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BRIEF ARTICLE

Comparative analysis of radiofrequency ablation and resection for resectable colorectal liver metastases

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Abstract

AIM: To evaluate the therapeutic efficacy of radiofrequency ablation (RFA) for resectable colorectal liver metastases (CRLM) compared with that of resection.

METHODS: Between June 2004 and June 2009, we retrospectively analyzed 29 patients with resectable CRLMs; 17 patients underwent RFA, and 12 underwent hepatic resection. All of the patients were informed about the treatment modalities and were allowed to choose either of them. RFA including an intraoperative approach was performed by a radiologist; otherwise, hepatic resection was performed by a surgeon. Comparative analysis of the two groups was performed, including comparisons of gender, age, and clinical outcomes, such as primary tumor stage and survival rates.

RESULTS: The mean tumor size was significantly larger in the resection group (3.59 cm *vs* 2.02 cm, $P < 0.01$), and the 5-year overall survival (OS) rate for all patients was 44.7%. There was no difference in the 5-year OS rates between the RFA and resection groups (37.8% *vs* 66.7%). Univariate analysis indicated significantly lower 5-year OS rates for patients with a tumor size > 3 cm. The 5-year disease-free survival (DFS) rates were 17.6% and 22.2% in the RFA and resection groups, respectively ($P = 0.119$). Univariate analysis revealed that in cases of male gender, age > 65 years, T stage < Ⅳ, absence of lymphatic metastasis, and tumor size > 3 cm, RFA resulted in significantly inferior 5-year DFS rates compared with surgical resection.

CONCLUSION: Surgical resection revealed superior outcomes in the treatment of resectable CRLMs, particularly in cases with a hepatic tumor size > 3 cm.

Key words: Colorectal neoplasm; Metastasis; Radiofrequency; Hepatectomy; Survival

Core tip: Colorectal liver metastasis is diagnosed in approximately 50% of patients with colorectal cancer. Surgical resection is the optimal treatment strategy. Alternative local treatment modalities can be adapted, and radiofrequency ablation (RFA) is widely accepted. We examined whether RFA is an appropriate alternative method to surgery for resectable colorectal liver metastases. This study retrospectively compared the therapeutic efficacy of RFA and compared it with that of surgical resection in a single institute.

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INTRODUCTION

A 2005 annual report of cancer incidence indicated that colorectal cancer (CRC) is the third most common malignancy worldwide and the second most common (12.5%) in Korea, following gastric cancer. The 5-year survival rate of CRC is reportedly 61%[1,2], and hepatic metastasis develops in approximately 40%-50% of patients with CRC; approximately 50% of diagnosed patients present the synchronous type[3-5]. Although surgical resection is the most effective current treatment for resectable colorectal cancer liver metastases (CRLMs)[6,7], only 10%-15% of such cases are suitable for the procedure[8,9]. Several alternative treatment modalities for unresectable CRLMs have been developed, of which radiofrequency ablation (RFA) is widely accepted as an effective alternative local treatment modality[10].

Surgical hepatic resection is the treatment of choice for resectable CRLMs. Although RFA is an alternative to resection in hepatocellular carcinoma[11,12], there is little information regarding indications for RFA in resectable CRLMs. RFA is performed within a limited number of clinical settings for resectable CRLMs[13,14]. The purpose of the present study was to compare the therapeutic efficacies of RFA and hepatic resection for resectable CRLMs within a single institution.

MATERIALS AND METHODS

In this study, we compared the treatment outcomes of 12 patients who underwent hepatic resection with 17 who underwent RFA for synchronous or metachronous resectable CRLMs between June 2004 and June 2009 at the Department of Surgery, Pusan National University Hospital (Busan, South Korea). The inclusion criteria for this study were as follows: (1) no signs of preoperative extrahepatic metastases; (2) tumor size < 5 cm; and (3) a single metastatic tumor. The exclusion criteria were as follows: (1) simultaneous performance of resection and RFA; (2) resection of hepatic recurrence after RFA; (3) lymph node metastases identified during or after resection; and (4) associated multiple hepatic metastases. The selection of patients for each treatment modality was fully based on the patient's decision.

Diagnosis of CRLM

The diagnosis of hepatic or extrahepatic metastasis was confirmed on the basis of the findings of serum carcinoembryonic antigen (CEA), contrast-enhanced computed tomography (CT) of the abdomen and chest, magnetic resonance imaging (MRI), and ^{18}F-2'-fluoro-2'-deoxyglucose positron emission tomography (FDG-PET). Hepatic metastasis was defined as any newly developed hepatic tumors detected during patient follow-up after curative resection of CRC. A needle biopsy was not routinely performed before RFA but was performed in patients with atypical hepatic mass enhancement.

RFA

RFA for hepatic metastases was performed when patients refused surgical hepatic resection after being informed of the treatment method, complications, and survival rates. RFA was performed percutaneously under local anesthesia or during and simultaneously with CRC resection. RFA was performed using a 200-W generator in the impedance control mode and a monopolar single or clustered internally cooled electrode (Covidien, Boulder, CO, United States). Written informed consent was obtained from all patients before initiating treatment.

Table 1 Types of surgery for colorectal liver metastasis

Type of surgery		*n* (%)
Major resection	Right hemihepatectomy	5 (41.7)
Minor resection	Segmentectomy	6 (50.0)
	Left lateral sectionectomy	1 (8.3)
Total		12

Surgical resection

A major resection was defined as resection of more than three hepatic segments and minor resection as two segments or less. Major and minor resections were performed in five and seven patients, respectively (Table 1). None of the patients received perioperative transfusion, and there was no incidence of postoperative mortality.

Follow-up protocol

Seven days after resection or RFA, contrast-enhanced CT of the abdomen was performed, and serum CEA levels were measured to determine the baseline values. The same evaluations were repeated every four months during the initial two years and every six months thereafter. Endoscopic analysis and FDG-PET were performed annually, and chest CT or MRI was added when tumor recurrence was suspected.

Statistical analysis

Overall survival (OS) and disease-free survival (DFS) rates were analyzed using the Kaplan-Meier method, and the statistical significance of differences in the survival rates was evaluated using the log-rank test. A two-tailed *P*-value < 0.05 was considered statistically significant. The statistical analysis was performed using SPSS statistical software (ver. 12.0; SPSS Inc., Chicago, IL, United States).

RESULTS

Clinicopathological data

Information regarding the patients and pathological results is provided in Tables 2 and 3. The mean tumor diameter in the RFA group (2.02 cm; range, 0.8-4.6 cm) was significantly smaller than that in the resection group (3.59 cm; range, 1.6-4.9 cm). There were no other significant differences between the two groups. Four of the 17 patients in the RFA group and 7 of the 12 in the resection group presented a hepatic tumor > 3 cm in size; no significant difference was evident between the two

Table 2 Summary of patient information

No.	Age (yr)	Sex	Comorbidity	Treatment modality	Location	Timing of metastasis	Recurrence	Results
1	51	M		RFA	Colon	Meta	Yes	S
2	60	M		RFA	Colon	Meta	Yes	D
3	69	M		Resection	Colon	Meta	Yes	D
4	76	M	DM, HT	Resection	Rectum	Meta	Yes	D
5	62	M		RFA	Colon	Syn	No	S
6	61	M	DM	RFA	Rectum	Meta	Yes	D
7	70	F		Resection	Colon	Meta	Yes	S
8	70	M		Resection	Rectum	Meta	No	S
9	71	F		Resection	Rectum	Meta	Yes	S
10	69	F	DM, HT	Resection	Colon	Syn	Yes	S
11	74	F		Resection	Colon	Syn	No	S
12	71	M		Resection	Colon	Meta	Yes	S
13	82	M		Resection	Rectum	Meta	Yes	D
14	58	F		RFA	Colon	Meta	No	S
15	60	M		RFA	Colon	Syn	Yes	D
16	56	F		RFA	Colon	Meta	Yes	S
17	56	M		RFA	Colon	Meta	Yes	S
18	54	F		RFA	Colon	Meta	Yes	D
19	52	F		RFA	Rectum	Meta	No	S
20	60	M		RFA	Colon	Meta	Yes	D
21	55	M		RFA	Rectum	Meta	Yes	D
22	75	M		Resection	Colon	Syn	Yes	D
23	54	F		RFA	Rectum	Meta	Yes	D
24	63	F		RFA	Colon	Syn	Yes	D
25	66	M		Resection	Rectum	Syn	Yes	S
26	56	F		RFA	Rectum	Meta	Yes	D
27	67	M		Resection	Colon	Meta	Yes	D
28	58	M		RFA	Rectum	Syn	No	S
29	71	M		Resection	Colon	Meta	Yes	S

DM: Diabetes mellitus; HT: Hypertension; RFA: Radiofrequency ablation; Meta: Metachronous; Syn: Synchronous; S: Survival; D: Death; M: Male; F: Female.

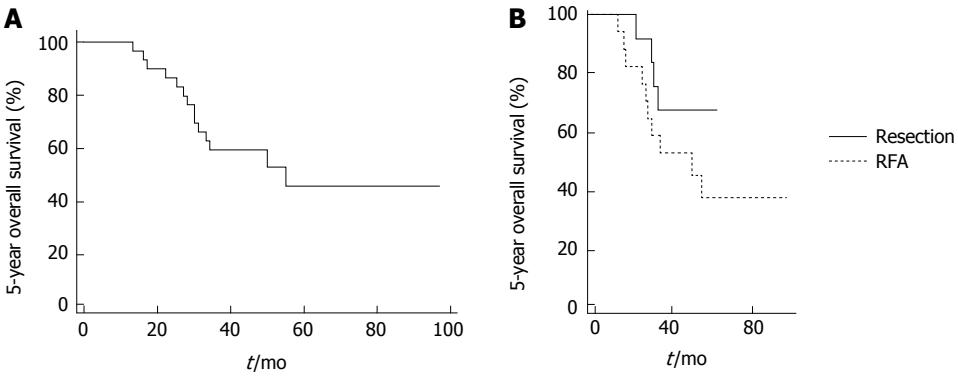

Figure 1 The 5-year overall survival rate. A: For all patients (44.7%); B: In the surgical resection (66.7%) and radiofrequency ablation (RFA) groups (37.8%).

groups (Table 4).

Survival rates

The 5-year OS rate was 44.7% among all patients with CRLMs, 37.8% in the RFA group, and 66.7% in the resection group (P = 0.29; Figure 1). The 5-year OS rate was lower in patients with a hepatic tumor size > 3 cm than in those with a tumor size < 3 cm (Table 5). Moreover, the 5-year DFS rates were 17.6% and 22.2% in the RFA and resection groups, respectively (P = 0.119; Figure 2). The variables associated with lower DFS rates included male gender, age > 65 years, CRC T stage < Ⅳ, absence of lymphatic invasion, and tumor size > 3 cm (Table 6).

DISCUSSION

Surgical resection is the treatment of choice for resectable CRLMs, whereas RFA has been used for unresectable CRLMs as an alternative treatment to improve patient survival[13,14]. While some series have reported RFA equivalent to resection, others have shown RFA to be inferior to resection based on overall survival[15-17]. However, the efficacy of RFA for resectable CRLMs remains controversial. Reuter *et al*[18] reported superior DFS rates in patients with resectable CRLMs following surgical resection than follow-

Table 3 Summary of pathological findings

No.	Metastatic tumor size (cm)	Diff	T	N	M	LNR	LV	PN
1	2.5	Mod	3	2	0	0.23	Pos	Pos
2	1.6	Mod	3	2	0	0.17	Pos	Pos
3	4	Mod	4	2	0	0.37	Pos	Pos
4	4.2	Mod	4	1	0	0.43	Pos	Pos
5	3.2	Mod	3	1	1	0.07	Pos	Neg
6	4.2	Mod	2	2	0	0.25	Pos	Pos
7	4	Mod	3	0	1	0	Pos	Pos
8	2.8	Mod	4	0	0	0	Pos	Pos
9	4.4	Mod	1	2	0	0.06	Neg	Neg
10	4.9	Well	3	1	1	0.03	Pos	Neg
11	2.8	Mod	3	0	0	0	Neg	Pos
12	2.3	Mod	4	1	0	0.08	Neg	Neg
13	3.2	Mod	4	2	1	0.33	Neg	Pos
14	1.2	Mod	3	2	0	0.14	Pos	Pos
15	0.9	Poor	3	2	0	0.12	Pos	Pos
16	1.7	Poor	3	1	0	0.04	Pos	Pos
17	2	Mod	3	1	0	0.03	Neg	Neg
18	1	Mod	3	2	0	0.34	Pos	Pos
19	2.5	Mod	4	0	0	0	Neg	Neg
20	2	Mod	3	1	0	0.14	Pos	Pos
21	1.6	Mod	3	1	0	0.08	Pos	Pos
22	1	Mod	3	1	0	0.04	Pos	Pos
23	3.8	Mod	2	0	0	0	Neg	Neg
24	3.7	Mod	3	0	1	0	Neg	Neg
25	1	Mod	3	0	0	0	Neg	Neg
26	3.6	Mod	4	2	1	0.58	Neg	Pos
27	1.2	Mod	3	0	0	0	Pos	Pos
28	0.8	Mod	4	1	1	0.03	Neg	Neg
29	1.3	Mod	3	0	0	0	Neg	Neg

Diff: Differentiation of primary tumor; T: T stage; N: N stage; M: M stage; LNR: Lymph node ratio; LN: Lymphovascular invasion; PN: Perineural invasion; Mod: Moderate; Poor: Poorly; Pos: Positive; Neg: Negative.

Table 4 Clinicopathological data of colorectal liver metastasis *n* (%)

		RFA (*n* = 17)	Resection (*n* = 12)	*P*-value
Sex	Male	7 (41)	4 (33)	0.49
	Female	10 (59)	8 (67)	
Age (yr)		61.35 ± 8.33	67.50 ± 7.44	0.07
Age (yr)	≤ 65	12 (71)	4 (33)	0.07
	> 65	5 (29)	8 (67)	
Timing of metastasis	Synchronous	5 (29)	3 (25)	1.00
	Metachronous	12 (71)	9 (75)	
Primary site	Colon	10 (59)	8 (67)	0.72
	Rectum	7 (41)	4 (33)	
T stage	I - III	13 (76)	8 (67)	0.68
	IV	4 (24)	4 (33)	
Lymphovascular	Positive	8 (47)	8 (67)	0.45
Invasion	Negative	9 (53)	4 (33)	
Perineural invasion	Positive	10 (59)	7 (58)	1.00
	Negative	7 (41)	5 (42)	
Lymph node metastasis	Positive	11 (65)	9 (75)	0.69
	Negative	6 (35)	3 (25)	
Size of metastasis (cm)		2.02 ± 1.17	3.59 ± 0.81	0.03
Size of metastasis	≤ 3 cm	13 (76)	5 (42)	0.07
	> 3 cm	4 (24)	7 (58)	
Recurrence	Yes	14 (82)	9 (75)	0.67
	No	3 (18)	3 (25)	

RFA: Radiofrequency ablation.

ing RFA. By contrast, Mulier *et al*[19] reported no significant difference in OS between RFA and surgical resection for local control of CRLMs. Furthermore, in a recent study, Kanas *et al*[20] reported a 5-year OS rate of 30%-40% in

Table 5 Univariate analysis of 5-year overall survival

		RFA (n = 17)		Resection (n = 12)		*P*-value
		3-yr	5-yr	3-yr	5-yr	
Sex	Female	42.9%	42.9%	100%	100%	0.083%
	Male	60.0%	30.0%	50.0%	50.0%	0.925%
Age (yr)	≤ 65	58.3%	38.9%	50.0%	50.0%	0.848%
	> 65	40.0%	40.0%	75.0%	75.0%	0.187%
Primary	1-3	50.0%	33.3%	75.0%	75.0%	0.194%
T stage	4	66.7%	66.7%	50.0%	50.0%	0.847%
Timing of	Synchronous	33.3%	33.3%	100%	100%	0.093%
Metastasis	Metachronous	63.6%	42.4%	55.6%	55.6%	0.975%
Preoperative chemotherapy	No	50.0%	50.0	66.7	66.7	0.410
	Yes	54.5%	36.4%	66.7%	66.7%	0.495%
Primary site	Colon	50.0%	37.5%	75.0%	75.0%	0.202%
	Rectum	57.1%	38.1%	50.0%	50.0%	0.992%
Metastatic	Negative Positive	50.0%	50.0%	100%	100%	0.175%
Lymph node		54.5%	32.7%	55.6%	55.6%	0.502%
Lymphovascular invasion	Negative	55.6%	55.6%	100%	100%	0.140%
	Positive	50.0%	25.0%	50.0%	50.0%	0.638%
Perineural invasion	Negative Positive	71.4%	71.4%	100%	100%	0.214%
		40.0%	20.0%	42.9%	42.9%	0.515%
Primary	≤ 3 cm	69.2%	49.50%	80.0%	80.0%	0.464%
Tumor size	> 3 cm	0.0%	0.0%	57.1%	57.1%	0.005%
Postoperative chemotherapy	No	20.0%	20.0%	0.0%	0.0%	0.929%
	Yes	66.7%	47.6%	80.0%	80.0%	0.341%

RFA: Radiofrequency ablation.

Table 6 Univariate analysis of 5-year disease-free survival

		RFA (n = 17)		Resection (n = 12)		*P*-value
		3-yr	5-yr	3-yr	5-yr	
Sex	Female	28.6%	28.6%	50.0%	50.0%	0.350
	Male	10.0%	10.0%	50.0%	33.3%	0.039
Age (yr)	≤ 65	25.0%	25.0%	50.0%	25.0%	0.449
	> 65	0.0%	0.0%	46.9%	46.9%	0.012
Primary	I -Ⅲ	7.1%	7.1%	50.0%	25.0%	0.023
T Stage	Ⅳ	66.7%	66.7%	50.0%	50.0%	0.702
Timing of	Synchronous	16.7%	16.7%	66.7%	66.7%	0.201
Metastasis	Metachronous	18.2%	18.2%	41.7%	20.8%	0.172
Preoperative chemotherapy	No	16.7%	16.7%	53.3%	53.3%	0.112
	Yes	18.2%	18.2%	33.3%	0.0%	0.617
Primary site	Colon	10.0%	10.0%	50.0%	25.0%	0.048
	Rectum	28.6%	28.6%	37.5%	37.5%	0.385
Metastatic	Negative	16.7%	16.7%	100.0%	100.0%	0.037
Lymph node	Positive	18.2%	18.2%	29.6%	14.8%	0.325
Lymphovascular invasion	Negative	22.2%	22.2%	50.0%	50.0%	0.137
	Positive	12.5%	12.5%	50.0%	33.3%	0.197
Perineural invasion	Negative	28.6%	28.6%	40.0%	40.0%	0.423
	Positive	10.0%	10.0%	57.1%	28.6%	0.074
Primary	≤ 3 cm	23.1%	23.1%	60.0%	30.0%	0.204
Tumor size	> 3 cm	0.0%	0.0%	38.1%	38.1%	0.013
Postoperative chemotherapy	No	0.0%	0.0%	50.0%	50.0%	0.151
	Yes	25.0%	25.0%	50.0%	33.3%	0.235

RFA: Radiofrequency ablation.

patients with resectable CRLMs. Moreover, they observed that the survival rate in the resection group was favorable and reported that statistical significance could be expected using a larger patient population, even in the actual 5-year OS rate in the RFA group and in the nonactual survival in the resection group. Our 5-year OS rates were 66.7% in the resection group and 37.8% in the RFA group (actuarial 5-year survival rates), which is comparable to those reported in other published studies. In patients with hepatic tumors < 3 cm, the 5-year OS rate was 80.0% in the RFA group and 49.5% in the resection group (P = 0.46). In patients with a hepatic tumor size > 3 cm, the 5-year OS rates were 0% in the RFA group and 57.1% in the resection group (P = 0.005). In addition, the DFS rate in the resection group was superior to that in the RFA group.

To date, there exist some controversies regarding the

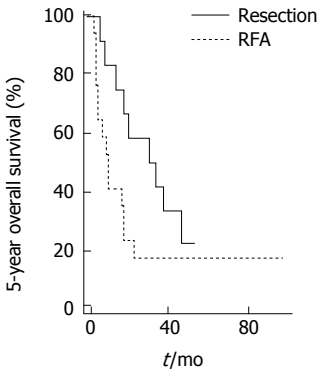

Figure 2 Disease-free survival rates in the surgical resection (22.2%) and radiofrequency ablation groups (17.6%). RFA: Radiofrequency ablation.

contribution of clinicopathological factors to survival following surgery for resectable CRLMs[21]. Surgical resection in CRLM is considered the treatment of choice for local tumor control rather than systemic therapy. RFA, which has the advantages of minimal invasiveness and sparing the liver parenchyma, might be favorable for the local control of CRLMs, which requires adjuvant chemotherapy as well[19]. However, less definitive evidence exists regarding the risk of intrahepatic or hematogenous metastases after RFA for patients with CRLMs. Fourteen patients who underwent RFA in our study experienced recurrences of multiple liver metastases and peritoneal carcinomatosis, and two patients developed metastases in the lung and spleen. The local recurrence rates after RFA are reportedly 2%-40%[22-25], and Abitabile *et al*[26] reported that local recurrence rates reached 8.8% overall and 1.6% for CRLMs < 3 cm in diameter. In the present study, one patient developed tumor recurrence following RFA and was excluded; the patient was followed up for 37 mo without recurrence after consecutive hepatic resection.

The statistical analysis in the present study identified the following risk factors for poor DFS in the RFA group compared with the resection group: male gender, age > 65 years, lower T stage, colon cancer, and absence of lymph node metastasis. These findings might be the result of the omission of intensive adjuvant chemotherapy in patients with less-advanced CRC stages.

Some limitations to the present study include its retrospective design and the small number of included cases. However, to our knowledge, this is the first report regarding the actuarial 5-year survival rate after RFA, which was 37.8% in patients with resectable CRLMs. Surgical resection is believed to be superior to RFA for resectable CRLMs; nevertheless, RFA displayed some interesting advantages to justify its adoption in patients with resectable CRLMs. Although a randomized controlled study of RFA is warranted, more strict indication criteria are needed before adopting RFA as a replacement for surgical resection in resectable CRLMs.

COMMENTS

Background

Hepatic metastasis develops in approximately 40%-50% of patients with colorectal cancer, and approximately 50% of diagnosed patients present the synchronous type. Surgical resection is the most effective current treatment for colorectal cancer liver metastasis (CRLM), and several alternative treatment modalities for CRLM have been developed.

Research frontiers

Radiofrequency ablation (RFA) is widely accepted as an effective alternative local treatment modality for CRLM. However, there is little information regarding indications for RFA in resectable CRLMs.

Innovations and breakthroughs

The authors retrospectively reviewed 29 patients with resectable CRLMs, who were treated with either RFA or surgical resection. This comparison was performed to determine whether RFA can be an effective alternative treatment for resectable CRLMs.

Applications

The authors suggest that RFA can be an alternative treatment for resectable CRLMs, primarily in patients with hepatic tumors < 3 cm in size.

Terminology

RFA is a procedure in which tissue ablation is performed using the heat generated by a high-frequency alternating current.

Peer review

This article examined the usefulness of RFA in patients with resectable CRLMs. In this study, the authors found that RFA can be useful in patients with CRLMs < 3 cm in diameter.

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