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A Comparison of Short-Term Outcomes between Laparoscopic and Open Liver Resection in Elderly Patients

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Purpose: The aim of this study was to compare the short-term outcomes between laparoscopic liver resection (LLR) and open liver resection (OLR) in elderly patients with hepatic tumors.

Methods: From January 2013 to December 2019, a retrospective study was conducted for a total of 143 patients with over 70 years of age, who underwent liver resection for hepatic tumors. Forty-five patients who received biliary reconstruction at the same time were excluded. According to surgical approaches, 98 patients were classified into LLR and OLR groups. All postoperative complications were classified according to the Clavien-Dindo grading system and the Comprehensive Complication Index (CCI).

Results: Incidence of the postoperative complications was not statistically different between LLR and OLR groups. The CCI was significantly lower in the LLR group, with a median of 8.556, and a median of 19.698 in the OLR group (p=0.042). The length of hospital stay in the LLR group was significantly shorter than in the OLR group (p=0.008).

Conclusion: LLR is safe and feasible as a treatment for hepatic tumor in elderly patients with potentially less postoperative complications compared to OLR.

Keywords: Hepatectomy, Laparoscopy, Laparotomy, Aged, Postoperative complications

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INTRODUCTION

Advancements in laparoscopic surgery have achieved a decrease in the overall postoperative complications in many different surgical subspecialties, including gynecology, urology, colorectal surgery, and gastric surgery.[1-4] Many case series and comparative studies have also reported similar advantages in terms of postoperative morbidity, hospital length of stay, and postoperative pain in the hepatobiliary field.[5-7]

With the increase in life expectancy worldwide, the prevalence of neoplastic disease of the hepatobiliary system has gradually increased and the need to perform liver resections in elderly patients has increased.[8] Since elderly patients are more likely to have decreased life expectancy and a greater prevalence of comorbidities, the decision on whether and how to perform a liver resection should be carefully made by weighing the benefits and risks of the surgery. It is currently accepted that liver resection in elderly patients can be safely performed with acceptable postoperative morbidity and mortality rates.[9-12] However, the issue of whether to perform a laparoscopic liver resection (LLR) or an open liver resection (OLR) arises from considerations of the operative time, technical difficulties, and the greater prevalence of comorbidities and decreased physiologic reserve of elderly patients. Although some reports have shown that LLR in the elderly is feasible, with acceptable postoperative outcomes compared to OLR,[5,7,13] more research toward improving the surgical outcomes of elderly patients would be considered valuable. Therefore, the aim of this retrospective study was to compare the short-term

outcomes between LLR and OLR in elderly patients with hepatic tumors.

MATERIALS AND METHODS

Study design and subjects

We retrospectively analyzed the medical data from the charts and surgical records of 143 patients over 70 years of age who underwent elective liver resections for hepatic tumors from January 2003 to December 2019 at the Department of Hepatobiliary Surgery, Yeungnam University Medical Center. Forty-five patients who underwent biliary reconstruction at the same time were excluded. Finally, 98 patients were divided into the LLR and OLR groups, 48 patients in the LLR group and 50 patients in the OLR group, according to the surgical approach adopted. Patient characteristics, surgical procedures and outcomes, and postoperative complications were evaluated. All postoperative complications were classified according to the Clavien-Dindo grading system and the Comprehensive Complication Index (CCI). This study was reviewed and approved by the Institutional Review Board of Yeungnam University Hospital (IRB No. 2020-08-039).

Preoperative evaluation

The preoperative investigations included complete blood counts, liver function tests, the indocyanine green retention rate at 15 minutes, and routine cardiopulmonary evaluation including electrocardiogram and spirometry. Patients with a history of cardiac problems or ongoing symptoms underwent echocardiography and consultations with cardiology were conducted. Computed tomography or magnetic resonance imaging was routinely performed to assess the tumor characteristics. The surgical risk was assessed using criteria of the American Society of Anesthesiologists (ASA) and liver resection was not recommended for patients with a score >3. However, surgery was performed for patients desiring surgical treatment.

Surgical procedures

The method of the procedure was decided according to the surgeon's preference, considering the location and the size of the tumor and the surgical risk of the patient. Tumors located on the periphery in anterolateral segments (Couinaud segments 2, 3, 4b, 5, or 6) were resected using laparoscopy, mostly. Tumors in the deep central part of the liver were resected in open manners. If the concomitant surgical procedures of other departments were planned as open surgical methods, the liver resections were also held in open manners.

During the operation, central venous pressure was decreased with fluid restriction and diuretics if needed. Parenchymal transection was performed with various instruments, such as the Cavitron Ultrasonic Surgical Aspirator, energy devices, and electrocautery. In most cases in the OLR group, the Pringle maneuver was performed to decrease intraoperative blood loss during liver transection. It was also performed in some cases in the LLR group by the decision of the surgeon. A closed suction drain was placed near each cut surface of the liver.

Postoperative outcomes

The postoperative complications were graded according to the Clavien-Dindo classification, and major complications were defined as those with Clavien-Dindo grade ≥III.[14] Biliary leakage was defined as a bilirubin concentration in the drainage fluid >3-fold that in serum on or after postoperative day 3.[15] Post-hepatectomy liver failure was defined according to the International Study Group of Liver Surgery criteria on postoperative day 5.[16] Hemorrhage was defined as a drop in the hemoglobin level of >3 g/dL after surgery compared to the postoperative baseline level, any postoperative transfusion of packed RBC units for a falling hemoglobin level, or the need for invasive reintervention.[17] Ascites was defined as an abdominal drainage output of >10 mL/kg/d after postoperative day 3.[18] Postoperative delirium was diagnosed by consulting with a psychiatrist and the patients were prescribed antipsychotic treatments by a psychiatrist.

Statistical analysis

The quantitative variables are expressed as medians (range) and the qualitative variables as frequencies (%). A Student's t-test was used for the intergroup comparisons of quantitative variables and a chi-squared test or Fisher's exact test was used to compare the categorical data. A p value of <0.05 was considered significant. All statistical analyses were performed using IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Preoperative data

A total of 98 patients underwent hepatic resections. Forty-eight and 50 were treated with laparoscopic and open approaches, respectively. The baseline characteristics and preoperative laboratory results are summarized in Table 1. There was no significant difference between the groups in terms of gender, age, history of previous abdominal surgery, and most preoperative laboratory results. The LLR group showed significantly lower platelet counts (p=0.002), ASA scores (p=0.031), a remarkably higher incidence of viral hepatitis (p<0.001), and higher body mass index (p=0.041)

Table 1. Baseline characteristics and laboratory results

Characteristic	LLR (n=48)	OLR (n=50)	*p* value
Gender, n (%)			
Male	35 (72.9)	32 (64.0)	0.343
Female	13 (27.1)	18 (36.0)	
Age (yr), median (range)	75 (70~86)	74.5 (70~85)	0.576
BMI (kg/m^2) , median (range)	24.6 (18.5~29.7)	23.4 (15.8~29.8)	0.041
ASA score ≤2, n (%)	30 (62.5)	41 (82.0)	0.031
Platelet count (×10^3/μL), median (range)	187 (71~378)	219 (82~588)	0.002
Total bilirubin (mg/dL), median (range)	0.65 (0.28~2.09)	0.63 (0.21~1.57)	0.905
PT INR, median (range)	1.10 (0.91~1.39)	1.06 (0.87~2.13)	0.824
Albumin (g/dL), median (range)	3.93 (1.54~4.90)	3.90 (2.91~4.91)	0.832
Creatinine (mg/dL), median (range)	0.94 (0.52~1.82)	0.90 (0.40~1.60)	0.218
ICG R15 (%), median (range)	12.5 (1.0~26.0)	9.7 (1.5~39.0)	0.279
Comorbidity, n (%)			
Hypertension	31 (64.6)	24 (48.0)	0.098
Diabetes	18 (37.5)	14 (28.0)	0.316
Cardiovascular disease	4 (8.3)	8 (16.0)	0.247
Cerebrovascular disease	7 (14.6)	8 (16.0)	0.846
Chronic kidney disease	7 (14.6)	6 (12.0)	0.706
Pulmonary disease	8 (16.7)	6 (12.0)	0.509
Charlson comorbidity index, median (range)	6 (3~11)	4 (3~9)	0.004
Previous abdominal surgery, n (%)	21 (43.8)	25 (50.0)	0.535
Positive viral markers, n (%)	20 (41.7)	5 (10.0)	<0.001
HBV	13 (27.1)	3 (6.0)	
HCV	7 (14.6)	2 (4.0)	

LLR = laparoscopic liver resection; OLR = open liver resection; BMI = body mass index; ASA = the American Society of Anesthesiologists; PT = prothrombin time; INR = international normalized ratio; ICG R15 = indocyanine green retention rate at 15 minutes; HBV = hepatitis B virus; HCV = hepatitis C virus.

and Charlson comorbidity index scores (p=0.004) than the OLR group.

Perioperative data and pathologic results

The perioperative data and pathologic results of the two groups are summarized in Table 2. There was no significant difference between the groups in operative time (p=0.070), whereas the number of perioperative blood transfusions was significantly less in the LLR group (p=0.002). Synchronous surgery was frequently conducted in the OLR group. Anatomical resection was performed in 19 patients (39.6%) in the LLR group and 23 patients (46.0%) in the OLR group with no statistical difference (p=0.521). Five patients (10.4%) in the LLR group were converted to open surgery.

Regarding the pathologic outcomes, R0 resection margins were obtained in 38 patients (79.2%) in the LLR group and 40 patients (80.0%) in the OLR group with no significant difference (p=0.918). The LLR group showed significantly more liver cirrhosis (p=0.008), and smaller tumor sizes (p=0.001) than the OLR group.

Postoperative outcomes

The data about postoperative outcomes and complications are shown in Table 3. Postoperative complications occurred in 12 patients (25.0%) in the LLR group and 21 patients (42.0%) in the OLR group with no statistical difference. Two patients (4.0%) in

Table 2. Perioperative data and pathologic results

Characteristic	LLR (n=48)	OLR (n=50)	*p* value
Operative time (min), median (range)	150 (70~325)	180 (40~310)	0.070
Anatomical resection, n (%)	19 (39.6)	23 (46.0)	0.521
Resection type, n (%)			
Major resection	6 (12.5)	20 (40.0)	0.002
Minor resection	42 (87.5)	30 (60.0)	
Conversion to open surgery, n (%)	5 (10.4)	-	-
Perioperative blood transfusion, n (%)	5 (10.4)	19 (38.0)	0.002
Synchronous operation, n (%)	3 (6.3)	12 (24.0)	0.015
Colon	2 (4.2)	8 (16.0)	
GIT, other than colon	0 (0.0)	1 (2.0)	
Others	1 (2.1)	3 (6.0)	
Final pathologic diagnosis, n (%)			
Benign lesion of liver	4 (8.3)	6 (12.0)	
Primary malignancy	35 (72.9)	26 (52.0)	
Metastatic tumor	9 (18.8)	18 (36.0)	
Underlying liver cirrhosis, n (%)	18 (37.5)	7 (14.0)	0.008
Number of tumors, median (range)	1 (1~3)	1 (1~4)	0.228
Maximal tumor size (cm), median (range)	22.5 (3~97)	35 (6~130)	0.001
R1 resection, n (%)	5 (10.4)	4 (8.0)	0.918

LLR = laparoscopic liver resection; OLR = open liver resection; GIT = gastrointestinal tract. Major resection was defined as the resection of 3 or more segments.

the OLR group died within 30 days without having a chance to be discharged, whereas there was no mortality in the LLR group.

Although the number of events in each category of postoperative complications was not statistically different between the groups, the CCI was significantly lower in the LLR group, with a median of 8.556, and a median of 19.698 in the OLR group (p=0.042). Most patients with C-D grade IIIa complications had bile leakage and underwent percutaneous drainage with or without endoscopic retrograde biliary drainage. All patients with C-D grade complications over IVa had acute kidney injury, which required hemodialysis.

The length of hospital stay in the LLR group was significantly shorter than in the OLR group (p=0.008), even though three patients had to be readmitted within 30 days after surgery. Two of them were admitted 1 month after the surgery due to intraabdominal abscesses, and percutaneous drainage catheters were placed under fluoroscopic guidance. The other patient was hospitalized 15 days after the surgery due to mild dyspnea and diagnosed as focal pneumonia. He was discharged 3 days later with improved symptoms.

DISCUSSION

Since Reich et al.[19] reported LLR in 1991, the use of LLR as a treatment for neoplastic disease has gradually increased. Many studies have reported that LLR showed improved surgical and postoperative outcomes.[6,13,20-22] With these evidences, the indications for LLR have been expanded to malignancies and major hepatectomies, and further studies have proven the safety and acceptable morbidity and mortality rates of LLR. Also, advancements in postoperative care and improvements in laparoscopic instruments have made LLR more feasible for the treatment of neoplastic liver disease.

However, a question about the feasibility of LLR in elderly patients remains unanswered. The aging process makes elderly people lose their reserve capacity gradually. This process may induce a greater incidence of complications and in-hospital mortality, not only during the surgery but also after surgery. Pneumoperitoneum may result in decreases in lung compliance, venous return, and the vascular perfusion of intra-abdominal organs, which can lead to postoperative cardiovascular complications and acute kidney injury.[23,24]

Table 3. Postoperative outcomes and complications

Characteristic	LLR (n=48)	OLR (n=50)	*p* value
Hospital stay (day), median (range)	14 (6~52)	18 (8~63)	0.008
Patients with morbidity, n (%)	12 (25.0)	21 (42.0)	0.075
In-hospital mortality, n (%)	0 (0.0)	2 (4.0)	0.495
Transfer to rehabilitation center, n (%)	4 (8.3)	9 (18.0)	0.158
Readmission within 30 days, n (%)	3 (6.3)	0 (0.0)	0.114
Highest C-D grade ≥IIIa, n (%)	7 (14.6)	12 (24.0)	0.238
I	1 (2.1)	2 (4.0)	
II	4 (8.3)	8 (16.0)	
IIIa	3 (6.3)	6 (12.0)	
IIIb	0 (0.0)	0 (0.0)	
IVa	4 (8.3)	3 (6.0)	
IVb	0 (0.0)	1 (2.0)	
V	0 (0.0)	2 (4.0)	
CCI, median (range)	8.556 (0~51.7)	19.698 (0~100)	0.042
Postoperative complications, n (%)			
Superficial SSI	1 (2.1)	6 (12.0)	0.112
Deep SSI	2 (4.2)	4 (8.0)	0.678
Pneumonia	3 (6.3)	4 (8.0)	1.000
Ascites	4 (8.3)	4 (8.0)	1.000
Delirium	1 (2.1)	3 (6.0)	0.617
Bile leakage	4 (8.3)	8 (16.0)	0.247
Liver failure	1 (2.1)	5 (10.0)	0.205
Renal failure	3 (6.3)	5 (10.0)	0.715
Bleeding	4 (8.3)	10 (20.0)	0.099

LLR = laparoscopic liver resection; OLR = open liver resection; C-D grade = Clavien-Dindo grade; CCI = Comprehensive Comorbidity Index; SSI = surgical site infection.

Despite the shortcomings of laparoscopy mentioned above, our study showed no difference in pulmonary and renal complications between the two groups. Recent LLR studies in elderly patients also reported similar results for cardiopulmonary and renal complications.[5,20,25,26] The absence of large abdominal incisions in the LLR group, which resulted in less postoperative pain and the preservation of pulmonary function, might have counterbalanced the adverse effects of pneumoperitoneum and less blood loss might have been a counterpart of the risk of renal injury in the LLR group.[27]

Consistent with recent studies, our study showed the non-inferiority, or even the superiority of LLR compared to OLR in terms of postoperative complications.[5,20,25,26] Although the complication rate for each category was not significantly different, the CCI scores were significantly lower in the LLR group, indicating that patients in the OLR group had multiple complications in each category. The explanation for the lower CCI scores might be the lower invasiveness of the LLR surgical procedure. Previous studies showed that LLR required longer operation time, which was even shorter in our study, and the rate of major resection in the LLR group was lower than that in the OLR group. The length of hospital stay was significantly lower in the LLR group, which might be the result of lower CCI scores.

We designed the study period from 2003 to 2019. The study period had to be relatively long to achieve an adequate statistical power. Since the indications of LLR have been expanded over time, the large proportion of the LLR was held recently. Thus, there would be a performance bias in terms of surgical skills between the two groups, which would result in a favorable outcome toward the LLR group.

Although our center performed a complete analysis of cardiopulmonary function and other comorbidities, many unmeasured factors, which are usually termed 'frailty', can affect the postoperative outcomes of elderly patients. Rockwood et al. defined frailty as a multidimensional syndrome involving the loss of reserves that gives rise to vulnerability, and established the Canadian Study of Health and Aging Clinical Frailty Scale to measure cognition, function, or comorbidity, and predict the risk of death.[28] Since our study was designed retrospectively, the frailty of the patients was not measured.

Propensity score matching was not necessarily performed since the aim of the study was to confirm the non-inferiority of LLR compared to OLR and the factors that significantly differed between each group were thought to cause better results in the OLR group. However, the pathologic data revealed that the number and size of the tumors were larger in the OLR group, which may have resulted in selection bias. Studies on the long-term oncologic outcomes of LLR are still needed. Randomized prospective trials are required to compare LLR and OLR in elderly patients.

CONCLUSION

In conclusion, we determined that LLR is safe and feasible as a treatment for neoplastic liver disease in elderly patients with potentially less postoperative complications compared to OLR.

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CONFLICT OF INTEREST

None.

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