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Original Article

Comparison of short- and long-term outcomes of laparoscopic hepatectomy for colorectal liver metastasis in the posterosuperior and anterolateral segments

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Abstract: Hepatectomy is the main curative strategy for patients with colorectal liver metastasis (CRLM). In recent years, laparoscopic hepatectomy (LH) has gradually been adopted for the treatment of CRLM. However, in most cases reported in previous studies, CRLM was located in the anterolateral segments. The aim of the current analysis was to compare the short- and long-term outcomes of LH for CRLM in the posterosuperior segments. Clinical and follow-up data of patients with CRLM, undergoing LH at our hospital from March 2009 to October 2016 were retrospectively analyzed. Patients were divided into the posterosuperior group (38 cases) and the anterolateral group (81 cases) based on the location of CRLM. Compared with the anterolateral group, the posterosuperior group had longer operative time, greater intraoperative blood loss, and higher rate of conversion. There was no statistical difference in the rate and severity of postoperative 30-day complications, postoperative 30-day mortality, length of hospital stay, pathological results, 5-year overall survival, and disease-free survival. In summary, although LH for CRLM in the posterosuperior segments has shortcomings such as long operative time, high intraoperative blood loss, and high rate of conversion, the incidence of postoperative complications, severity of complications, postoperative 30-day mortality, and long-term survival outcomes in the PS group were not different from those in the anterolateral segments.

Keywords: Colorectal liver metastasis, laparoscopic hepatectomy, minimally invasive surgery, posterosuperior segments

Introduction

Hepatectomy is the primary treatment for patients with colorectal liver metastasis (CRLM) [1-5]. In recent years, improvements in laparoscopic instruments and promotion of laparoscopic surgery have led to the gradual adoption of laparoscopic hepatectomy (LH) for the treatment of CRLM [6-13]. Compared with open hepatectomy, LH has the advantages of reduced blood loss and more rapid recovery with similar long-term survival outcomes [6-13]. Clinically, the liver is divided into two anatomical regions: the posterosuperior segments (Couinaud segments 2, 3, 4b, 5, and 6) and the anterolateral segments (Couinaud segments 1, 4a, 7, and 8) [14]. LH for lesions of the posterosuperior segments is more difficult than that for the anterolateral segments [15-23]. In previously reported studies, LH for CRLM has been mainly applied primarily for anterolateral segments [6-13]. Thus far, there has been no report in the English literature on the short- and long-term outcomes of LH for CRLM located in the posterosuperior segments. Therefore, this study aimed to report the short- and long-term outcomes of LH for CRLM in the posterosuperior segments versus those in the anterolateral segments.

Patients and methods

The research was approved by our local ethics committees. The requirement of informed con-

Table 1. Comparison of the preoperative data between the two groups

Variables	Anterolateral group (*n* = 81)	Posterosuperior group (*n* = 38)	*P* value
Age (years)	63 (42-71)	60 (40-69)	0.380
Gender (Male:Female)	49 (60.5%):32 (39.5%)	24 (63.2%):14 (36.8%)	0.781
BMI (kg/m^2)	22 (19-27)	21 (20-25)	0.236
Primary tumor location			0.396
Colon	38 (46.9%)	21 (55.3%)	
Rectum	43 (53.1%)	17 (44.7%)	
Primary tumor stage			0.745
I	15 (18.5%)	6 (15.8%)	
II	23 (28.4%)	14 (36.8%)	
III	43 (53.1%)	18 (47.4%)	
Time of occurrence			0.337
Metachronous	67 (74.1%)	34 (89.5%)	
Synchronous	14 (17.3%)	4 (10.5%)	
Disease-free interval			0.615
< 36 months	24 (29.6%)	13 (34.2%)	
≥ 36 months	57 (70.4%)	25 (65.8%)	
Preoperative CEA level			0.681
< 5 ng/ml	13 (16.0%)	5 (13.2%)	
≥ 5 ng/ml	68 (84.0%)	33 (86.8%)	
ASA score			0.873
I	67 (82.7%)	31 (81.6%)	
II	12 (14.8%)	6 (15.8%)	
III	4 (4.9%)	1 (2.6%)	
Tumor number			0.234
Single	71 (87.7%)	36 (94.7%)	
Multiple	10 (12.3%)	2 (5.3%)	

CEA: carcinoembryonic antigen; ASA: American Society of Anesthesiologists.

sent from patients was waived because of the retrospective nature of the research, since it was not a prospective study.

From March 2009 to October 2016, a total of 143 patients with CRLM underwent LH at our institution. Inclusion criteria were: (1) primary radical hepatectomy, (2) CRLM lesions located in one segment, (3) no other operations, such as radiofrequency ablation, and (4) complete clinical and follow-up data. Exclusion criteria included: (1) palliative hepatectomy or liver biopsy only and (2) intraoperative death. A total of 119 patients met the inclusion criteria and were included in the study. Based on the location of CRLM, patients were divided into the posterosuperior group (38 cases) and the anterolateral group (81 cases).

All patients underwent abdominal imaging to determine the location and number of CRLM lesions and identify the adjacent vasculature. The indications for LH are as follows: (1) primary colorectal cancer having received radical resection (R0 resection, open or laparoscopic surgery), (2) metastasis only in the liver, and (3) preoperative examination suggesting single or two metastatic lesions located within a segment, with a diameter less than 5 cm, and not adjacent to the hepatic portal and large vessels. Routine intraoperative ultrasonography was performed during LH to localize the tumor, identify the adjacent vasculature, and maintain an appropriate resection margin. Detailed surgical procedures have been previously reported [19].

Postoperative 30-day complications were defined as complications within 30 days after surgery, and severity of 30-day postoperative complications was assessed according to the Dindo-Clavien classification as follows: grade 1, oral medication or bedside medical care required; grade 2, intravenous medical therapy required; grade 3, radiologic, endoscopic, or operative intervention required; grade 4, chronic deficit or disability associated with the event; grade 5, death related to surgical complication. Major complications were classified into grades 3, 4, and 5. Minor complications were defined as grades 1 and 2 [24-30]. Postoperative 30-day mortality was defined as any cause of death within 30 days after surgery.

Patients were registered with their permanent home address and contact information when discharged. Outpatient visits, home visits, and phone calls were used for follow-up. Patients were followed every 3 months for the first 2

Table 2. Comparison of short-term outcomes of the two groups

Variables	Anterolateral group (*n* = 81)	Posterosuperior group (*n* = 38)	*P* value
Conversion	2 (2.5%)	6 (15.8%)	0.021
Operative time (min)	150 (100-240)	180 (110-260)	0.021
Blood loss (ml)	240 (180-460)	290 (160-560)	0.030
Surgical procedure			0.286
Nonanatomical hepatectomy	59 (72.8%)	24 (63.2%)	
Anatomical hepatectomy	22 (27.2%)	14 (36.8%)	
Postoperative hospital stay (d)	10 (7-22)	11 (9-29)	0.098
Patients with postoperative complications	17 (21.0%)	8 (21.1%)	0.994
Patients with major complications	3 (3.7%)	2 (5.3%)	1.000
Tumor size (cm)	2.6 (1.0-6.0)	3.0 (0.9-5.0)	0.158
Resection margin (cm)	1.6 (0.2-4.0)	1.4 (0.1-4.6)	0..320
Adjuvant chemotherapy	54 (66.7%)	20 (52.6%)	0.193

Table 3. Comparison of follow-up and cancer recurrence of the two groups

Variables	Anterolateral group (*n* = 81)	Posterosuperior group (*n* = 38)	*P* value
Death	24 (29.6%)	12 (31.6%)	0.829
Cancer recurrence	22 (27.2%)	11 (26.3%)	
Non-neoplastic diseases	2 (2.5%)	1 (2.6%)	
Tumor recurrence	28 (34.6%)	17 (44.7%)	0.286
Recurrence pattern			0.990
Extrahepatic	7 (8.6%)	4 (10.6%)	
Intrahepatic	18 (22.2%)	11 (26.3%)	
Both	3 (3.7%)	2 (5.3%)	
Time to recurrence (median)	16 (10-44)	14 (9-55)	0.407

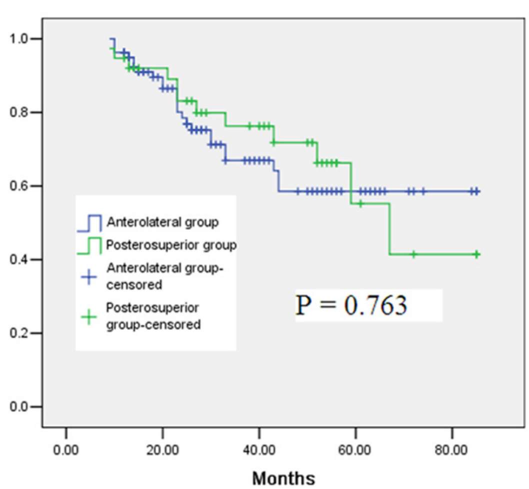

Figure 1. Comparison of overall survival between the two groups.

years and then once every 6 months. Follow-up included routine physical examination, tumor marker detection, and abdominal imaging examination [31-36]. Patients suspected of tumor recurrence and other discomforts received hospital treatment at any time. The last follow up visit was in November 2016.

Data are presented as means and standard deviations for variables with a normal distribution. For data with a non-normal distribution, results are expressed as medians and ranges. Survival rates were analyzed using the Kaplan-Meier method. Univariate analyses were performed to identify prognostic variables related to overall survival (OS) and disease free survival (DFS). Univariate analyses were performed to identify the prognostic variables related to survival. Univariate variables with probability values < 0.05 were selected for inclusion in the multivariate Cox proportional hazard regression model. $P < 0.05$ was considered statistically significant. SPSS 13.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analysis.

Results

Preoperative data of the two groups

Preoperative data for the two groups are shown in **Table 1**. There was no significant difference in preoperative data such as age, sex, body mass index, American Society of Anesthesiologists (ASA) score, carcinoembry-

Table 4. Univariate and multivariate analysis of overall survival

Factors	Univariate analysis			Multivariate analysis			
	OR	95% CI	*P* value	OR	95% CI	Beta value	*P* value
Sex (Male vs. Female)	1.102	0.415-1.320	0.501				
CEA (≥ 5 vs. < 5 ng/ml)	1.398	1.102-1.784	0.030	1.489	0.845-1.548	0.584	0.120
Time of occurrence (Synchronous vs. Metachronous)	1.069	0.459-1.269	0.307				
Primary tumor location (Rectum vs. Colon)	1.075	0.749-1.236	0.198				
ASA score (III vs. I-II)	1.197	0.489-1.980	0.360				
Tumor number (Multiple vs. Single)	1.200	0.870-1.903	0.109				
Primary tumor stage (Stage III vs. Stage I-II)	2.029	1.250-3.602	0.012	1.987	1.258-2.902	1.580	0.009
Disease-free interval (< 36 vs. ≥ 36 months)	2.503	1.210-4.203	0.023	2.803	1.518-5.109	1.804	0.025
Tumor size (≥ 2.5 vs. < 2.5 cm)	1.360	0.540-2.250	0.158				

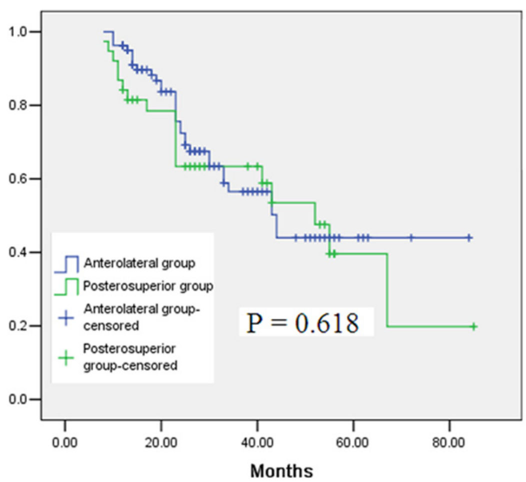

Figure 2. Comparison of disease-free survival between the two groups.

onic antigen (CEA) level before hepatectomy, primary tumor location, primary tumor stage, time of occurrence and disease-free interval.

Short-term outcomes of the two groups

Short-term outcomes are shown in **Table 2**. Compared with the anterolateral group, the posterosuperior group had a longer operation time (*P* = 0.021), greater intraoperative blood loss (*P* = 0.030), and higher rate of conversion (*P* = 0.021). Two patients in the anterolateral group were converted to open surgery due to uncontrolled intraoperative bleeding. Six patients were converted to open surgery in the posterosuperior group, including four due to uncontrolled intraoperative bleeding and 2 due to deeper tumor location making it difficult to ensure a R0 margin with LH. There was no statistically significant difference between the two groups in the type of surgery, postoperative hospital stay, and the incidence and severity of postoperative 30-day complications. Neither group had a patient death within 30 days after surgery. Detailed pathological results are shown in **Table 2**. There was no significant difference between the two groups in terms of tumor size and resection margin (**Table 2**).

Long-term overall survival outcomes of the two groups

At final follow-up, 12 patients and 24 patients in the posterosuperior and anterolateral groups died, respectively. The majority of deaths were due to tumor recurrence, while only a small proportion was attributed to non-neoplastic diseases (**Table 3**). The 5-year OS was 56% and 58% in the posterosuperior and anterolateral groups, respectively; this difference was not statistically significant (**Figure 1**, *P* = 0.763). Univariate analysis showed that TNM stage of the original colorectal cancer, recurrence-free interval, and CEA level before hepatectomy correlated with OS (**Table 4**). Multivariate analysis showed that TNM stage of the original colorectal cancer and recurrence-free interval were independent predictors of OS (**Table 4**).

Long-term disease free survival outcomes of the two groups

The 5-year disease free survival was 39% and 43% in the posterosuperior and anterolateral groups, respectively; this difference was not statistically significant (**Figure 2**, *P* = 0.618). Univariate analysis showed that colorectal cancer stage, recurrence-free interval, and preoperative CEA level were associated with disease-

Table 5. Univariate and multivariate analysis of disease-free survival

Factors	Univariate analysis			Multivariate analysis			
	OR	95% CI	*P* value	OR	95% CI	Beta value	*P* value
Sex (Male vs. Female)	1.239	0.584-1.549	0.259				
CEA (≥ 5 vs. < 5 ng/ml)	1.287	1.125-1.855	0.044	1.478	1.128-1.789	2.500	0.030
Time of occurrence (Synchronous vs. Metachronous)	1.148	0.587-1.420	0.159				
Primary tumor location (Rectum vs. Colon)	1.109	0.726-1.548	0.258				
ASA score (III vs. I-II)	1.240	0.489-1.509	0.201				
Tumor number (Multiple vs. Single)	1.197	0.703-1.536	0.213				
Primary tumor stage (Stage III vs. Stage I-II)	3.010	1.590-3.980	0.008	2.159	1.480-3.057	1.508	0.018
Disease-free interval (< 36 vs. ≥ 36 months)	1.258	1.105-2.108	0.041	1.200	1.129-2.328	0.658	0.080
Tumor size (≥ 2.5 vs. < 2.5 cm)	1.360	0.540-2.250	0.158				

free survival (**Table 5**). Multivariate analysis showed that colorectal cancer stage and CEA level before hepatectomy were independent predictors of disease free survival (**Table 5**).

Discussion

In this study, we compared short- and long-term outcomes of LH for posterosuperior and anterolateral CRLM. The results showed that the technical difficulty of LH was higher for CRLM in the posterosuperior segments than that in the anterolateral segments, demonstrated by longer operation time, greater intraoperative blood loss, and higher rate of conversion to open laparotomy. However, the incidence of 30-day complications, 30-day mortality, and long-term survival outcomes were not significantly different between the posterosuperior and anterolateral groups.

In this study, six patients were converted to open procedure in the posterosuperior group, including four due to uncontrolled bleeding and two due to deeper tumor location making it difficult to ensure a R0 margin with LH. In comparison, only 2 patients in the anterolateral group were converted to open laparotomy. Due to anatomical reasons, the surgical field of view is relatively narrow for posterosuperior liver lesions [15-23]. The drawback associated with a narrow surgical field of view is the difficulty in determining the resection margins and in achieving intraoperative hemostasis [15-23]. Additionally, the lack of laparoscopic surgical equipment specifically designed for posterosuperior tumors, the fact that it is a less common procedure, and the lack of experience among surgeons all contributed to the high conversion rate [15-23]. Surgeons have taken some measures to improve the technique, such as changing the incision location and patient position during surgery [15-23].

Because using LH is a more difficult procedure to treat liver metastasis in the posterosuperior segments [15-23], the clinical guidelines for LH list liver metastasis located in the posterosuperior segments as a contraindication. However, our study indicated that there was no statistically significant difference in the incidence of complications, severity of complications, and mortality in both groups 30 days postoperatively. These results suggest that liver metastasis located in the posterosuperior segments should not be considered a contraindication for LH. Nevertheless, surgeons who perform LH for liver metastasis in the posterosuperior segments need to have significant laparoscopic experience. Previous studies showed that the surgeon must perform 50-60 LH procedures in order to master the technique [37-43].

Previous studies demonstrated that LH and laparotomy for CRLM have similar long-term survival outcomes [6-13]. Large sample studies have found that 5-year OS and 5-year recurrence-free survival of patients with CRLM treated with LH were 45%-68% and 39%-54%, respectively [6-13]. In this study, the 5-year OS and 5-year relapse-free survival were similar in both groups, and these values were similar to those reported in the large sample study described above. These results strongly indicate that, as long as appropriate patients are chosen and physicians are skilled, the long-term outcomes of LH for liver metastasis in the posterosuperior and anterolateral segments are similar.

Limitations of this study include the fact that it was a single-center experience, small sample size, and had a retrospective design; therefore, the levels of evidence are low. In addition, none of the patients underwent major hepatectomy (resection of more than three segments), so the conclusion from this study is difficult to generalize to laparoscopic major hepatectomy. However, according to our extensive search using PubMed, Embase, Web of Science, and Google Scholar, currently, there are no reports in the English literature on the short- and long-term outcomes of LH for CRLM in the posterosuperior segments.

In conclusion, although LH for CRLM in the posterosuperior segments has shortcomings including longer operative time, greater intraoperative blood loss, and high conversion rate, the incidence and severity of postoperative 30-day complications, postoperative 30-day mortality, and long-term survival outcomes were similar to patients with anterolateral segments. As long as surgeons are skillful, LH is feasible and effective for the treatment of CRLM in the posterosuperior segments.

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Disclosure of conflict of interest

None.

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