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ORIGINAL ARTICLE

A comparative study of laparoscopic microwave ablation with laparoscopic radiofrequency ablation for colorectal liver metastasis

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Summary

Purpose: *Laparoscopic thermal ablation is a common alternative to surgical resection for treating colorectal liver metastasis, particularly for metastases located in difficult-to-reach regions. This study aimed to compare the short- and long-term outcomes of laparoscopic radiofrequency ablation (LRFA) and laparoscopic microwave ablation (LMWA) used for treating colorectal liver metastasis.*

Methods: *Data from patients with colorectal liver metastasis who had undergone LRFA or LMWA from January 2010 to January 2016 were examined. Baseline data, postoperative 30-day complications, complete ablation rates, local tumor progression rates, and disease-free (DFS) and overall survival (OS) rates were compared between the two treatment groups.*

Results*: A total of 179 patients with colorectal liver metastasis (71 with LMWA and 108 with LRFA) were treated via the laparoscopic approach. Major postoperative 30-day complication rates were 11.1% and 12.7% in the LRFA and LMWA groups, respectively (p=0.046). No perioperative or postoperative 30-day deaths occurred. Local tumor progression (LTP) rates were 10.2% (11/108) and 1.4% (1/71) in the LRFA and LMWA groups (p=0.046), respectively. Five-year OS rates were 56% and 58% (p=0.498) and 5-year DFS rates were 41% and 39% (p=0.557) in the LRFA and LMWA groups, respectively.*

Conclusions: *LRFA and LMWA appear to be safe for treating colorectal liver metastasis. The OS and DFS rates were similar, although LTP rates were lower in the LMWA group than in the LRFA group.*

Key words: *colorectal liver metastasis, hepatectomy, laparoscopic radiofrequency ablation, laparoscopic microwave ablation, survival*

Introduction

Treatment options for colorectal liver metastasis include radical hepatic resection, thermal ablation (by percutaneous, laparoscopic, or open approach), and chemotherapy [1-7]. Among them, percutaneous RFA is one of the most commonly used techniques for treating colorectal liver metastases with small diameters [8-11]. Thus, percutaneous RFA can be used to treat small tumors with lesser blood loss and fewer postoperative complications than those in radical hepatic resection [8-11]. One limitation of percutaneous RFA is that it cannot be used to treat tumors larger than 3 cm in size or around nearby blood vessels that may act as a heat sink [8-11]. Incomplete ablations in these circumstances may lead to high rates of LTP [8-11]. Surgeons have begun addressing these limitations using high-powered MWA systems, which utilize an electric field to heat tissues. Com-

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pared with RFA, this penetrating electric field in MWA can create larger ablation zones and heat tumor tissue to hotter temperatures [12-14].

Despite the benefits associated with percutaneous ablation, few colorectal liver cancer cases are still not amenable to a direct percutaneous approach because of the location of the nodule, particularly if it is near the capsule or the diaphragm [12-14]. An alternative method for treating these nodules is to utilize a laparoscopic approach, which allows the surgeon to grossly examine the tumor spread, detect a new nodule via intraoperative ultrasound (IOUS), and identify safer insertion paths to treat tumors located in difficult-to-reach locations. Laparoscopic treatment strategies with MWA or RFA have only recently been adopted to reduce complication rates [15-19]. Long-term clinical results from laparoscopic MWA treatment of colorectal liver metastasis have not yet been characterized. This retrospective study aimed to compare laparoscopic MWA and RFA in patients with colorectal liver metastasis in terms of their respective technical success, postoperative 30-day complication rates, LTP rates, and OS and DFS rates.

Methods

This retrospective study complied with the tenets of the Declaration of Helsinki and was approved by the local ethics committee. The need for informed consent from all patients was waived because the study was retrospective.

All patients with colorectal liver metastasis who were treated with either LMWA or LRFA from January 2010 to January 2016 were included in this study. The indications for laparoscopic ablation therapies (LMWA or LRFA) were as follows: a single lesion of ≤ 5 cm in diameter or 2 to 3 lesions of ≤ 3 cm in diameter unresectable because of the high risk of postoperative complications, without cirrhosis, and/or superficial lesions adjacent to abdominal viscera or deeply seeded lesions that were not amenable to percutaneous approaches. Patients who underwent radical hepatic resection with ablation therapy were excluded from this study.

Preoperative assessment included abdominal ultrasound (US) and computed tomography (CT) of the abdomen to confirm the diagnosis and location of colorectal liver metastasis. In selected cases wherein CT or US imaging was equivocal, magnetic resonance imaging (MRI) of the abdomen was utilized. All patients underwent IOUS for detecting a new nodule, which was not discovered by preoperative examinations. The techniques used for laparoscopic ablation have been reported elsewhere [20]. Postoperative morbidity and mortality were defined as complications and death, respectively, within 30 days after laparoscopic ablation. The Clavien–Dindo classification was used to grade complications 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; and Grade 5, death related to surgical complications. Major complications were classified as Grades 3–5, whereas minor complications were classified as Grades 1 and 2 [21-25].

Abdominal US and CT scans were performed at 1 and 3 months after laparoscopic ablation to evaluate treatment response. Subsequently, the post-treatment response was evaluated by CT every 6 months. Technical success was defined by the tumor lesion being completely covered by the ablation zones at the 1-month follow-up examinations using contrast-enhanced imaging [26-29]. LTP was defined by the reappearance of tumor foci within the edge of the ablation zone.

Patients who did not exhibit a complete local response after the first ablation session immediately underwent additional ablation sessions or chemotherapy. Patients with intrahepatic or extrahepatic recurrence were treated with appropriate therapies following the current guidelines for colorectal liver metastasis [30-36]. OS rate was assessed from the day of RFA till the last follow-up or death due to any cause. DFS rate was calculated from the day of RFA till the day of cancer recurrence or death due to any cause. The follow-up period ended in November 2016.

Statistics

Data are presented as means and standard deviations for variables that followed normal distribution. For data following non-normal distribution, the results were expressed as medians and ranges. Survival rates were analyzed using the Kaplan-Meier method and log-rank test. Univariate analyses were performed to identify prognostic variables related to OS and DFS. Univariate variables with p values <0.10 were selected for inclusion in a multivariate Cox proportional hazards regression model. Adjusted hazard ratios and the corresponding 95% confidence intervals were calculated. $P < 0.05$ was considered statistically significant. SPSS 13.0 for Microsoft Windows version (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses.

Results

A total of 179 patients with colorectal liver metastasis treated via the laparoscopic approach were analyzed (71 underwent LMWA and 108 LRFA). The baseline characteristics of patients allocated to LMWA or LRFA are described in Table 1. A significant difference in the maximum diameter of colorectal liver metastatic nodules was observed between patients treated with LMWA and those treated with LRFA.

The conversion rate to open approach during the laparoscopic access was 0%, and no periop-

Table 1. Comparison of clinical data between LMWA and LRFA group

Data	*LMWA (n=71) n*	*LRFA (n=108) n*	*p value*
Age (years), median (range)	51 (39-71)	50 (42-72)	0.310
Sex			0. 405
Male	49	68	
Female	22	40	
CEA pre ablation (ng/ml), median (range)	16 (3-49)	14 (2-39)	0.209
Primary tumor			0.466
Colon cancer	44	61	
Rectal cancer	27	47	
Original cancer stage			0.594
I	12	19	
II	28	47	
III	31	42	
ASA score			0.908
I	52	76	
II	14	23	
III	5	9	
Number of lesions			0.832
1	33	51	
2	26	34	
3	12	23	
Maximum tumor size (cm), n (range)	3 (1-5)	2 (1-4)	0.040

Table 2. Comparison of surgical outcomes and complications between LMWA and LRFA group

	LMWA (n=71) n	*LRFA (n=108) n*	*p value*
Ablation time (min), n (range)	70 (30-100)	60 (40-110)	0.120
Blood loss (ml), n (range)	40 (20-90)	50 (30-80)	0.205
Length of hospital stay (d), n (range)	7 (5-19)	9 (4-18)	0.108
Patients with complications	9	12	0.750
Patients with major complications	0	0	-
Patients with minor complications	9	12	0.750
Perihepatic fluid collection	3	3	
Urinary tract infection	2	3	
Pleural effusion	1	4	
Ascites	3	2	

erative or postoperative 30-day deaths occurred. The overall morbidity rates were 12.7 and 11.1% in the LMWA and LRFA groups, respectively; however, this difference was not significant. The severity of postoperative 30-day complications, as per Clavien–Dindo classification, was comparable between the two groups (Table 2).

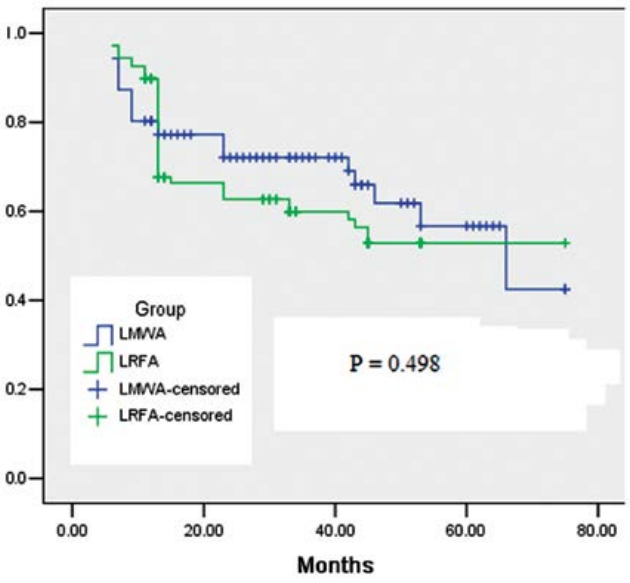

Figure 1. Overall survival of patients with colorectal liver metastasis undergoing laparoscopic microwave ablation and radiofrequency ablation (p=0.498).

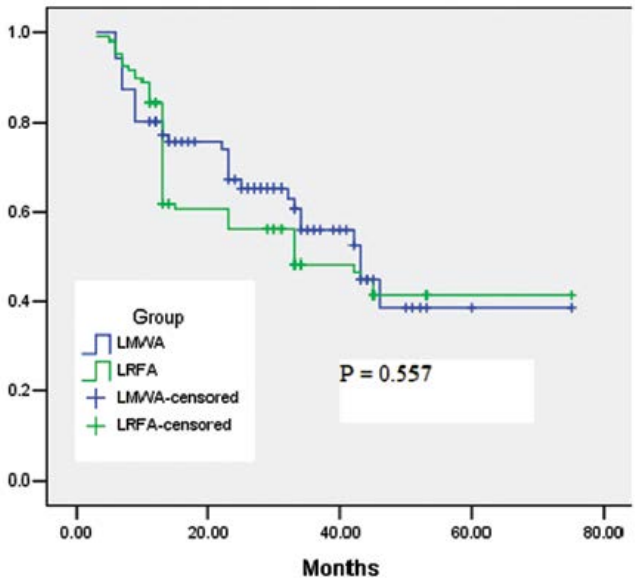

Figure 2. Disease-free survival of patients with colorectal liver metastasis undergoing laparoscopic microwave ablation and radiofrequency ablation (p=0.557).

The median follow-up period of all patients was 39 months. Technical success was achieved in 96% (68/71) of patients treated with LRFA and 95% (108/103) of patients treated with LMWA. LTP rates were 10.2% (11/108) and 1.4% (1/71) in the LRFA and LMWA groups, respectively. A significantly higher LTP rate was observed in the LRFA group compared with the LMWA group (p=0.046). Five-year OS rates were 56 and 58% and 5-year DFS rates were 41 and 39% in the LRFA and LMWA groups, respectively (Figures 1 and 2). The two groups demonstrated similar rates

Table 3. Univariate analysis of overall survival

Variables	*Five-year overall survival (%)*	*p value*
Age, years		0.195
<65	61	
≥65	53	
Gender		0.285
Male	62	
Female	54	
Disease-free interval, months		0.036
> 24	69	
≤ 24	41	
ASA score		0.208
I-II	59	
III	54	
Primary tumor		0.295
Colon cancer	63	
Rectal cancer	55	
Original cancer stage		0.028
I-II	65	
III	42	
CEA, ng/ml		0.190
≤10	59	
>10	51	
Maximum tumor size, cm		0.079
≤2	61	
>2	49	
Ablation method		0.498
LMWA	58	
LRFA	56	

Table 5. Univariate analysis of disease-free survival

Variables	*Five-year overall survival (%)*	*p value*
Age, years		0.207
<65	49	
≥65	32	
Gender		0.362
Male	43	
Female	37	
Disease-free interval, months		0.059
	51	
> 24	32	
≤ 24		
ASA score		0.403
I-II	43	
III	37	
Primary tumor		0.198
Colon cancer	46	
Rectal cancer	37	
Original cancer stage		0.039
I-II	47	
III	29	
CEA, ng/ml		0.042
≤10	53	
>10	36	
Dominant tumor size, cm		0.049
≤2	46	
>2	31	
Ablation method		0.557
LMWA	67	
LRFA	55	

of OS (p=0.498) and DFS (p=0.557).

Univariate and multivariate analyses identified DFS and original pathological stage as factors with independent effects on OS (Tables 3 and 4). LMWA or LRFA did not influence OS. Univariate and multivariate analyses revealed that pathological stage and CEA levels before ablation had independent effects on DFS. LMWA or LRFA did not influence DFS (Tables 5 and 6).

Discussion

Laparoscopic approaches for thermal ablation provide access to difficult-to-reach tumors, particularly if the tumors are located underneath the liver capsule or adjacent to the gallbladder or the diaphragm [15-20]. In this study, we compared the efficacy, incidence and severity of postoperative 30-day complications, and long-term survival outcomes between LMWA and LRFA procedures. Our results demonstrated that both laparoscopic approaches were associated with near-complete technical success and low postoperative 30-day complications, similar to previously reported results on percutaneous RFA for treating colorectal liver metastasis [9-11]. No significant differences were found between ablation groups in terms of recurrence, DFS, and OS rates. However, our study revealed a lower incidence of LTP in the LMWA group than in the LRFA group.

With regard to the safety of both LMWA and LRFA, the present study found no perioperative or postoperative 30-day mortality and a low incidence of postoperative 30-day complication. These values are comparable to the safety profiles found in previous studies on clinical ablation [15-20]. Recent studies comparing RFA and MWA also reported similar data for both techniques, with

Table 4. Cox proportional hazards model for overall survival

Variables	*Hazard ratio (95% CI)*	*p value*
Disease-free interval > 24 versus ≤ 24 months	1.879 (1.250-3.002)	0.023
Original cancer stage I-II versus III	2.069 (1.129-2.950)	0.038
Dominant tumor size ≤2 cm versus >2 cm	1.205 (0.698-1.589)	0.109

Table 6. Cox proportional hazards model for disease-free survival

Variables	*Hazard ratio (95% CI)*	*p value*
CEA ≤10 ng/ml versus >10 ng/ml	2.006 (1.358-2.990)	0.030
Original cancer stage I-II versus III	3.098 (1.980-3.500)	0.031
Disease-free interval > 24 versus ≤ 24 months	1.369 (0.590-1.680)	0.198
Dominant tumor size ≤2 cm versus >2 cm	1.250 (0.480-1.503)	0.206

low complications rates [9-13].

Current literature concerning complete ablation and LTP rates of LMWA versus LRFA is controversial [37-40]. In our study, a lower incidence of LTP was observed in the LMWA group than in the LRFA group. LMWA systems create larger margins and overcome the heat-sink effect, blocking the vessels implicated in LTP.

Long-term survival outcomes after LRFA for colorectal liver metastasis can be improved by minimizing the risk of LTP. We found that LTP was significantly higher in the LRFA group than in the LMWA group, but both processes had similar OS and DFS rates. Survival rates may have been related to our protocol of immediate treatment with repeat LRFA, LMWA, or chemotherapy after LTP detection. Notably, only 4 patients had no follow-up treatment.

Our study design has certain limitations. The retrospective, unblinded nature of our analysis may have introduced bias, especially as LRFA procedures were performed earlier in the study, whereas LMWA procedures were predominantly performed later in the study. At our institute, we prefer to use LMWA if the colorectal liver metastasis nodule diameter is 2–3 cm and LRFA for smaller nodules. This preference presents a potential bias that could influence OS. However, overall recurrences were not statistically different, and LTP rates in patients treated with LRFA were higher than those in patients treated with LMWA-treated patients, despite their smaller nodules. As previously described, repeated treatments received by patients at recurrence could represent a potential confounder for interpreting survival data.

In summary, our study showed that laparoscopic ablations with LRFA or LMWA are safe and effective alternatives for patients with colorectal liver metastases located in difficult-to-reach locations. There was no mortality in either group, and no difference in the postoperative complication rates. The LTP rates in patients treated with LMWA were lower than those in patients treated with LRFA; however, this finding had little impact on OS and DFS, which was similar between the two groups. A multicenter, prospective, randomized controlled trial in the future is warranted to confirm these results.

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Conflict of interests

The authors declare no confict of interests.

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