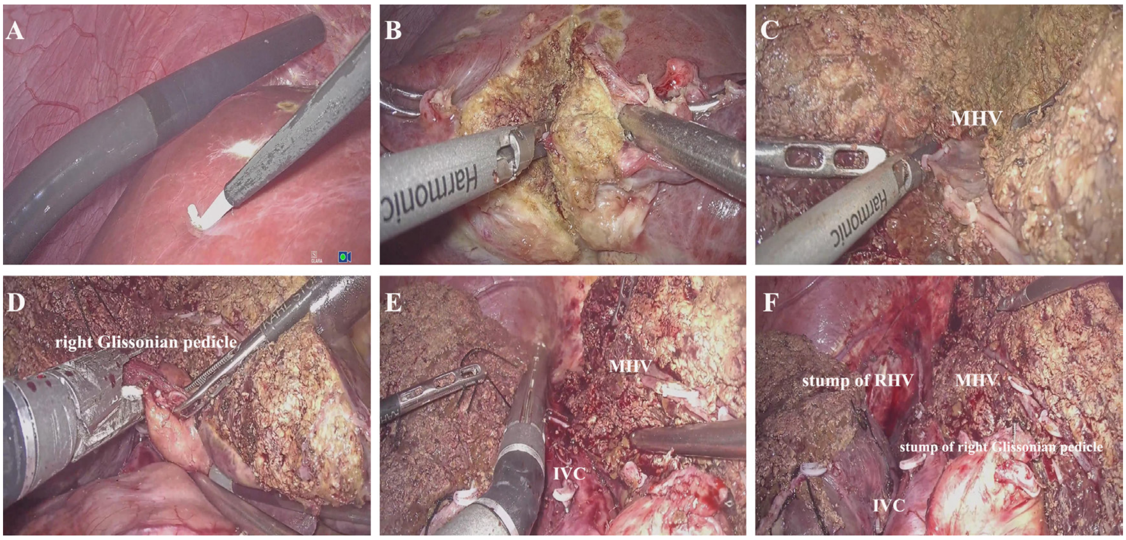

Figure 3. Laparoscopic technique and procedure for LARH-HPFM. (A) IOUS was used to mark the the tumor range and central position and to determine the courses of main trunk of MHV; **(B)** Parenchymal resection was carried out firstly using harmonic scalpel; **(C)** Parenchymal transection along the MHV; **(D)** exposing and dividing right Glissonian pedicle; **(E)** exposing and dividing RHV; **(F)** Findings after anatomic hemihepatectomy. *Abbreviation*: LARH-HPFM, laparoscopic anatomical right hemihepatectomy *via* a hepatic parenchymal transection-first approach guided by the middle hepatic vein; MHV,Middle hepatic vein.

hepatic veins were clipped. After sufficient opening of the hepatic parenchyma around the ventral and dorsal side of the right Glissonian pedicle, the right Glissonian pedicle was isolated by cotton tape and then transected. It is noteworthy that transecting was done while the tape was retracted toward the contralateral side. Then, parenchymal dissection was advanced from the caudal to cranial side along the plane consisting of ventral side of the inferior vena cava (IVC), MHV and ischemic line. After accomplishing parenchymal dissection, the right hepatic vein (RHV) was divided (Figure 3).

In the LARH-EG group, the peritoneum of the hepatoduodenal ligament was meticulously dissected at the hepatic hilum and the dorsal side of the hepatoduodenal ligament. The dissection was performed between the hepatic parenchyma and the bifurcation of the right Glissonian pedicle. The right Glissonian pedicle was encircled laparoscopically. When the corresponding Glissonian pedicle was occluded, we marked the ischemic line by electrocautery on the liver capsule. The superficial parenchyma was dissected along the demarcation line, while the deeper tissue was dissected along the MHV. The caudate process was cut from the back side. Short hepatic veins were clipped. After sufficient parenchymal dissection, so that the whole bifurcating Glissonian pedicle was exposed, the right Glissonian pedicle was transected by a laparoscopic linear stapler. After accomplishing parenchymal dissection, the RHV was divided (Figure 4).

2.3. Propensity score matching (PSM)

The PSM analysis is a useful method and widely used in retrospective studies to reduce confounding and selection bias (*11*). In our research, the LARH-HPFM group and the LARH-EG group were compared with a 1:1 PSM analysis in an attempt to minimize intergroup disparities. A propensity score for each patient was calculated using logistic regression based on the imbalanced variables, and a 1:1 the nearest-neighbor matching method was performed between the two groups. Patients who fail to meet the matching criteria were excluded.

2.4. Surgical outcomes

The following analyzed variables were included: operative time, estimated blood loss (EBL), intraoperative transfusion, conversion, bowel function recovery, postoperative hospital stay, postoperative liver function, postoperative complications according to Clavien–Dindo grade (*12*) and mortality. Prolonged operative time was defined as ≥ 240 min (*13*). Massive hemorrhage during operation was defined as EBL > 400 mL (*14*). All patients were regularly followed at the outpatient department every 1-3 months for the first year and every 3-6 months thereafter. All patients underwent routine blood tests, liver function tests, tumor markers tests, and abdominal ultrasound and computed tomography (CT) or magnetic resonance imaging (MRI) were performed when necessary. The follow-up ended in February 2023.

The quality of surgical care was assessed using textbook outcome (TO), which was considered in patients fulfilling and cumulating all of the following 6 previously described endpoints (*15*): R0 (≥ 1 cm) surgical margin, absence of perioperative transfusion, absence of postoperative complications (considering all Dindo-Clavien grades), absence of prolonged length

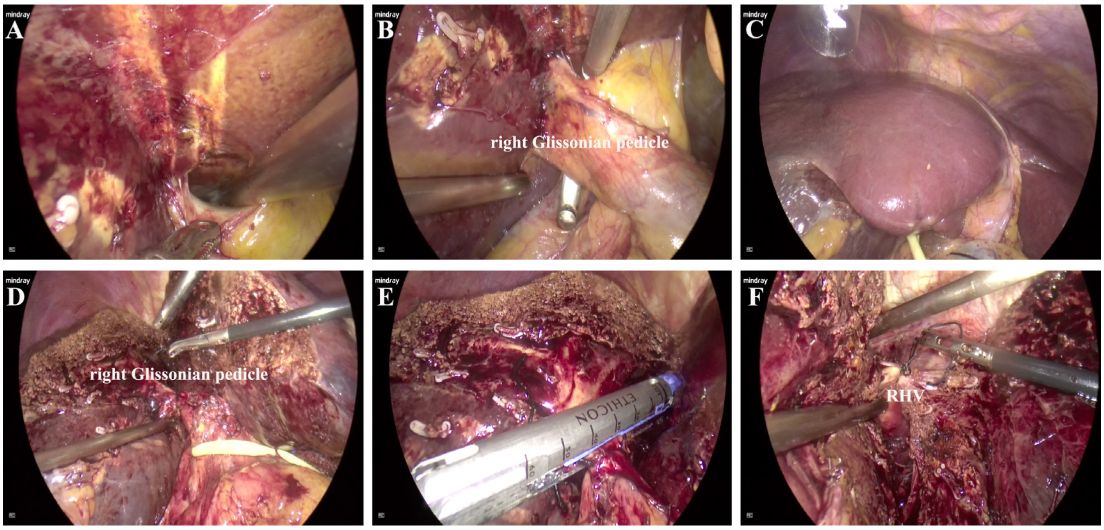

Figure 4. Laparoscopic technique and procedure for LARH-GA. (A) The peritoneum of the hepatoduodenal ligament was meticulously dissected at the hepatic hilum and the dorsal side of the hepatoduodenal ligament; **(B)** The golden finger was inserted into the latent anatomic space between the hepatic parenchyma and the bifurcation of the right Glissonian pedicles; **(C)** When the right Glissonian pedicle was isolated and occluded, the ischemic line was marked by electrocautery on the liver capsule; **(D)** After sufficient parenchymal dissection, the right Glissonian pedicle was exposed; **(E)** Right Glissonian pedicle was transected by a laparoscopic linear stapler with 60-mm blue cartridge; **(F)** RHV was isolated and ligated. *Abbreviation*: LARH-HPFM, laparoscopic anatomical right hemihepatectomy *via* a hepatic parenchymal transection-first approach guided by the middle hepatic vein; RHV, Right hepatic vein.

of stay (LOS) as defined as a postoperative stay < 50th percentile of the total cohort (LOS ≤ 10 days), absence of unplanned readmission, and absence of postoperative mortality.

2.5. Statistical analysis

The characteristics of patients were expressed as mean ± standard deviation or median with interquartile range for continuous variables and frequency with proportion for categorical variables. Differences between the groups were compared using *t* test for continuous data and Chi-square test for categorical variables. Survival curves were estimated by the Kaplan–Meier method with log-rank comparison. Prior to multivariate logistic regression modeling, multicollinearity among candidate predictors was assessed using Pearson correlation; variables with $|r| > 0.7$ were excluded. Variables significant in univariate analysis ($p < 0.05$) or deemed clinically relevant based on prior knowledge were included as candidates for the multivariate logistic regression model. The final model was constructed using backward stepwise selection (removal criterion $p \geq 0.05$), retaining variables significant at $p < 0.05$ or considered clinically essential. The $p < 0.05$ were considered statistically significant. Statistical analyses and PSM were performed using R version 4.3.1 and SPSS version 26.0 (IBM SPSS, Inc, Chicago, IL).

3. Results

3.1. Baseline characteristics

Between January 2017 and December 2019, a total of 105 HCC patients who underwent LARH were included in this study, of whom 48 patients underwent LARH-HPFM and 57 the LARH-EG.

All patients underwent blood biochemistry and tumor markers analyses, imaging examination (Figure 5), indocyanine green clearance test, and 3-dimensional reconstruction (Figure 6) before the operation. The patients' baseline characteristics in the two groups are shown in Table 1. The two groups differed before PSM in terms of ALB ($p = 0.017$). After PSM, 41 patients in each group were well-matched and the baseline demographics were comparable (Table 1).

3.2. Surgical data and postoperative outcomes

The Table 2 summarized the surgical data and postoperative outcomes between LARH-HPFM and LARH-EG group. The operative time was shorter in the LARH-HPFM group than in the LARH-EG group ($p = 0.029$). The blood loss in LARH-HPFM group was less than that of LARH-EG group ($p = 0.023$). The Pringle's time of LARH-HPFM group was shorter than that of LARH-EG group ($p = 0.035$). One patients in the LARH-HPFM group and two patients in the LARH-EG group converted to formal open surgery due to difficult control of intraoperative bleeding and intra-abdominal adhesions.

For postoperative recovery, there were no significant differences between the RH-HPFM and LARH-EG groups in terms of length of stay, diet recovery, and conversion rates. In terms of postoperative liver function, there were no significant differences in serum ALT, total bilirubin and albumin levels between LARH-HPFM group and LARH-EG group at 1, 3 and 5 days

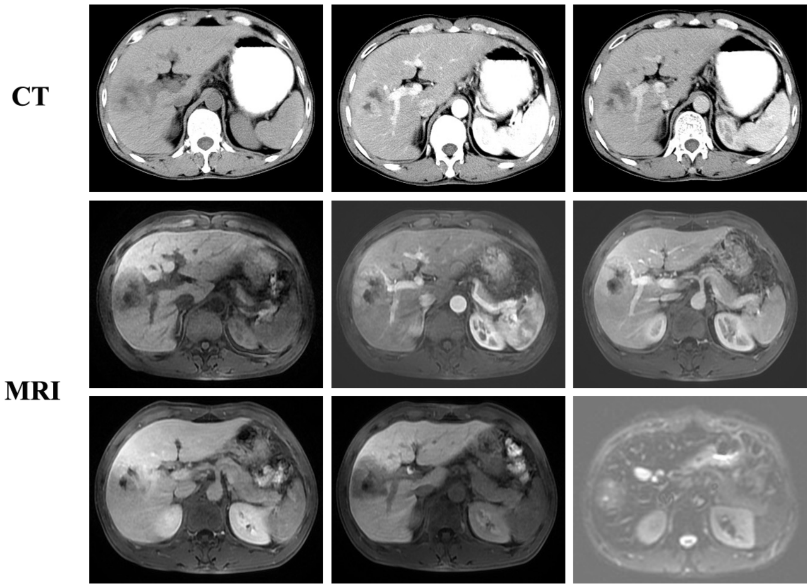

Figure 5. Preoperative CT (A) and MRI (B) of the liver.

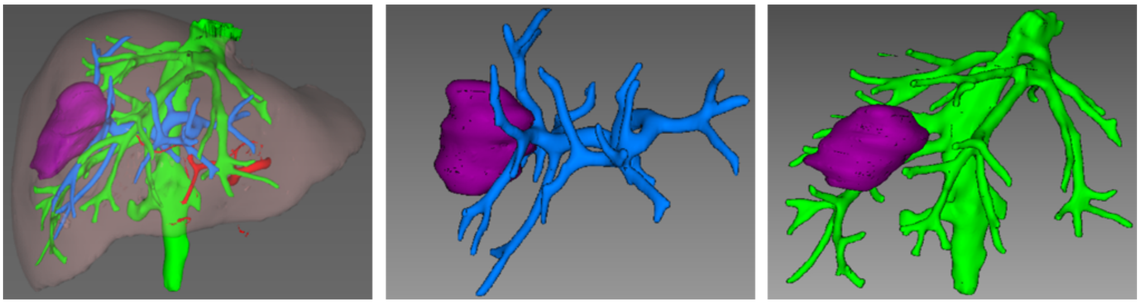

Figure 6. Preoperative 3D-CT reconstruction.

after surgery. In terms of complications, there was no significant difference in the total complication rate between LARH-HPFM group and LARH-EG group (29.3% *vs.* 41.5%, $p = 0.248$). Similarly, there were no significant differences in the type of complications and the incidence of grade I and grade II complications between the two groups. No patients suffered Grade III and above complications in LARH-HPFM group. In the LARH-EG group, one patient suffered from pleural effusion was submitted to thoracentesis with continuous chest drainage, and one intra-abdominal collection secondary to bile leak, treated with ultrasound-guided abdominal puncture and drainage, who were noted as grade III complications. There was no mortality case within 30 days in both groups.

3.3. Univariable and multivariable analyses of risk factors associated with EBL ≥ 400 mL in HCC patients undergoing LARH-HPFM or LARH-EG after PSM

All univariable and multivariable analyses of risk factors associated with EBL ≥ 400 mL in two groups after PSM are shown in Figure 7. Univariable analysis identified surgical approaches, cirrhosis, maximum tumor diameter > 5 cm, macrovascular invasion as risk factors of EBL ($p < 0.05$). Multivariate analysis revealed that maximum tumor diameter > 5 cm (8.59, 95% CI 1.91 - 38.77, $p = 0.005$), cirrhosis (7.17, 95% CI 1.71 - 30.12, $p = 0.007$) and macrovascular invasion (12.51, 95% CI 1.67 - 93.64, $p = 0.014$) were independent risk factors for EBL ≥ 400 mL. However, LARH-HPFM (compared to LARH-EG) (0.14, 95% CI 0.04 - 0.53, $p = 0.004$) was protective factors for EBL ≥ 400 mL.

3.4. Univariable and multivariable analyses of risk factors associated with prolonged operative time in HCC patients undergoing LARH-HPFM or LARH-EG after PSM

All univariable and multivariable analyses of risk factors associated with operative time ≥ 240 min in two groups after PSM are shown in Figure 8. Univariable analysis identified surgical approaches, maximum tumor diameter > 5 cm, tumor encapsulation incomplete, and macrovascular invasion as risk factors of prolonged operative time ($p < 0.05$). Multivariate analysis revealed that maximum tumor diameter > 5 cm (5.89, 95% CI 1.54 - 22.52, $p = 0.010$) and macrovascular invasion (11.69,

Table 1. Patient characteristics before and after PSM

Variables	Before PSM		*p*	After PSM		*p*
	LARH-HPFM *n* = 48	LARH-EG *n* = 57		LARH-HPFM *n* = 41	LARH-EG *n* = 41	
Age (years), mean (SD)	52.29 ± 10.45	54.6 ± 11.45	0.288	52.34 ± 10.50	52.56 ± 11.6	0.929
Gender, *n* (%)						
Male	38 (79.2)	39 (68.4)	0.215	32 (78.0)	31 (75.6)	0.794
Female	10 (20.8)	18 (31.6)		9 (22.0)	10 (24.4)	
BMI (kg/m^2), mean (SD)	23.30 ± 2.96	23.39 ± 2.94	0.873	23.24 ± 3.16	23.37 ± 3.19	0.852
ASA II, *n* (%)	24 (48.9)	26 (43.7)		20 (48.8)	14 (34.1)	0.179
Child-Pugh B, *n* (%)	9 (18.8)	7 (12.3)	0.358	7 (17.1)	8 (19.5)	0.775
BCLC stage B, *n* (%)	10 (20.8)	18 (31.6)	0.483	8 (19.5)	14 (34.1)	0.135
Previous abdominal surgery, *n* (%)	5 (10.4)	10 (17.5)	0.298	5 (12.2)	5 (12.2)	1.000
Hepatitis B viral infection, *n* (%)	34 (75.6)	37 (77.1)	0.862	35 (85.4)	36 (87.8)	0.746
Cirrhosis, *n* (%)	9 (18.8)	11 (19.3)	0.943	9 (22.0)	6 (14.6)	0.391
Clinically significant portal hypertension, *n* (%)	4 (8.3)	4 (7.0)	0.800	2 (4.9)	3 (7.3)	0.644
ICG-R15 (%), mean (SD)	7.17 ± 2.94	7.72 ± 2.25	0.278	7.49 ± 2.95	7.56 ± 2.25	0.867
Hypertension, *n* (%)	9 (18.8)	7 (12.3)	0.358	7 (17.1)	3 (7.3)	0.177
Diabetes mellitus, *n* (%)	6 (12.5)	6 (10.5)	0.751	5 (12.2)	4 (9.8)	0.724
Heart disease, *n* (%)	3 (6.7)	2 (4.2)	0.593	2 (4.9)	1 (2.4)	0.556
Largest tumor size(cm), mean (SD)	5.38 ± 1.61	5.35 ± 2.31	0.952	5.37 ± 1.59	5.17 ± 2.04	0.630
Surgical margin (cm), mean (SD)	3.08 ± 0.74	2.91 ± 0.58	0.186	3.15 ± 0.73	2.98 ± 0.61	0.253
Microvascular invasion, *n* (%)						
M1, *n* (%)	8 (16.7)	11 (19.3)	0.921	4 (9.8)	8 (19.5)	0.207
M2, *n* (%)	4 (8.3)	4 (7.0)		4 (9.8)	1 (2.4)	
Macrovascular invasion, *n* (%)	7 (14.6)	9 (15.8)	0.062	5 (12.2)	6 (14.6)	0.746
Tumor encapsulation incomplete, *n* (%)	37 (77.1)	42 (73.7)	0.688	30 (73.2)	30 (73.2)	1.000
Edmondson–Steiner grade, *n* (%)						
I/II	31 (64.6)	40 (70.2)	0.542	26 (63.4)	28 (68.3)	0.641
III/IV	17 (35.4)	17 (29.8)		15 (36.6)	13 (31.7)	
HGB (g/L), mean (SD)	139.10 ± 16.96	133.00 ± 16.90	0.069	139.85 ± 15.9	137.63 ± 14.79	0.515
AST (IU/L), mean (SD)	29.70 (17.00-139.30)	37.10 (12.20-306.30)	0.069	29.00 (17.00-139.30)	33.50 (10.90-113.50)	0.970
ALT (IU/L), mean (SD)	35.00 (11.00-152.00)	36.10 (16.10-287.40)	0.412	32.30 (10.70-144.80)	33.50 (10.10-156.10)	0.742
TB (μmol/L), mean (SD)	16.25 ± 7.70	15.42 ± 6.50	0.551	15.93 ± 8.16	15.51 ± 6.19	0.796
ALB (g/L), mean (SD)	44.67 ± 4.62	42.49 ± 4.53	0.017	44.29 ± 4.67	43.63 ± 4.24	0.505
PT (s), mean (SD)	11.44 ± 1.05	11.70 ± 1.18	0.232	11.39 ± 1.05	11.71 ± 1.10	0.185
INR, mean (SD)	1.02 ± 0.11	1.04 ± 0.12	0.190	1.01 ± 0.107	1.04 ± 0.10	0.266
PLT (109 /L), mean (SD)	185.0 ± 72.15	175.0 ± 62.89	0.453	190.29 ± 74.68	174.07 ± 59.29	0.279

Abbreviation: PSM, propensity score matching; LARH, laparoscopic anatomical right hemihepatectomy; HPFM, hepatic parenchymal transection-first approach (HPF) guided by the middle hepatic vein (MHV); EG, Glissonian approach; BMI, body mass index; ASA, American society of anesheslologists physical status classification system; SD, standard deviation.

95% CI 1.96 - 69.83, 0.007) were independent risk factors for prolonged operative time. However, LARH-HPFM (compared to LARH-EG) (0.23, 95% CI 0.06 - 0.81, p = 0.023) was protective factor for prolonged operative time.

3.5. Distribution of TO criteria and number of cumulated TO criteria

LARH-HPFM cumulated more TO criteria (p = 0.025) and had higher rate of TO (46.3% *vs.* 24.4%; 2.68, 95% CI 1.05 - 6.86, p = 0.038) than LARH-EG. The distribution of TO criteria and the cumulated number of TO criteria according to LARH-HPFM and LARH-EG is displayed in Figure 9A and B.

3.6. Survival

The median follow-up time in the LARH-HPFM group was 40.2 months and in the LARH-EG group was 37.1 months (p = 0.871). The oncological outcomes between LARH-HPFM group and LARH-EG group did not differ with regard to overall survival (OS) (p = 0.539) and disease-free survival (DFS) (p = 0.846). The 1- and 3-year OS rates were 97.6% and 67.7%, respectively, in the LARH-HPFM group and 95.1% and 76.7%, respectively,

Table 2. Intraoperative data and postoperative outcomes

	LARH-HPFM *n* = 41	LARH-EG *n* = 41	*p*
Surgical data			
Operative time (min), mean (SD)	207.59 ± 37.70	226.44 ± 39.30	0.029
Blood loss (mL), mean (SD)	333.90 ± 94.52	382.32 ± 94.01	0.023
Conversion to open, *n* (%)	1 (2.4)	2 (4.9)	1.000
Pringle time (min), mean (SD)	41.7 ± 13.35	47.68 ± 11.89	0.035
Postoperative outcomes			
TO	19 (46.34)	10 (24.39)	0.038
No. of cumulated TO creteria, mean (SD)	5.15 ± 1.04	4.59 ± 1.18	0.025
Mortality within 30d, *n* (%)	0	0	NA
Perioperative transfusion, *n* (%)	7 (17.1)	16 (39.0)	0.027
Prolonged hospitalization time, *n* (%)	7 (17.1)	13 (31.7)	0.123
Negative margins, *n* (%)	35 (85.4)	33 (80.5)	0.557
Readmission, *n* (%)	3 (7.3)	3 (7.3)	1.000
Complications, *n* (%)	12 (29.3)	17 (41.5)	0.248
Clavien–Dindo classification, *n* (%)			0.364
I, *n* (%)	10 (24.4)	11 (26.8)	
II, *n* (%)	2 (4.9)	4 (9.8)	
III, *n* (%)	0	2 (4.9)	
Liver decompensation, *n* (%)	0	2 (4.9)	0.494
Ascites, *n* (%)	10 (24.4)	7 (17.1)	0.414
Hemorrhage, *n* (%)	1 (2.4)	3 (7.3)	0.305
Bile leakage, *n* (%)	1 (2.4)	1 (2.4)	1.000
Pulmonary infection, *n* (%)	4 (9.8)	5 (12.2)	0.724
Pleural effusion, *n* (%)	1 (2.4)	3 (7.3)	0.305
Hospitalization time(days), mean (SD)	10.07 ± 3.67	11.56 ± 4.38	0.099
Bowel function recovery (days), mean (SD)	2.95 ±0.77	3.46 ± 1.53	0.060
Postoperative liver function			
POD1			
TB, μmol/L, mean (SD)	29.07 ± 15.06	30.71 ± 21.44	0.691
AST, IU/L, mean (SD)	240.44 ±212.60	292.95 ± 261.66	0.322
ALT, IU/L, mean (SD)	239.80 ± 179.83	274.29 ± 211.02	0.428
POD3			
TB, μmol/L, mean (SD)	27.00 ± 16.65	31.07 ± 17.21	0.279
AST, IU/L, mean (SD)	61.59 ± 42.27	65.12 ± 60.66	0.760
ALT, IU/L, mean (SD)	120.15 ± 87.95	116.02 ± 76.17	0.821
POD5			
TB, μmol/L, mean (SD)	22.51 ± 10.95	26.02 ± 12.77	0.185
AST, IU/L, mean (SD)	39.78 ± 16.30	38.02 ± 23.35	0.694
ALT, IU/L, mean (SD)	65.22 ± 33.77	53.37 ± 25.87	0.078

Abbreviation: LARH, laparoscopic anatomical right hemihepatectomy; HPFM, hepatic parenchymal transection-first approach guided by the middle hepatic vein; EG, Glissonian approach; TO, textbook outcome; POD, post-operative day; SD, standard deviation.

in the LARH-EG group (Figure 10A). The 1-and 3-year DFS rates were 87.8% and 63.6%, respectively, in the LARH-HPFM group and 90.2% and 72.0%, respectively, in the LARH-EG group (Figure 10B).

4. Discussion

In recent years, laparoscopic major hepatectomies are increasingly used in different centers worldwide, while LARH is the most commonly performed laparoscopic major liver resection (*16*). Although recent studies demonstrated the safety and reproducibility of LARH with favorable surgical outcomes in comparison with open surgery, this procedure remains technically challenging with a steep learning curve (*17,18*). In LARH, the main difficulty lies in the choice of surgical approach. The choice of laparoscopic surgical approach for a LARH is not simply a "road of entry" but a series of strategic decisions on how to accomplish the surgical goals while ensuring the safety and effectiveness of the surgery (*19,20*).

The Glissonian approach and HD can be used in LARH. HD is difficult and time-consuming to operate under the laparoscope and is suitable for the treatment of bileduct stones and portal vein tumor thrombus (PVTT) (*21,22*). The Glisson approach is based on hepatectomy with Glissonian pedicle transection proposed by Takasaki. It can be divided into the extrahepatic, intrahepatic, and transfissural approaches (*23,24*). It has a better safety profile, shortens the separation time of Glissonian pedicle, and advances the laparoscopic surgical process. If there is liver cirrhosis, severe fatty liver disease, Glissonian pedicle anatomical variation, short portal vessels, narrow hepatic hilar region, or difficulty in exposure of the hilar plate, and due to limitations of endoscopic instruments, the Glissonian approach is harder (*25-28*). The Laennec capsule can be used as a marker and

Characteristics	Univariate analysis OR	95%CI	P-value	Multivariate analysis OR	95%CI	P-value
LARH-HPFM vs. LARH-EG	0.26	0.11 , 0.66	0.005	0.14	0.04 , 0.53	0.004
Male	0.68	0.24 , 1.89	0.454			
Age>60	1.16	0.44 , 3.06	0.759			
ASA II	0.4	0.16 , 1.01	0.053			
BMI≥24kg/m2	1.27	0.40 , 4.01	0.688			
Hypertension	0.48	0.11 , 2.00	0.313			
Diabetes mellitus	0.97	0.24 , 3.91	0.965			
Previous abdominal surgery	0.79	0.20 , 3.03	0.729	0.38	0.05 , 2.73	0.334
Clinically significant portal hypertension	1.98	0.52 , 7.64	0.319	0.37	0.06 , 2.49	0.31
Cirrhosis	3.52	1.29 , 9.61	0.014	7.17	1.71 , 30.12	0.007
BCLC stage B	1.31	0.49 , 3.48	0.591			
Child-Pugh B	0.71	0.16 , 3.17	0.65			
Edmondson–Steiner III/IV	1.35	0.54 , 3.37	0.523			
Tumor diameter>5 cm	3.52	1.29 , 9.61	0.014	8.59	1.91 , 38.77	0.005
Tumor encapsulation incomplete	1.87	0.74 , 4.76	0.186	1.75	0.52 , 5.90	0.37
Microvascular invasion	1.49	0.51 , 4.34	0.468			
Macrovascular invasion	6.91	1.39 , 34.38	0.018	12.51	1.67 , 93.64	0.014
PLT≥100×109 /L	0.63	0.19 , 2.06	0.44			
ALT>44 U/L	1.08	0.43 , 2.71	0.864			
AST>44 U/L	2.61	0.90, 7.52	0.077			
ALB≥35 g/L	1.7	0.35 , 8.11	0.508			
TBIL>17 mol/L	1.49	0.58 , 3.83	0.408			
PT>12 s	2.96	0.91 , 9.64	0.071	1.68	0.35 , 8.05	0.514
HBV infection	0.44	0.15 , 1.27	0.128			

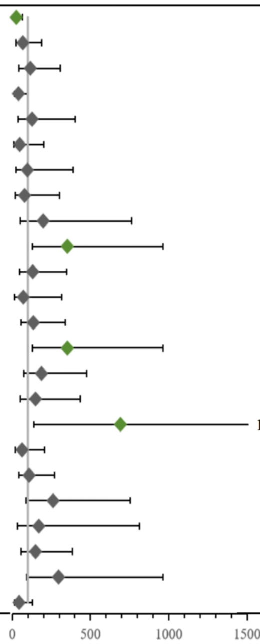

Figure 7. Univariable and multivariable analyses of risk factors associated with EBL > 400 mL in HCC patients undergoing LARH-HPFM or LARH-EG after PSM. *Abbreviation*: EBL, estimated blood loss; LARH, laparoscopic anatomical right hemihepatectomy; HPFM, hepatic parenchymal transection-first approach guided by the middle hepatic vein; EG, Glissonian approach; PSM, propensity score matching; ASA, American society of Aneshesiologists physical status classification system.

Characteristics	Univariate analysis OR	95%CI	P-value	Multivariate analysis OR	95%CI	P-value
LARH, HPFM vs. LARH, EG	0.32	0.12 , 0.90	0.030	0.23	0.06 , 0.81	0.023
Male	0.8	0.26 , 2.44	0.696			
Age>60	0.87	0.29 , 2.59	0.805			
ASA II	0.68	0.25 , 1.84	0.445			
BMI≥24kg/m2	2.09	0.72 , 6.07	0.176			
Hypertension	1.86	0.47 , 7.31	0.375			
Diabetes mellitus	2.27	0.55 , 9.36	0.255			
Previous abdominal surgery	1.11	0.26 , 4.74	0.884	0.940	0.15 , 6.03	0.945
Clinically significant portal	1.78	0.28 , 11.40	0.544			
Cirrhosis	0.8	0.27 , 2.37	0.693	0.660	0.18 , 2.43	0.531
BCLC stage B	2.27	0.80 , 6.43	0.121			
Child-Pugh B	1.96	0.61 , 6.32	0.259			
Edmondson–Steiner III/IV	0.43	0.14 , 1.33	0.145			
Tumor diameter>5 cm	3.24	1.17 , 9.03	0.024	5.890	1.54 , 22.52	0.010
Tumor encapsulation incomplete	3.2	1.17 , 8.75	0.023	3.650	0.99 , 13.44	0.052
Macrovascular invasion	9.96	2.35 , 42.19	0.002	11.690	1.96 , 69.83	0.007
Microvascular invasion	1.09	0.34 , 3.53	0.888			
PLT≥100×109 /L	2.25	0.68 , 7.41	0.183			
ALT>44 U/L	1.04	0.38 , 2.86	0.94			
AST>44 U/L	0.62	0.18 , 2.11	0.441			
ALB≥35 g/L	0.4	0.05 , 3.53	0.411			
TBIL>17 mol/L	1.73	0.63 , 4.77	0.291			
PT>12 s	2.79	0.87 , 8.89	0.083			
HBV infection	0.41	0.11 , 1.50	0.177			

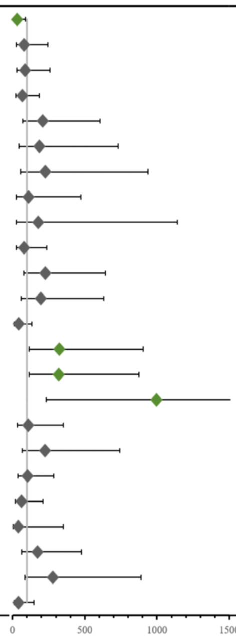

Figure 8. Univariable and multivariable analyses of risk factors associated with prolonged operative time in HCC patients undergoing LARH-HPFM or LARH-EG after PSM. *Abbreviation*: EBL, estimated blood loss; LARH, laparoscopic anatomical right hemihepatectomy; HPFM, hepatic parenchymal transection-first approach guided by the middle hepatic vein; EG, Glissonian approach; PSM, propensity score matching; ASA,A merican society of aneshesiologists physical status classification system.

approach for anatomical hepatectomy. The surgeon can achieve anatomical separation and management of the right Glissonian pedicle without anatomical damage to the liver parenchyma. The Laennec capsule approach for hepatectomy with Glissonian's pedicle transection is essentially an extrahepatic, extrathecal approach that can overcome some of the shortcomings of the conventional extrahepatic, extrathecal approach and is safe and effective (*29-31*).

The "easy first" strategy can be used for the LARH

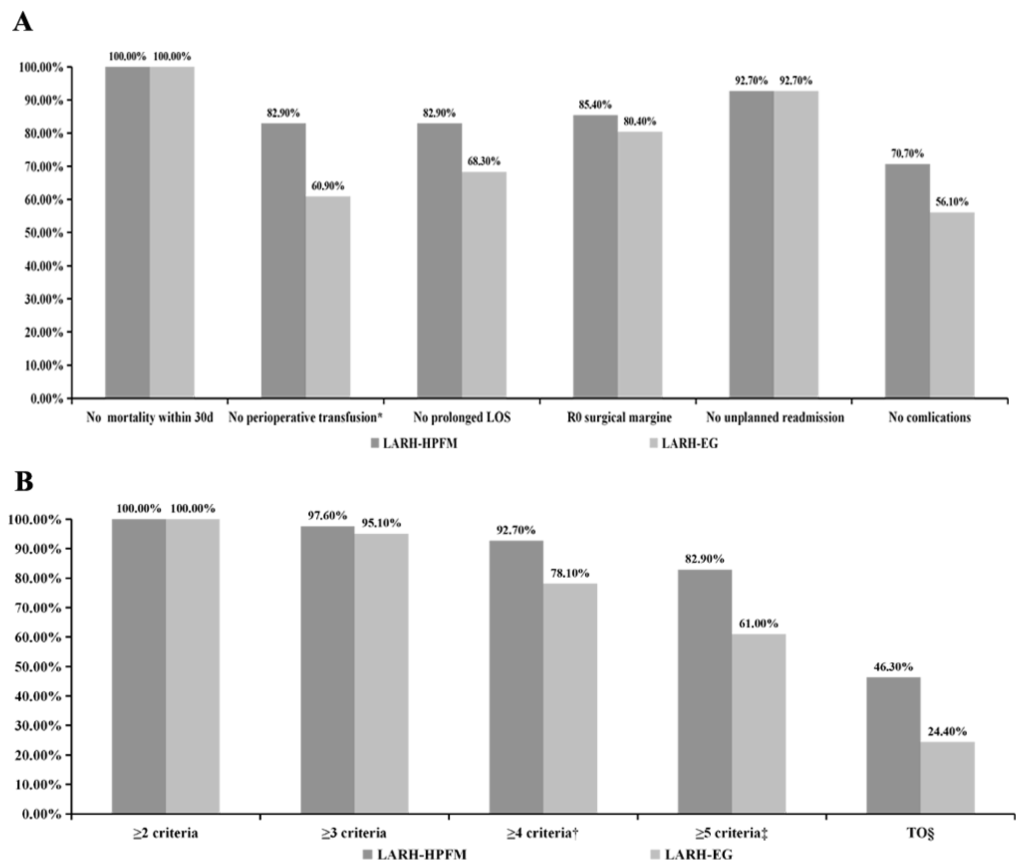

Figure 9. Distribution of TO criteria and number of cumulated TO criteria according to the type of surgical approach in the matched population. (A) TO criteria distribution. Levels of significance: $*p = 0.027$. **(B)** Distribution of number of cumulated TO criteria. Levels of significance: $\dagger p = 0.061$; $\ddagger p = 0.027$; $\S p = 0.038$. *Abbreviation*: TO, textbook outcome. LOS, length of stay.

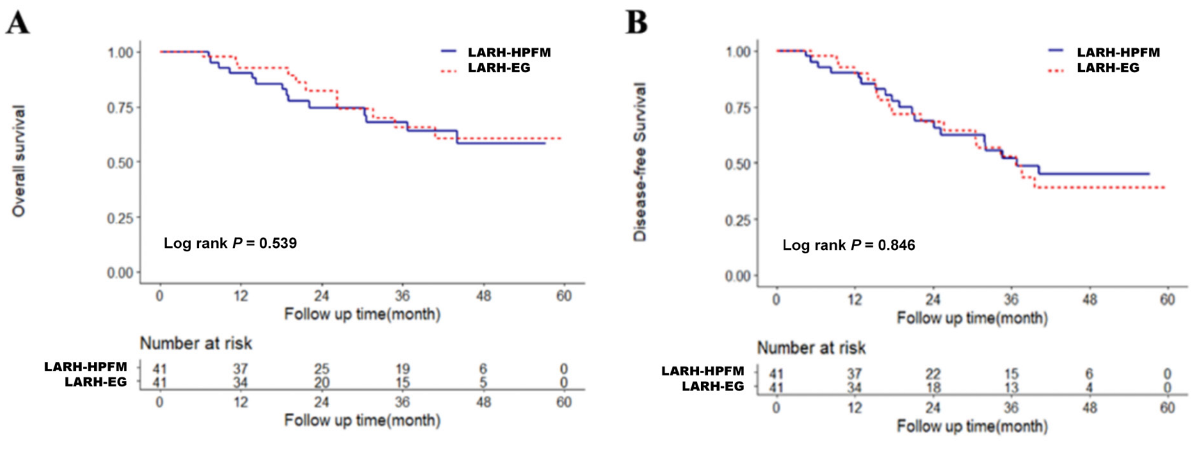

Figure 10. The survival curve between LARH-HPFM and LARH-GA groups, (A) OS rates and (B) DFS rates. *Abbreviation*: LARH, laparoscopic anatomical right hemihepatectomy; HPFM, hepatic parenchymal transection-first approach guided by the middle hepatic vein; EG, Glissonian approach; OS, overall survival; DFS, disease-free survival.

approach. According to the anatomical characteristics of the right hemiliver, the site that is relatively easy to dissect is dissected first to simplify the complex operation. We have explored this by using the HPFM for laparoscopic left hemihepatectomy in the early stage. By prioritizing the transection of the liver parenchyma, the left Glissonian pedicle is fully exposed, and the Glissonian pedicle is handled under adequate space conditions, making laparoscopic anatomical hepatectomy progression less difficult (*9*). Is this technique suitable for right hemihepatectomy? Based on the experience of other centers, combined with our own clinical experience, we continuously explored and practiced different sequences of the LARH approach and carried out LARH *via* HPFM. The resection was completed through the MHV as marker and fully exposing right Glissonian pedicle. To a certain extent, this technique overcomes the difficulties of complicated LARH operations, high technical risks, and long learning curves and can more simply and intuitively guide the transected liver plane, simplify the surgical procedure, shorten the surgical time, and reduce the risks of bleeding and postoperative complications, which is consistent with the concept of precision hepatectomy and amounts to a certain technical model. Of note, LARH-HPFM proved significantly superior to the LARH-EG in TO. The HPFM is both safe and effective for various liver resections, including right anterior hepatectomy, central hepatectomy, segment 4 segmentectomy, segment 8 segmentectomy, and others.

The precautions for LARH-HPFM are listed as follows: (*i*) Preoperative high resolution thin-sliced enhanced CT scanning, helical CT arterial portography, 3D reconstruction visualization system and magnetic resonance cholangiopancreatography (MRCP) are used to accurately assess and judge the location and courses of vessels and bile duct, and individualized treatment is performed according to the variation (*32*). (*ii*) IOUS is an important step. In the absence of IOUS, preoperative image analysis and liver anatomical surface marking can be used to locate the position of the MHV and its relationship with the tumor, as well as the location of the larger vein branches (*33*). The hepatectomy section can be delineated to improve the accuracy of the surgery. According to the intraoperative conditions, IOUS can be used to repeatedly adjust the liver transection plane. To reduce gas interference, water can be injected into the transection. (*iii*) In the first longitudinal liver transection plane, the left or right Glissonian pedicle can be temporarily clipped to form the ischemic line, and the pre-resection line can be determined. Generally, the Cantlie line can also be selected. It is better to expose the MHV to determine the liver transection plane to achieve anatomical hepatectomy. Active exposure of the MHV avoids the massive hemorrhage caused by accidental injury of the hepatic vein during the operation; the anatomical level of the Laennec capsule can be fully utilized for blunt separation while separating and protecting the vein (*34*). (*iv*) The procedure should be performed under CVP (3-5 cmH_2O) and intermittent blockage of the first hepatic portal to reduce the blood oozing from the wound during separation (*35*). (*v*) Full dissection was performed to expose the Glissonian pedicle so that the endoscopic linear stapler could be placed. The whole Glissonian pedicle was accurately exposed and identified, and then the transection could be done using endoscopic linear stapler. Hepatic parenchymal was sufficiently transected first to help protect the preserved lateral ducts and hepatic vein trunk, and long-arm detachment forceps were used to test-clamp target hepatic pedicle to accurately identify the right Glissonian pedicle. Attention needs to be paid to the protection of the IVC, and the endoscopic linear stapler must be inserted under direct vision and without violence to prevent damage to the IVC. (*vi*) According to the situation and experience of the surgeon, direct cauterization using bipolar or unipolar electrocoagulation, titanium clips, or vascular clips (first using the separation forceps to lift part of the venous wall) can be used to stop bleeding. Suturing can be used to stop bleeding if necessary, and an appropriate amount of absorbable hemostatic gauze can significantly reduce bleeding (*36*). (*vii*) The use of a special device, the "Goldfinger" (a specialized curved dissector) is conducive to the anatomical separation of the Glisson pedicle and can reduce iatrogenic injury.

The application value of the LARH-HPFM in laparoscopic anatomical hepatectomy is mainly reflected in the following aspects: (*i*) It follows the "easy first" strategy and avoids the fine anatomical separation of Glissonian pedicle and bypasses the surgical obstacles caused by the complex anatomical variation of the Glissonian pedicle. (*ii*) Adequately thinning the hepatic parenchymal and maintaining enough tension to expand the relative gap to expose the transection plane can help determine the position of the Glissonian pedicle in the parenchyma and the direction and angle of the endoscopic linear stapler placement, improving the efficiency of the endoscopic linear stapler, avoiding the risk of injury and bleeding caused by dissecting and separating the Glissonian pedicle without adequate exposure, simplifying the surgical procedure somewhat, shortening the operation time, and improving the safety of the operation. (*iii*) The use of mature anatomical landmarks to set the transection plane of the liver parenchyma avoided accidental injury caused by the wrong dissection level and direction, and the scope of resection can be easily and precisely located. (*iv*) The ineffective liver tissue without inflow and outflow tract can be completely removed, the possibility of postoperative tumor recurrence and postoperative complications can be reduced, so as to improve the survival rate of patients.

For HCC treatment, any surgical approach aims to improve the survival rate of patients. Previous studies demonstrated that the Glissonian approach could improve the postoperative survival in patients with HCC. The principal reason for this is that Glissonian approach could prevent intraoperative spread of cancer cells dislodged by surgical manipulation by isolating the blood supply of the tumor-bearing area from that of the other parts of the liver (*37,38*). Meanwhile, we found that the oncological outcomes were similar between the two groups. Previous reports (*39,40*) have demonstrated increased blood loss and blood transfusion are negative effects on the recurrence and prognosis of patients with HCC after hepatectomy. Moreover, favouring TO significantly improved the probability of cure. Based on these results, the LARH-HPFM seems to be a better choice to improve survival rates of the HCC patients. However, our results are limited to small sample size and further studies need to evaluate the oncological results.

In this study, several limitations need to be addressed. The potential effects of a learning curve in the laparoscopic approach may exist objectively. To limit the influence of learning curve as less as possible, we included patients who underwent LARH-HPFM only after the time period that we had passed the learning curve. The study is a retrospective analysis with small sample size, which may introduce potential selection bias. Although we introduced the PSM method to minimize selection bias, confounding variables could not be completely avoided. The follow-up period was not long enough, and a longer follow-up time is required in future studies to verify the effect of LARH-HPFM. This was a single-centre study, which may have limited the generalizability of the results. Therefore, further multicenter prospective or retrospective studies with large sample sizes and long-term follow-up are required to confirm these results.

The goal of laparoscopic anatomical hepatectomy is to simplify the complex surgery, with reasonable design, accurate efficacy, and high safety. We will combine the "easy first" strategy with LARH, and HPFM will be used. By preferentially dissecting the hepatic parenchyma, the Glissonian pedicle of the corresponding hepatic segment is fully exposed, and the Glissonian pedicle is treated with enough space to reduce the difficulty of progression of the laparoscopic anatomical hepatectomy and make its application easier. However, the selection of various approaches is not fixed and independent. It is necessary to conduct a comprehensive preoperative evaluation through careful image reading and three-dimensional reconstruction before surgery and to make a rational selection with a combination of various accesses according to their technical characteristics, the equipment, the surgical style, the lesion localization, and the individual characteristics of each case.

In conclusion, LARH-HPFM is safe and feasible for HCC with certain advantages over LARH-EG, but there are still many problems worth further exploration.

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