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Laparoscopic liver resection of hepatocellular carcinoma located in segments 7 or 8

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Abstract

Background Many centers consider hepatocellular carcinoma (HCC) located in segments 7 or 8 to be unsuitable for laparoscopic liver resection (LLR). We evaluated the safety of LLR of HCC in segments 7 or 8 following the introduction of new laparoscopic techniques.

Methods This retrospective study included 104 patients who underwent LLR ($n = 46$) or open liver resection (OLR) ($n = 58$) for HCC located in segments 7 or 8 between October 2004 and June 2015. The LLR group was subdivided into two subgroups according to whether LLR was performed before (Lap1; $n = 29$) or after (Lap2; $n = 17$) the introduction of the Pringle maneuver, intercostal trocars, and semi-lateral patient positioning.

Results Non-anatomical resection was more frequent (63.0 vs. 29.3%; $P < 0.001$) and tumor size was smaller (2.8 vs. 4.7 cm; $P < 0.001$) in the LLR group than in the OLR group. Blood transfusion ($P = 0.526$), operation time ($P = 0.267$), postoperative complications ($P = 0.051$), and resection margin ($P = 0.705$) were similar in both groups. LLR was associated with less blood loss (550 vs. 700 ml, $P = 0.030$) and shorter hospital stay (8 vs. 10 days; $P = 0.001$). The 3-year overall (90.2 vs. 81.2%, $P = 0.096$) and disease-free survival (15.1 vs. 12.1%; $P = 0.857$) rates were similar in both groups. The Lap2 group has less blood loss (230 vs. 500 ml; $P = 0.005$) and shorter hospital stay (7 vs. 9 days; $P = 0.038$) compared with the Lap1 group.

Conclusion LLR can be safely performed for HCC located in segments 7 or 8 with recent improvements in surgical techniques and accumulated experience.

Keywords Hepatectomy · Indication · Location · Complication · Technique

Laparoscopic liver resection (LLR) is increasingly being performed worldwide, and laparoscopic left lateral sectionectomy and minor LLR are now considered to be standard procedures [1, 2]. Some studies have shown that the short-term and long-term outcomes of LLR are comparable to those of open liver resection (OLR) [3, 4]. Tumors located in the anterolateral segments are considered suitable for LLR, while tumors located in the posterosuperior segments are still regarded as unfavorable for LLR [5]. Until recently, these locations were considered by most surgeons to be a poor indication for LLR owing to the limited visibility of these regions and the greater difficulty to control bleeding [6]. Several large case-series and extensive reviews have revealed that LLR is still rarely performed for tumors located in the posterior segments. Limited access to the portal triad, difficult pedicle control, large transection area, and anatomic location are among the factors that make it difficult to perform LLR for tumors in this region of the liver [7].

Segments 7 and 8 of the liver are the most difficult locations for laparoscopic access [8]. In fact, resection of these segments is only performed at a few centers worldwide, and only by surgeons with advanced experience in

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both open and minimally invasive surgery [9]. In an earlier study, resection of segments 7 or 8 was associated with longer operation time and greater blood loss compared to other segments [10].

The accumulating experience of laparoscopic major hepatectomy, the development of new instruments, the improvements in surgical skills, and the introduction of novel techniques have made it feasible to perform LLR of segments 7 or 8, and it is now performed at a greater number of centers than before. To date, however, no studies have compared the perioperative and long-term outcomes between LLR and OLR for hepatocellular carcinoma (HCC) located in segments 7 and 8. Therefore, the aims of this study were to compare the perioperative and long-term survival outcomes between LLR and OLR for HCC located in segments 7 and 8, and to evaluate the safety of LLR of segments 7 and 8 based on a retrospective review of patients treated at our institute before and after the introduction of new LLR tools and techniques.

Methods

Patients

We performed a retrospective analysis of 104 patients who underwent hepatic resection for HCC located at segments 7 or 8 at the Department of Surgery, Seoul National University Bundang Hospital between October 1, 2004 and June 30, 2015. This study was approved by the hospital's Institutional Review Board. Eight (15.4%) patients in the LLR group were converted to open surgery because of bleeding in five patients, an uncertain tumor margin in two patients, and poor visibility in one patient. These eight patients were excluded in statistical analyses. Most conversion occurred during our early experience. Therefore, the LLR group comprised 46 patients and the OLR group comprised 58 patients.

In 2012, we introduced several techniques into LLR of tumors located in segments 7 or 8, namely the semi-lateral French position [11], placement of intercostal trocars [12], and the use of the Pringle maneuver. Therefore, patients in the laparoscopic group were divided into two subgroups according to whether they underwent LLR before 2012 (Lap1 group, $n = 29$) or after 2012 (Lap2 group, $n = 17$).

Surgical technique

The indications for LLR were similar to those for OLR in terms of the preoperative assessment of liver function, type of liver resection, and postoperative care [4]. However, laparoscopic approaches were not usually considered in patients with tumors $\geq$5 cm in diameter and tumors invading or adjacent to the main portal pedicle or inferior vena cava, as well as patients with central lesions in the suprahepatic junction adjacent to the major hepatic vein [13].

The LLR techniques used at our institution have been described in more detail elsewhere [11, 14, 15]. Briefly, after inducing general anesthesia, the patients were tilted into the 30° reverse Trendelenburg position with their legs apart (French position) and with right-side-up adjustment. The surgeon stood between the legs at the start of surgery and then moved to the right of the patient to manipulate the instrument through the intercostal trocars. The scopist and the assistant stood on the left side of the patient. Four conventional ports were initially used. A 12-mm camera port was placed in the sub-umbilical region. Pneumoperitoneum was established and maintained at <13 mmHg. Two main working 12-mm ports were inserted where the subcostal area meets the midclavicular line and epigastric area, respectively. A 5-mm port was placed in the subcostal area where it meets the anterior axillary line. A flexible tipped laparoscope was used. After port insertion, intraoperative ultrasound was performed to detect the tumor and confirm the resection margin. For intercostal trocars, two additional intercostal trocars were placed in the seventh and ninth intercostal spaces [12]. Laparoscopic Pringle's maneuver was applied when non-anatomical resection was performed. After isolating the hepatoduodenal ligament, it was encircled with umbilical tape and both ends of the umbilical tape were passed through the long tube, as is usually performed during open surgery. Intermittent clamping of hepatoduodenal ligament <15 min was performed. For anatomical resection, Pringle's maneuver was not performed.

The right liver was mobilized from the inferior vena cava and the diaphragm. Similarly to Professor Gayet's techniques, for major LLRs, the retrohepatic veins larger than 5 mm draining into the inferior vena cava were clipped prior to transection [16]. After mobilizing the liver, the posterior side of the right liver was easily visualized. The laparoscope introduced through the intercostal trocar allowed clear visualization of the superior and posterior parts of the liver. The instruments introduced through these trocars facilitate meticulous dissection. The superficial hepatic parenchyma was transected using ultrasonic shears and deeper parenchymal dissection was performed using a laparoscopic Cavitron Ultrasonic Surgical Aspirator. Bleeding from small branches of the hepatic veins was controlled with endoclips and a sealing device. After achieving hemostasis, fibrin glue was applied to the cut surface of the liver. The resected specimen was inserted into a protective bag and retrieved through the epigastric or sub-umbilical port. Large specimens, especially right liver grafts, were retrieved through an additional suprapubic transverse incision [11].

Table 1 Preoperative characteristics

	LLR group ($n = 46$)	OLR group ($n = 58$)	P value
Age (years), median (range)	62 (48–80)	66 (39–83)	0.852
Gender			0.539
Male	35 (76%)	47 (81%)	
Female	11 (23.9%)	11 (19.0%)	
BMI (kg/m^2), median (range)	23.3 (18.79–30.08)	23.2 (19.86–33.1)	0.654
Albumin (g/dl), median (range)	4.1 (2.8–4.8)	4.1 (2.0–4.7)	0.164
Bilirubin (mg/dl), median (range)	0.8 (0.3–3.8)	0.8 (0–1.6)	0.734
Prothrombin time [24], median (range)	1.07 (0.4–1.76)	1.06 (0.6–1.6)	0.800
Platelet count (1000/μl), median (range)	141 (40–305)	166 (19–363)	0.661
SGPT (IU/l), median (range)	35 (15–338)	27 (13–249)	0.281
SGOT (IU/l), median (range)	36 (17–684)	33 (17–1910)	0.751
ICG-R15 (%), median (range)	9.8 (2.2–46.7)	7.2 (0.70–25.1)	0.253
AFP (ng/ml), median (range)	18.5 (1.5–9390)	15.2 (1.4–40,000)	0.458
Child–pugh class, n (%)			0.783
A	41 (89.1%)	51 (92.7%)	
B	2 (4.3%)	2 (3.6%)	
C	3 (6.5%)	2 (3.6%)	
Hepatitis, n (%)			0.149
Hepatitis B	36 (78.3%)	35 (60.3%)	
Hepatitis C	3 (6.5%)	7 (12.1%)	
Both positive	0 (0%)	0 (0%)	
Both negative	7 (15.2%)	16 (27.6%)	
Prior RFA, n (%)	3 (6.5%)	5 (9.3%)	0.615
Prior TACE, n (%)	13 (28.3%)	28 (48.3%)	0.038
Tumor size (cm), median (range)	2.8 (1.3–6.9)	4.7 (1.0–22.0)	<0.05
Number of tumors, n (%)			0.338
Solitary	41 (89.1%)	46 (79.3%)	
Multiple	5 (10.86%)	12 (20.6%)	

LLR laparoscopic liver resection, *OLR* open liver resection, *BMI* body mass index, *INR* international normalized ratio, *SGPT* serum glutamic pyruvic transaminase, *SGOT* serum glutamic-oxaloacetic transaminase, *AFP* alpha-fetoprotein, *ICG-R15* indocyanine green clearance rate at 15 min, *RFA* radiofrequency ablation, *TACE* transarterial chemo-embolization

Statistical analyses

All statistical analyses were performed using SPSS software version 23.0 (IBM Corp., Armonk, NY). Data are reported as the median (range). The χ^2 test was used to compare categorical variables and the Mann–Whitney U test was used to compare continuous variables between groups. Survival outcomes were analyzed using the Kaplan–Meier method and were compared using log-rank tests. P values of <0.05 were considered statistically significant.

Results

The preoperative characteristics of the LLR and OLR groups are shown in Table 1. The median tumor size was significantly smaller in the LLR group than in the OLR group (2.8 vs. 4.7 cm; $P < 0.05$). A greater proportion of patients in the OLR group underwent transarterial chemo-embolization before hepatectomy compared with the LLR group ($P = 0.038$). There were no significant differences between the two groups in terms of age, sex, body mass index, presence of hepatitis, liver function, severity of liver cirrhosis, and preoperative radiofrequency ablation. The preoperative serum alpha-fetoprotein and indocyanine green retention rate at 15 min (ICG-R15%) were similar in both groups.

Table 2 summarizes the perioperative outcomes of the two groups. Operation time and blood transfusion were similar in both groups. However, blood loss was lower in the LLR group than in the OLR group (550 vs. 700 ml; $P = 0.030$). Major liver resection was more frequent in the OLR group ($P = 0.026$) while non-anatomical resection, including tumorectomy or segmentectomy, was more frequent in the LLR group ($P = 0.001$).

Table 2 Perioperative outcomes

	LLR group ($n = 46$)	OLR group ($n = 58$)	P value
Operation time (min), median (range)	330 (195–790)	295 (170–720)	0.286
Blood loss (ml), median (range)	550 (200–5900)	700 (200–7000)	0.030
Blood transfusion, *n* (%)	8 (17.4%)	13 (22.4%)	0.524
Operation type, *n* (%)			0.026
Tumorectomy	19 (41.3%)	10 (17.2%)	
Segmentectomy	10 (21.7%)	7 (12.1%)	
Bisegmentectomy	1 (2.2%)	1 (1.7%)	
Right anterior sectionectomy	1 (2.2%)	6 (10.3%)	
Right posterior sectionectomy	6 (13%)	10 (17.2%)	
Right hepatectomy	8 (17.4%)	14 (24.1%)	
Extended right hepatectomy	0 (0%)	4 (6.9%)	
Central bisectionectomy	1 (2.2%)	6 (10.3%)	
Type of resection, *n* (%)			0.001
Anatomical	17 (37%)	41 (70.7%)	
Non-anatomical	29 (63%)	17 (29.3%)	

LLR laparoscopic liver resection, *OLR* open liver resection

Table 3 Pathologic and postoperative outcomes

	LLR group ($n = 46$)	OLR group ($n = 58$)	P value
Resection margin (cm), median (range)	0.7 (0.01–6.8)	0.7 (0.10–4.0)	0.473
Cirrhosis, *n* (%)	27 (58.7%)	38 (65.5%)	0.307
Satellite nodules, *n* (%)	4 (8.9%)	11 (19.6%)	0.131
Microvascular invasion, *n* (%)	17 (38.6%)	19 (32.8%)	0.538
Resection, *n* (%)			0.868
R0	45 (97.8%)	57 (98.3%)	
R1	1 (2.2%)	1 (1.7%)	
Postoperative complications, *n* (%)	8 (17.4%)	20 (34.5%)	0.048
Type of complication, *n* (%)			0.333
General	1 (2.2%)	2 (3.6%)	
Surgical	1 (2.2%)	6 (10.9%)	
Liver-related	3 (6.5%)	4 (7.3%)	
Mixed	2 (4.3%)	5 (9.1%)	
Clavien–Dindo grade, *n* (%)			0.150
I	0 (0%)	6 (10.3%)	
II	2 (4.3%)	2 (3.4%)	
IIIa	5 (10.9%)	8 (13.8%)	
IIIb	0 (0%)	1 (1.7%)	
IVa	0 (0%)	2 (3.4%)	
IVb	0 (0%)	1 (1.7%)	
V	0 (0%)	1 (1.7%)	
Major complications (grade $\geq$ IIIb), *n* (%)	0 (0%)	5 (8.62%)	0.150
Hospital stay (days), median (range)	8 (95–147)	10 (6–47)	0.013
Early mortality, *n* (%)	0 (0%)	1 (1.7%)	0.203

LLR laparoscopic liver resection, *OLR* open liver resection

The pathologic results, including resection margin, pathological cirrhosis, satellite nodules, microvascular invasion, and the rate of R0 resection, were similar in both groups (Table 3). The overall complication rate was greater in the OLR group than in the LLR group (34.5 vs. 17.4%; $P = 0.048$). The major complication rate (grade $\geq$ IIIb)

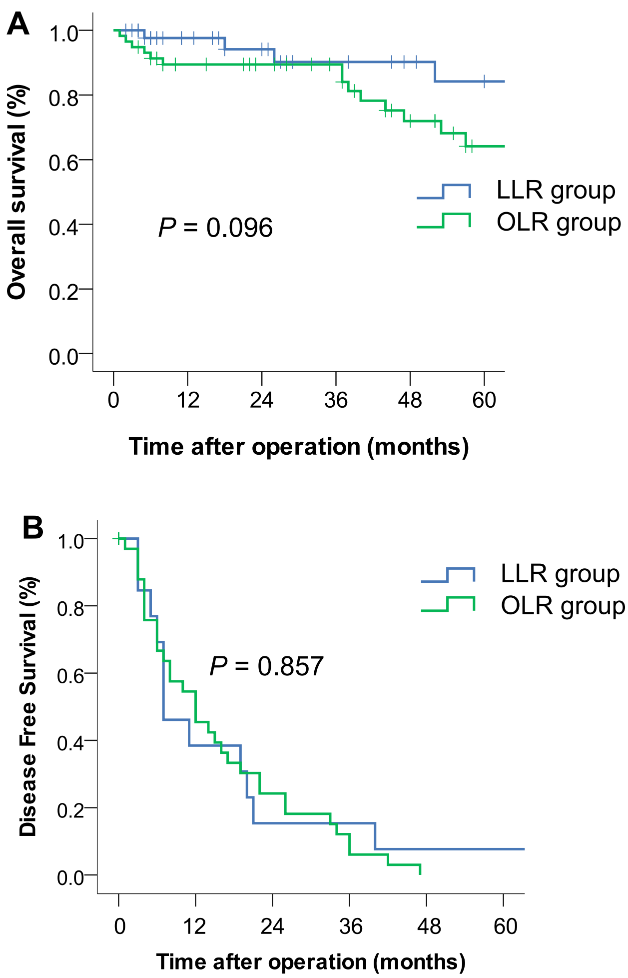

Fig. 1 Three-year overall survival rate (**A**) and 3-year disease-free survival rate (**B**)

was greater in the OLR group than in the LLR, although the difference was not significant (6.89 vs. 0%; $P = 0.150$). Hospital stay was significantly shorter in the LLR group than in the OLR group (8 vs. 10 days; $P = 0.013$). There was one mortality within 1 month of surgery in the OLR group that was caused by uncontrollable bleeding from a gastric ulcer.

The 3-year overall patient survival (90.2 vs. 81.2%; $P = 0.096$) and the 3-year disease-free survival (15.4 vs. 12.1%; $P = 0.857$) rates were similar in the LLR and OLR groups (Fig. 1).

We also compared the surgical outcomes between two subgroups of patients who underwent LLR either before (Lap1 group) or after (Lap2 group) the introduction of several new techniques. We found no significant differences between these subgroups in terms of operation time ($P = 0.070$), blood transfusion ($P = 0.115$), type of resection ($P = 0.417$), and postoperative complication rate ($P = 0.115$). However, blood loss (230 vs. 500 ml; $P = 0.005$) and hospital stay (7 vs. 9 days; $P = 0.038$) were significantly less in the Lap2 group than in the Lap1 group (Table 4).

Discussion

In this study, we compared the perioperative and long-term outcomes between LLR and OLR for HCC located in segments 7 or 8. Of note, blood loss and hospital stay were significantly less in the LLR group than in the OLR group. The 3-year overall survival and disease-free survival rates were similar in both groups. We also evaluated the safety of LLR in segments 7 or 8 by comparing the outcomes of patients who underwent LLR before and after the introduction of new techniques. This analysis revealed that blood loss and hospital stay were much lower after the introduction of the new techniques for LLR.

The technical challenges associated with laparoscopic resection of the posterosuperior segments include surgical field exposure, bleeding control, and determination of a safe resection margin [17]. Major hepatectomy or anatomical liver resection are more frequently required for tumors located in the posterosuperior segments to achieve an adequate resection margin [13]. Citing these challenges, an international consensus meeting recommended that major LLR should only be performed by experienced surgeons [1, 18].

Recent advances in laparoscopic techniques and surgical equipment mean that LLR is now feasible and safe for lesions located in the posterosuperior segments of the liver [19]. To overcome the challenges of LLR of posterosuperior segments, several modifications have been proposed to facilitate the surgical approach [20]. In recent years, our institution introduced three new techniques to overcome these challenges. To achieve better exposure of lesions located in segments 7 or 8, we modified the patient's position from the conventional 30° reverse Trendelenburg with the lower limbs apart into the semi-lateral French position. Proper positioning of the patient improves the operative field because gravity pulls the remnant liver down. Furthermore, lifting the right hepatic vein above the inferior vena cava may reduce venous bleeding [21, 22]. This position also facilitates a caudal approach to reduce blood loss and morbidity [23].

Another problem for lesions located in segments 7 or 8 is the poor operative field. Because the operative field is some distance from the conventional trocar site, the laparoscope and the instrument need to be advanced over a longer distance [4, 5]. Additional ports inserted through intercostal spaces will be beneficial in overcoming these difficulties. Inserting a laparoscope through the intercostal trocar can improve the operative field for posterosuperior lesions. Intercostal trocars can provide better access to the

Table 4 Comparison of perioperative outcomes between patients who underwent LLR before or after the introduction of new techniques

	Lap1 group (n = 29)	Lap2 group (n = 17)	P value
Operation time (min), median (range)	330 (195–790)	265 (90–695)	0.070
Blood loss (ml), median (range)	500 (300–5900)	230 (0–1000)	0.005
Blood transfusion, n (%)	7 (24.1%)	1 (5.9%)	0.115
Operation type, n (%)			0.540
Tumorectomy	10 (34.5%)	9 (52.9%)	
Segmentectomy	7 (24.1%)	3 (17.6%)	
Bisegmentectomy	0 (0%)	1 (5.9%)	
Right anterior sectionectomy	1 (3.4%)	0 (0%)	
Right posterior sectionectomy	5 (17.2%)	1 (5.9%)	
Right hepatectomy	5 (17.2%)	3 (17.6%)	
Central bisectionectomy	1 (3.4%)	0 (0%)	
Type of resection, n (%)			0.417
Anatomical	12 (41.4%)	5 (29.4%)	
Non-anatomical	17 (58.6%)	12 (40.6%)	
Hospital stay (days), median (range)	9 (5–147)	7 (4–13)	0.038
Postoperative complications, n (%)	7 (24.1%)	1 (5.9%)	0.115

Lap1 patients who underwent laparoscopic liver resection (LLR) before the introduction of new techniques in 2012, *Lap2* patients who underwent LLR after the introduction of new techniques in 2012

operative field and make it easier to manipulate the instruments. The feasibility of this method for liver resection of lesions located in segments 7 and 8 was demonstrated in the study by Lee et al. [12].

Bleeding is another challenge for LLRs located in segments 7 or 8, and is the main cause of conversion from laparoscopy to OLR, especially in cirrhotic patients [7]. In our institution, we started to use the Pringle maneuver to provide better control of bleeding. Maehara et al. [24]. reported that the Pringle maneuver helped to reduce intraoperative bleeding during laparoscopic hepatectomy. Similarly, Man et al. [25]. reported that the Pringle maneuver is beneficial in terms of reducing blood loss and shortening the time to complete liver transection. In their study, the Pringle maneuver was associated with a reduction in the blood transfusion volume, and only one-third of their patients needed blood transfusion. Outflow occlusion during the lateral laparoscopic approach to lesions in the posterior segments of the liver could additionally reduce bleeding although we did not introduce the technique yet [19].

This study has some limitations, which means we must interpret our results carefully. In particular, this was a retrospective study with a relatively small sample size, and there were some differences in the preoperative characteristics between the LLR and OLR groups. Another limitation of this study is long study period of more than 10 years. This could be associated with a bias. Nevertheless, to the best of our knowledge, this is first report to compare the outcomes of LLR with those of OLR for HCC located in segments 7 or 8.

In conclusion, our results suggest that LLR is feasible and can be safely performed for HCC located in segments 7 or 8 considering recent improvements of techniques and accumulated experience.

Compliance with ethical standards

Disclosures Drs. Hanisah Guro, Jai Young Cho, Ho-Seong Han, Yoo-Seok Yoon, YoungRok Choi, Jae Seong Jang, Seong, Uk Kwon, Sungho Kim and Jang Kyu Choi have no conflicts of interest or financial ties to disclose.

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