Oncology Research, Vol. 23, pp. 219–228
Printed in the USA.

0965-0407/16 $90.00 + .00
DOI: http://dx.doi.org/10.3727/096504016X14567549091260
E-ISSN 1555-3906
www.cognizantcommunication.com

Thermal Radiofrequency Ablation as an Adjuvant Therapy for Patients With Colorectal Liver Metastasis

Yaohua Fan,*†[1] Xiyan Zhu,*[1] Qiuping Lan,* Fang Lou,* Yu Zheng,* Haizhou Lou,* Yong Fang,* Wei Jin,* Hongming Pan,* and Kaifeng Wang*‡

*Department of Oncology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China
†Department of Oncology, Jiaxing the First Hospital, Jiaxing, China
‡Cancer Center, the Affiliated Hospital of Hangzhou Normal University, Hangzhou, China

Radiofrequency ablation (RFA) is a minimally invasive technology for the treatment of liver malignancies and is used as an adjuvant therapy in patients with colorectal liver metastasis (CLM). This study enrolled a total of 49 CLM patients who underwent RFA treatment. Univariate and multivariate analyses were performed using the log-rank test and Cox proportional hazard model, respectively. Univariate analysis showed that OS was closely correlated with tumor size, frequency of RFA treatment, resection of the liver lesion, and CEA levels before RFA ($p < 0.05$). Multivariate analysis revealed that resection of CLM lesions after RFA, frequency of RFA treatment, and serum CEA levels before RFA were independent risk factors for the survival of CLM patients ($p < 0.05$). Tumor lesion size, resection of the liver lesion after RFA, frequency of RFA treatment, and serum CEA levels before RFA may be important prognostic factors of CLM patients treated with RFA therapy.

Key words: Liver metastasis; Radiofrequency ablation (RFA); Influence factor

INTRODUCTION

Liver metastasis is one of the most common forms of metastatic colorectal cancer (CRC). Approximately 25% of patients with CRC present with liver metastasis at the time of initial diagnosis, and another 25% of patients will present with liver metastases after surgical resection of the primary tumor (1,2). Without appropriate treatment, the median survival of patients with colorectal liver metastasis (CLM) is only 8 months, and the 5-year survival rate is nearly zero. Of note, only 10~20% of CLM patients are suitable candidates for surgery (3,4). As a result, many nonsurgical ablative methods have been developed for the treatment of CLM patients, and the most widely utilized method is radiofrequency ablation (RFA).

The guidelines for resection of CRC liver metastases in the UK and the National Comprehensive Cancer Network (NCCN) 2012 (version 3, 2012) guidelines (5,6) recommend using RFA alone or in conjunction with surgical resection for the treatment of patients with CRC metastases to the liver. This recommendation was based on category 2A evidence, which is defined as lower level evidence, with uniform NCCN consensus.

It has been reported that RFA can improve treatment outcomes and prolong the survival of CLM patients (7,8). However, only a small number of large-scale clinical trials have been conducted to date that provide evidence of its effectiveness. Therefore, further studies are necessary to evaluate the true effectiveness of RFA and to identify the prognostic factors influencing the outcome of CLM patients undergoing RFA. This study aimed to investigate the various prognostic factors of survival of CLM patients who received palliative RFA treatment.

MATERIALS AND METHODS

Ethics Statement

This study was approved by the Ethics Committee of Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University (IRB: 20121120-4). All patients (or their legal representative) provided written informed consent prior to enrollment.

Patient Enrollment

A total of 49 patients with CLM received palliative RFA at Sir Run Run Shaw Hospital, Zhejiang University School

[1]These authors provided equal contribution to this work.
Address correspondence to Kaifeng Wang, Cancer Center, the Affiliated Hospital of Hangzhou Normal University, Hangzhou 310000, China. Tel: +86-0571-86006926; Fax: +86-0571-86436673; E-mail: wangkf2000@163.com

of Medicine from December 1, 2003, to December 30, 2010, according to the inclusion criteria of the study. All patients had evidence of liver metastases, as documented by computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), ultrasonography, or biopsy, before being treated with palliative RFA. The tumor-node-metastasis (TNM) stage was IV. The chemotherapy regimens used to treat patients included FOLFOX, FOLFIRI, or XELOX according to NCCN guidelines.

Inclusion Criteria

Patients satisfying the following inclusion criteria were enrolled in the study:

1. Ability to understand and willingness to sign a written informed consent for RFA treatment
2. Had received at least two prior different chemotherapy regimens
3. With less than three locations of the tumor treated with or without a single radiofrequency ablation and with the diameter of each tumor being less than 5 cm
4. Liver function classified as Child-Pugh Class A or B
5. Life expectancy of at least 12 weeks
6. Karnofsky Performance Status (KPS) score of over 60
7. Adequate bone marrow, liver, and renal function assessed within 7 days prior to RFA treatment.

Exclusion Criteria

Patients with the following conditions were excluded from the study:

1. Patients could benefit from chemotherapy or surgery
2. Uncontrolled extrahepatic disease and uncontrolled primary cancer
3. Patients with more than three locations or the diameter of tumor larger than 5 cm
4. Liver function classified as Child-Pugh Class C
5. Prolongation of serum PT and APTT
6. Presence of ascites
7. Presence of serious comorbid complications, such as intestinal obstruction, massive hemorrhage of the gastrointestinal tract, cardiopulmonary insufficiency, or fever over 38°C unrelated to cancer.

Clinical Evaluation

Physical examination was conducted for each patient before the RFA treatment. Routine preoperation tests [including routine blood tests, biochemical tests, PT/APTT, X-ray of chest, electrocardiography (ECG)], and evaluation of heart and respiratory function were completed to ensure safety of the surgery. The accurate number, location, and size of the liver lesions were evaluated by ultrasonography or CT scanning before RFA and were subsequently evaluated every 4–6 weeks. Serum CEA levels were measured within 1 week prior to RFA treatment and were evaluated every 4–6 weeks. Prior hepatectomy or systemic chemotherapy was carefully recorded. All the aforementioned tests were performed at the Department of Examination, Radiology, and ECG of Sir Run Run Shaw Hospital, Zhejiang University School of Medicine.

RFA Equipment

The Cool-Tip™ RFA system (Radionics, Burlington, MA, USA) was used in this study. This system consisted of an RF generator, with a maximum power output of 200 W. It can impulsively radiate while monitoring its power output, impedance, and the temperature of electrode and system. The length of the radiation probe was 15 cm long, with a 3-cm portion being exposed to air contact.

Treatment

RFA treatment was performed by physicians from the Department of Oncology at Sir Run Run Shaw hospital,

Table 1. Demographic and Clinical Characteristics of Patients (N=49)

Characteristics	No. (%)
Gender	
Male	27 (55.1)
Female	22 (44.9)
Age (years)	
<60	18 (36.7)
≥60	31 (63.3)
Primary location of cancer	
Rectum	20 (40.8)
Colon	29 (59.2)
Pathological types (adenocarcinoma)	
Highly differentiated	12 (24.5)
Moderately differentiated	22 (44.9)
Highly/moderately differentiated	5 (10.2)
Moderately/poorly differentiated	2 (4.1)
Not clear	8 (16.3)
Number of CLM	
Single	18 (36.7)
Multiple (≥2)	31 (63.3)
Resection of CLM	
Resection after RFA treatment	9 (18.4)
No resection after RFA treatment	38 (77.6)
Unknown	2 (4.0)
Maximum diameter of CLM (cm)	
≤3	25 (51.1)
>3	18 (36.7)
Unknown	6 (12.2)
Frequency of RFA treatment	
<Twice	27 (55.1)
≥Twice	22 (44.9)
Survival status	
Survived	23 (46.9)
Dead	26 (53.1)

Zhejiang University School of Medicine. After precise identification of the tumor location in the liver by ultrasonography or by CT scanning, the patients received local anesthesia. The RFA probe was placed at the bottom of the tumor along its longest diameter guided by B ultrasound. The ablation treatment lasted for 12–16 min. Vital signs of the patients were closely monitored during the treatment. Regular care that including stanching bleeding, pain relief, and liver care was provided for 3 days after RFA treatment.

Patients underwent surgical resection of the liver metastatic lesions after RFA treatment at the time of disease recurrence and when they were deemed to be surgically operable.

Survival Data

The survival data of each patient were obtained through telephone calls or during outpatient follow-ups. Survival time was defined as the survival time after RFA. This was determined from the time when the first RFA treatment was administered until the death of the patient or the end of follow-up time (February 28, 2011). The main outcomes were 1- and 3-year survival rate, median overall survival (OS) time, and median progression-free survival (PFS) time.

Statistical Analysis

The SPSS statistical software, version 16.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. The OS and PFS were presented as median values with a 95% confidence interval (95% CI). Survival rates were determined using the Kaplan–Meier method and the log-rank test. Multivariate analysis was performed using the Cox regression model. The significance level was set at 5% for each analysis.

RESULTS

Demographic and Clinical Characteristics of Patients

A total of 49 cases were included in this study. The demographic and clinical characteristics of patients are presented in Table 1. Among the 49 CLM patients who received RFA treatment, the median OS was 24.8 months, and the median PFS was 15.3 months. The 1-, 2-, 3-, 4-, and 5-year survival rates were 66.7%, 33.3%, 10.4%, 4.2%, and 4.2%, respectively.

Correlation Between the Diameter of CLM Lesions and Survival

After RFA treatment, the median OS of patients with maximum tumor diameter of less than 3 cm was higher (29.0 months; 95% CI: 14.0–44.0 months), when

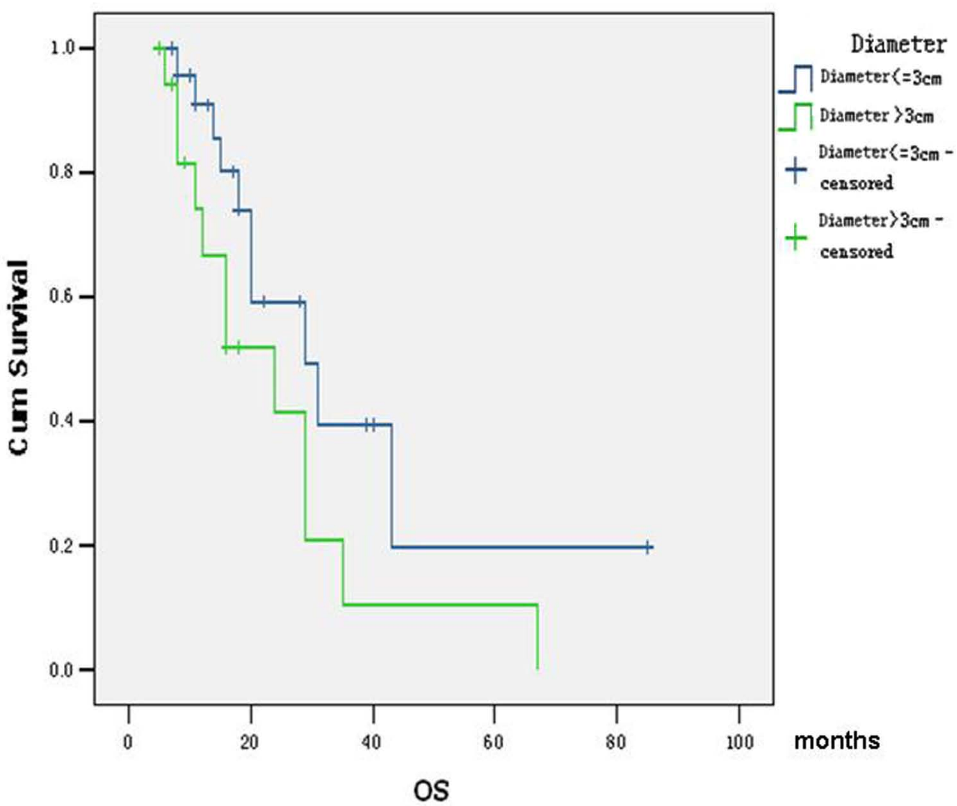

Figure 1. Kaplan–Meier curves depict OS of RFA-treated CLM patients with liver lesions of different maximum diameters.

compared to that in patients with a maximum tumor diameter of greater than 3 cm (24.0 months; 95% CI: 10.8–37.2 months; $p = 0.074$) (Fig. 1). The median PFS was 22.0 months (95% CI: 4.0–40.0 months) for patients with a maximum tumor diameter less than 3 cm and 15.0 months (95% CI: 2.9–27.1) for patients with a maximum tumor diameter greater than 3 cm ($p = 0.407$) (Fig. 2).

Correlation Between Frequency of RFA Treatment and Prognosis

Of the 49 patients, 22 patients had received subsequent RFA treatments. The median OS of these patients was significantly higher (31.0 months; 95% CI: 20.8–42.2 months) than that of patients who had received single RFA treatment (20.0 months; 95% CI: 11.4–28.6 months; $p = 0.017$) (Fig. 3). The median PFS for the two groups was 22.0 months (95% CI: 10.6–3.4 months) and 7.0 months (95% CI: 4.8–9.2 months), respectively ($p = 0.054$) (Fig. 4).

Correlation Between Resection of CLM Lesions and Prognosis

The median OS of patients who underwent resection of metastatic liver lesions after RFA treatment was 55.3 months (95% CI: 35.1–75.4 months). In contrast, the median OS was significantly shorter at 20.5 months (95% CI: 17.0–24.0 months) in those patients who did undergo surgical resection after RFA treatment ($p = 0.003$). Figure 5 shows the Kaplan–Meier OS curves of the two groups. The median PFS of patients who had resection of liver metastasis after RFA was 26.0 months (95% CI: 15.3–36.7 months) and was 12.6 months (95% CI: 8.4–16.8 months) for those who did have follow-up surgery. This difference between the two groups was not statistically significant ($p = 0.113$). Figure 6 shows the Kaplan–Meier PFS curves of the two groups.

Correlation Between Serum CEA Levels and Prognosis

Figure 7 shows that the median OS in patients with CEA levels <5 ng/ml was higher (35.0 months; 95% CI: 3.3–66.7 months) than those with CEA levels ≥5 ng/ml (20.0 months; 95% CI: 11.7–28.3 months; $p = 0.012$). The median PFS of these two groups was 25.0 months (95% CI: 18.8–31.2 months) and 8.0 months (95% CI: 5.5–10.5 months; $p = 0.042$) (Fig. 8), respectively.

Multivariate Analysis of Independent Prognostic Factors

Using the Cox regression model, we also analyzed potential factors that may influence the prognosis of

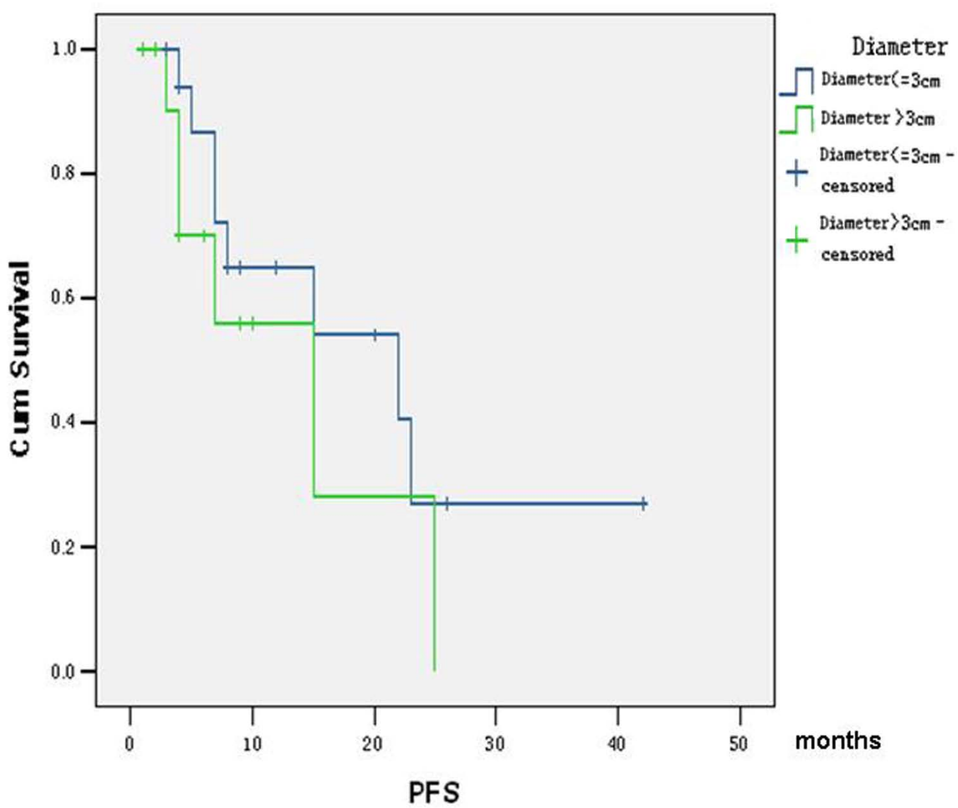

Figure 2. Kaplan–Meier PFS curves of RFA-treated CLM patients with liver lesions of different maximum diameters.

CLM patients undergoing RFA treatment (Table 2). We found that resection of CLM lesion after RFA, frequency of RFA treatments, and serum CEA levels before RFA were independent prognostic factors for CLM patients.

DISCUSSION

RFA is currently the most commonly used ablative technique, and a number of studies have shown that this procedure is relatively safe (9–13). As a result of its technical simplicity and safety, RFA is gaining popularity in many tumor centers as the preferred method for local ablation of unresectable tumors. However, there are no published large-scale randomized controlled trials to clarify the efficacy of RFA in CLM treatment.

There are numerous published case series and retrospective studies on the use of RFA in the treatment of CRC metastases in the liver (2,14–20). Lee et al. (21) found that the cumulative 3- and 5-year local recurrence-free survival rates were markedly higher in the hepatic resection group (88.0% and 84.6%) than those in the RFA group (53.3% and 42.6%, respectively) ($p \leq 0.001$). Despite a higher local recurrence rate, RFA may be considered as a potential therapeutic option for patients who are considered unsuitable for conventional surgical treatment. Berber et al. (22) concluded that the median actuarial survival from the date of surgery in the RFA group was lower than that in the resection group. They indicated that higher risk patients were channeled to RFA, leaving a highly selected group of patients for resection with a very favorable survival. RFA still achieved long-term survival in patients who were otherwise not deemed to be appropriate surgical candidates for resection. Kim et al. (23) found that in patients with solitary CLM <3 cm, OS and disease-free survival (DFS) rates did not differ between the RFA group and the surgery group ($p = 0.962$ and $p = 0.980$). In patients with solitary CLM ≥3 cm, DFS was significantly lower in the RFA group as compared with that of the resection group ($p = 0.015$). They indicated that RFA might be a safe alternative treatment for patients with solitary CLM less than 3 cm, with outcomes equivalent to hepatic resection. In the present study, the median survival time of patients receiving RFA was 24.8 months, the median PFS time was 15.3 months, and the 1- and 3-year survival rates were 66.7% and 10.4%, respectively. Gilliams and Lees (24,25) and Kuehl et al. (26) reported that 1- and 3-year survival rates for CLM patients were 85–90% and 34–58% after RFA treatment alone, respectively, which are higher than what we have reported in our study. When the data from case series and retrospective studies are taken together, the outcomes reported in these studies consistently suggest that RFA

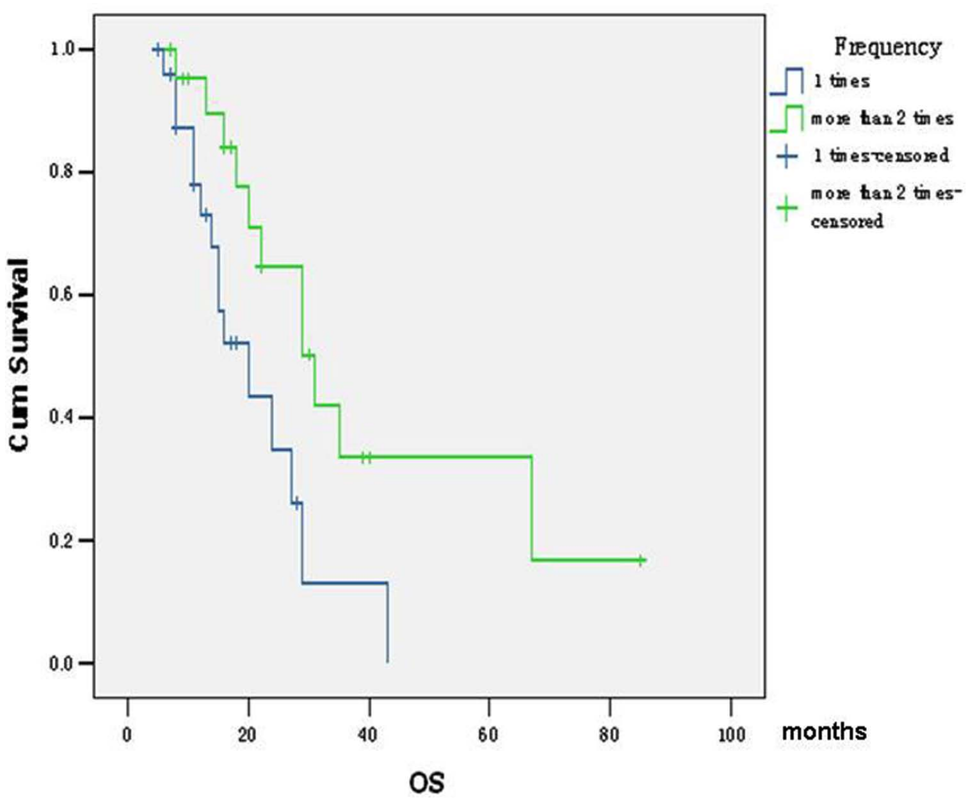

Figure 3. Kaplan–Meier OS curves of CLM patients who received single or multiple RFA treatments.

treatment result in higher 1-, 3-, and 5-year survival rates than those from currently available chemotherapy.

RFA has the advantage of being minimally invasive and is a relatively low-risk procedure for the treatment of discrete liver tumors, especially when compared to open surgical resection (27). There are several factors, including the number of metastatic tumors, their size and location, the use of systemic treatment before RFA treatment, and tumor metastasis outside liver, that may influence the long-term prognostic of RFA treatment (14,28).

Our study showed that the clinical parameters of the CLM patients receiving RFA treatment were closely correlated with prognosis. One important parameter is the diameter of the CLM lesion. Although the overall survival curves of two groups were not significantly different, the curves clearly separated and the difference approached statistical significance, which indicated that patients might have improved survival with tumor diameter of less than 3 cm. As our study was relatively small, it was not sufficiently powered to detect a survival difference. Previous studies have also demonstrated the importance of tumor diameter in CLM prognosis. Kingham et al. concluded that a tumor size over 1 cm was associated with an increased tumor recurrence rate in CLM patients (29). Therefore, it has been suggested that resection might be a better treatment option in the event of tumor recurrence after RFA therapy (30). In our study, it has also been demonstrated that resection for recurrence after RFA was associated with significant long-term survival benefit. Furthermore, patients who had received multiple RFA procedures had better prognosis than patients receiving RFA only once. Our results showed that the median OS time values for the two groups were significantly different.

There is also evidence demonstrating the potential correlation between the expression of tumor markers and prognosis of colorectal cancer with liver metastasis. The average CEA level is 32.3 ng/ml (1–184 ng/ml) in CLM patients (31). Low CEA levels have been positively correlated with good prognosis (32,33). Our study also demonstrated a similar correlation in that the median OS and PFS time of patients with CEA levels <5 ng/ml were significantly longer than those of patients with CEA levels ≥5 ng/ml, which highlights the importance of CEA monitoring in evaluating the effectiveness of RFA treatment in CLM patients. CEA is a glycoprotein produced by CRC and lung cancer cells. It may facilitate the growth and proliferation of cancer cells. Thus, CEA positivity and increased CEA levels may indicate growth or active proliferation of CRC cells.

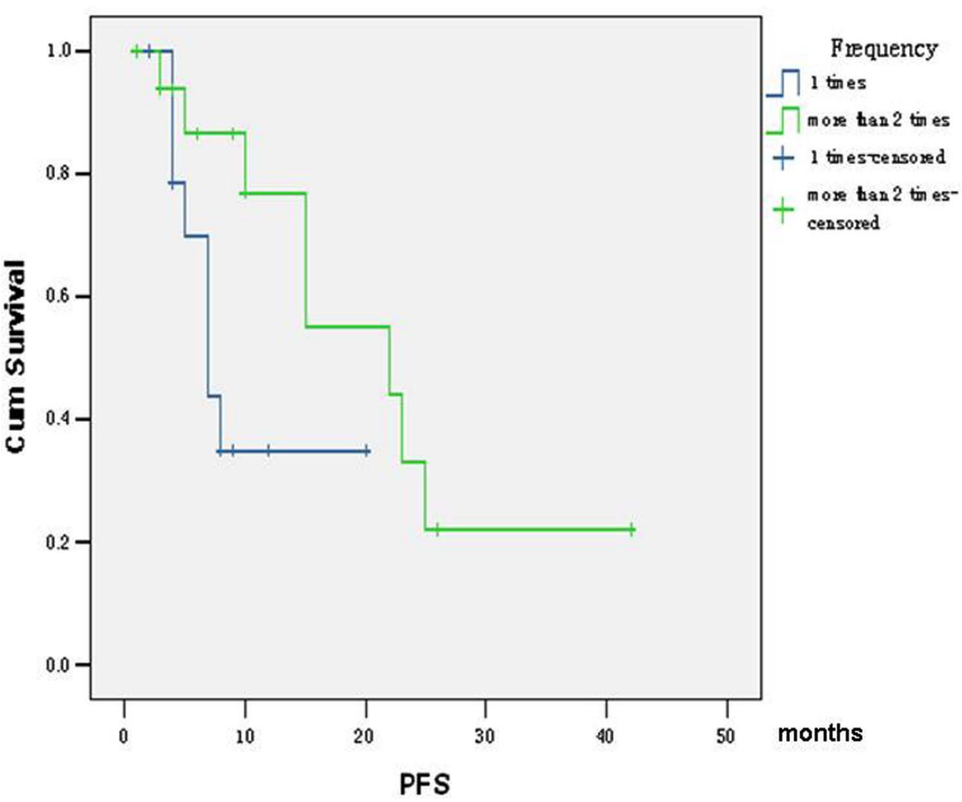

Figure 4. Kaplan–Meier PFS curves of CLM patients who received single or multiple RFA treatments.

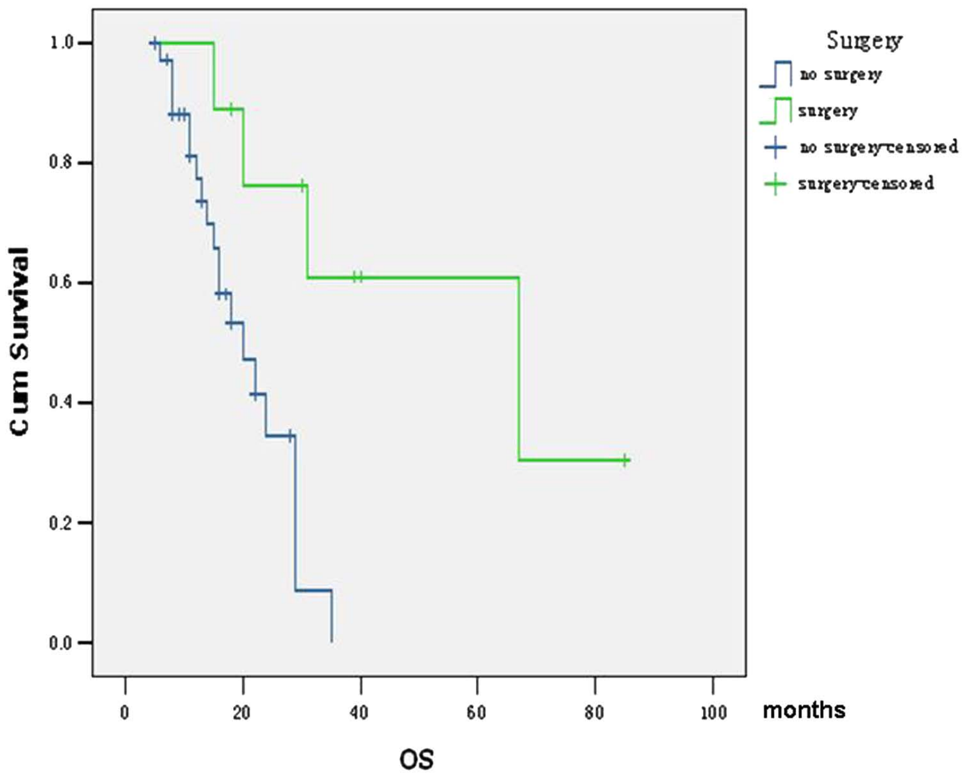

Figure 5. Kaplan–Meier OS curves of CLM patients who underwent subsequent surgical resection after RFA treatment.

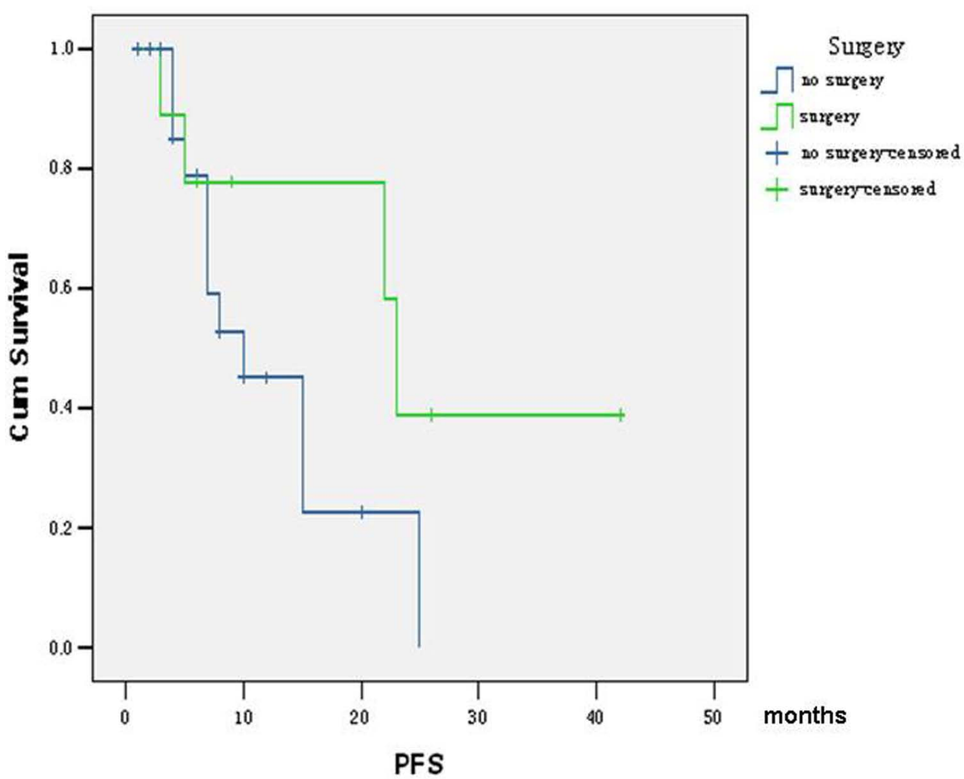

Figure 6. Kaplan–Meier PFS curves of CLM patients who underwent subsequent surgical resection after RFA treatment.

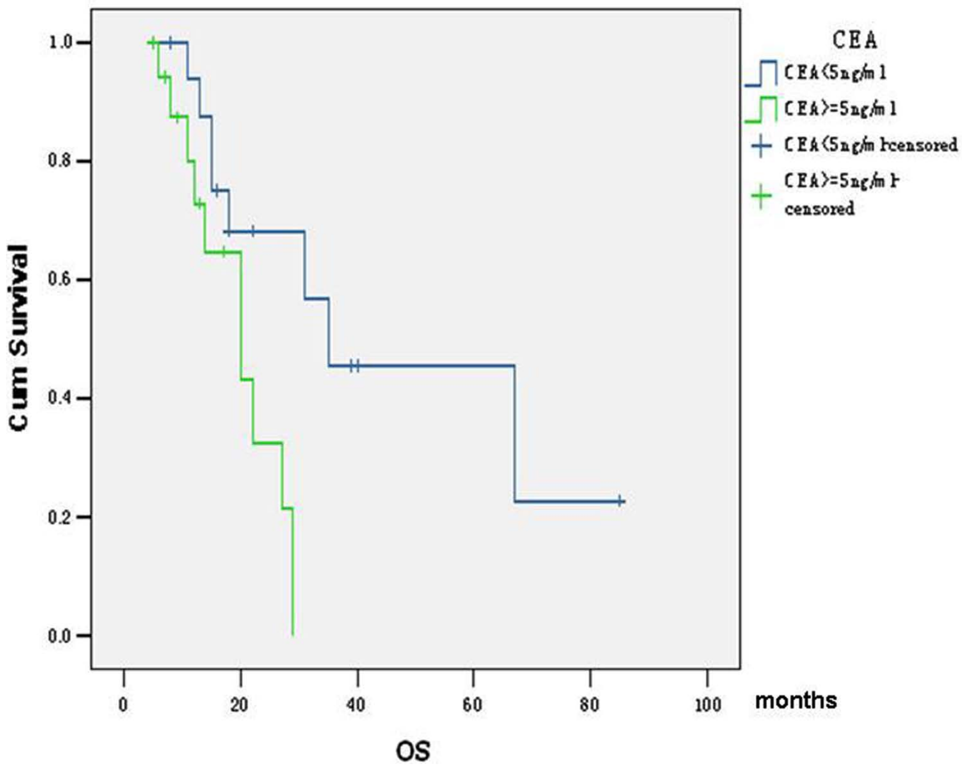

Figure 7. Kaplan–Meier OS curves of CLM patients with different CEA levels (<5 ng/ml or ≥5 ng/ml) before RFA treatment.

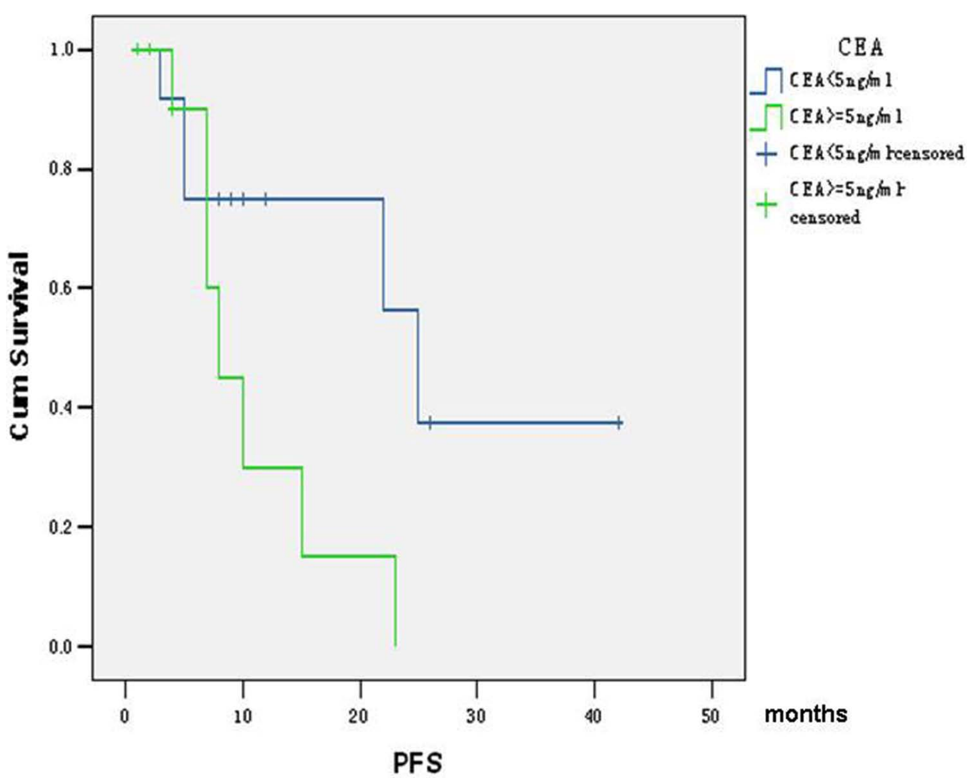

Figure 8. Kaplan–Meier PFS curves of CLM patients with different CEA levels (<5 ng/ml or ≥5 ng/ml) before RFA treatment.

Table 2. Multivariate Analysis of Prognostic Factors of CLM Patients After RFA

Factor	*p* Value
Gender	0.865
Age	0.147
Pathological types	0.168
Number of CLM lesions	0.807
Location of CLM lesions	0.462
Diameter of CLM lesions	0.234
Resection of CLM lesions	0.023*
Frequency of RFA treatments	0.002*
CLA before RFA	0.003*
Extrahepatic disease	0.855

*$p<0.05$.

Multivariate analysis revealed that resection of CLM lesions after RFA, frequency of RFA treatments ≥2, and serum CEA levels <5 ng/ml before RFA were all independent prognostic factors associated with better survival in CLM patients.

CONCLUSIONS

The findings from our study have shown that tumor lesion size, resection of recurrence CLM lesion after RFA, frequency of RFA treatment, and serum CEA levels before RFA may represent important prognostic factors of CLM patients treated with RFA therapy. It is clear that RFA therapy represents an important treatment option that must be considered when evaluating colorectal cancer patients with metastatic involvement of the liver.

ACKNOWLEDGMENTS: This study was supported in part by the Medical and Health Platform Backbone Personnel Plan (Department of Health of Zhejiang Province, 2012RCB028), National Natural Science Foundation of China (30872945), Natural Science Foundation of Zhejiang Province (LY15H 160015), Health Department Foundation of Zhejiang Province (2008B110), Jinhua Science and Technology Plan of Zhejiang Province (2008-3-049), Foundation of China Society of Clinical Oncology (CSCO) for young researcher (Y-B2010-030), and Horizontal Topic Study of Zhejiang University (12-491030-072). The authors would like to thank Dr. Wei Chen for her constructive discussions and proofreading of this manuscript.

REFERENCES

1. Leonard, G. D.; Brenner, B.; Kemeny, N. E. Neoadjuvant chemotherapy before liver resection for patients with unresectable liver metastases from colorectal carcinoma. J. Clin. Oncol. 23(9):2038–2048; 2005.
2. Mckay, A.; Dixon, E.; Taylor, M. Current role of radiofrequency ablation for the treatment of colorectal liver metastases. Br. J. Surg. 93(10):1192–1201; 2006.
3. Bismuth, H.; Adam, R.; Lévi, F.; Farabos, C.; Waechter, F.; Castaing, D.; Majno, P.; Engerran, L. Resection of nonresectable liver metastases from colorectal cancer after neoadjuvant chemotherapy. Ann. Surg. 224(4):509–520; 1996.
4. Petrelli, N. J.; Abbruzzese, J.; Mansfield, P.; Minsky, B. Hepatic resection: The last surgical frontier for colorectal cancer. J. Clin. Oncol. 23(20):4475–4477; 2005.
5. Garden, O. J.; Rees, M.; Poston, G. J.; Mirza, D.; Saunders, M.; Ledermann, J.; Primrose, J. N.; Parks, R. W. Guidelines for resection of colorectal cancer liver metastases. Gut 55(Suppl. 3):iii1–iii8; 2006.
6. National Comprehensive Cancer Network. NCCN guidelines. 2015. Retrieved from http://www.nccn.org/professionals/physician_gls/f_guidelines.asp
7. Gervais, D. A.; Goldberg, S. N.; Brown, D. B.; Soulen, M. C.; Millward, S. F.; Rajan, D. K. Society of Interventional Radiology position statement on percutaneous radiofrequency ablation for the treatment of liver tumors. J. Vasc. Interv. Radiol. 20(Suppl. 7):S342–347; 2009.
8. Bale, R.; Widmann, G.; Schullian, P.; Haidu, M.; Pall, G.; Klaus, A.; Weiss, H.; Biebl, M.; Margreiter, R. Percutaneous stereotactic radiofrequency ablation of colorectal liver metastases. Eur. Radiol. 22(4):930–937; 2012.
9. Pearson, A. S.; Izzo, F.; Fleming, R. Y.; Ellis, L. M.; Delrio, P.; Roh, M. S.; Granchi, J.; Curley, S. A. Intraoperative radiofrequency ablation or cryoablation for hepatic malignancies. Am. J. Surg. 178(6):592–599; 1999.
10. Bilchik, A. J.; Wood, T. F.; Allegra, D.; Tsioulias, G. J.; Chung, M.; Rose, D. M.; Ramming, K. P.; Morton, D. L. Cryosurgical ablation and radiofrequency ablation for unresectable hepatic malignant neoplasms: A proposed algorithm. Arch. Surg. 135(6):657–662; 2000.
11. Elias, D.; Baton, O.; Sideris, L.; Boige, V.; Malka, D.; Liberale, G.; Pocard, M.; Lasser. P. Hepatectomy plus intraoperative radiofrequency ablation and chemotherapy to treat technically unresectable multiple colorectal liver metastases. J. Surg. Oncol. 90(1):36–42; 2005.
12. Curley, S. A.; Marra, P.; Beaty, K.; Ellis, L. M.; Vauthey, J. N.; Abdalla, E. K.; Scaife, C.; Raut, C.; Wolff, R.; Choi, H.; Loyer, E.; Vallone, P.; Fiore, F.; Scordino, F.; De Rosa, V.; Orlando, R.; Pignata, S.; Daniele, B.; Izzo, F. Early and late complications after radiofrequency ablation of malignant liver tumors in 608 patients. Ann. Surg. 239(4):450–458; 2004.
13. Mulier, S.; Mulier, P.; Ni, Y.; Miao, Y.; Dupas, B.; Marchal, G.; De Wever, I.; Michel, L. Complications of radiofrequency coagulation of liver tumors. Br. J. Surg. 89(10):1206–1222; 2002.
14. Abdalla, E. K.; Vauthey, J. N.; Ellis, L. M.; Ellis, V.; Pollock, R.; Broglio, K. R.; Hess, K.; Curley, S. A. Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. Ann. Surg. 239(6):818–825; discussion 825–827; 2004.
15. Lencioni, R.; Crocetti, L.; Cioni, D.; Della Pina, C; Bartolozzi, C. Percutaneous radiofrequency ablation of hepatic colorectal metastases: Technique, indications, results, and new promises. Invest. Radiol. 39(11):689–697; 2004.
16. Kemeny, N. Management of liver metastases from colorectal cancer. Oncology (Williston Park) 20(10):1161–1176; 2006.
17. Ruers, T. J.; Joosten, J. J.; Wiering, B.; Langenhoff, B. S.; Dekker, H. M.; Wobbes, T.; Oyen, W. J.; Krabbe, P. F.; Punt, C. J. Comparison between local ablative therapy and chemotherapy for non-resectable colorectal liver metastases: A prospective study. Ann. Surg. Oncol. 14(3):1161–1169; 2007.
18. de Jong, M. C.; Pulitano, C.; Ribero, D.; Strub, J.; Mentha, G.; Schulick, R. D.; Choti, M. A.; Aldrighetti, L.; Capussotti, L.; Pawlik, T. M. Rates and patterns of recurrence following curative intent surgery for colorectal liver

metastasis: An international multi-institutional analysis of 1669 patients. Ann. Surg. 250(3):440–448; 2009.
19. Van Tilborg, A. A.; Meijerink, M. R.; Sietses, C.; Van Waesberghe, J. H.; Mackintosh, M. O.; Meijer, S.; Van Kuijk, C.; Van Den Tol, P. Long-term results of radiofrequency ablation for unresectable colorectal liver metastases: A potentially curative intervention. Br. J. Radiol. 84(1002):556–565; 2011.
20. Guenette, J. P.; Dupuy, D. E. Radiofrequency ablation of colorectal hepatic metastases. J. Surg. Oncol. 102(8):978–987; 2010.
21. Lee, W. S.; Yun, S. H.; Chun, H. K.; Lee, W. Y.; Kim, S. J.; Choi, S. H.; Heo, J. S.; Joh, J. W.; Choi, D.; Kim, S. H.; Rhim, H.; Lim, H. K. Clinical outcomes of hepatic resection and radiofrequency ablation in patients with solitary colorectal liver metastasis. J. Clin. Gastroenterol. 42(8):945–949; 2008.
22. Berber, E.; Tsinberg, M.; Tellioglu, G.; Simpfendorfer, C. H.; Siperstein, A. E. Resection versus laparoscopic radiofrequency thermal ablation of solitary colorectal liver metastasis. J. Gastrointest. Surg. 12(11):1967–1972; 2008.
23. Kim, K. H.; Yoon, Y. S.; Yu, C. S.; Kim, T. W.; Kim, H. J.; Kim, P. N.; Ha, H. K.; Kim, J. C. Comparative analysis of radiofrequency ablation and surgical resection for colorectal liver metastases. J. Korean Surg. Soc. 81(1):25–34; 2011.
24. Gillams, A. R.; Lees, W. R. Survival after percutaneous, image-guided, thermal ablation of hepatic metastases from colorectal cancer. Dis. Colon Rectum 43(5):656–661; 2000.
25. Gillams, A. R.; Lees, W. R. Radiofrequency ablation of colorectal liver metastases. Abdom. Imaging 30(4):419–426; 2005.
26. Kuehl, H.; Stattaus, J.; Hertel, S.; Hunold, P.; Kaiser, G.; Bockisch, A.; Forsting, M. Mid-term outcome of positron emission tomography/computed tomography-assisted radiofrequency ablation in primary and secondary liver tumours—A single-centre experience. Clin. Oncol. 20(3): 234–240; 2008.
27. Livraghi, T.; Solbiati, L.; Meloni, M. F.; Gazelle, G. S.; Halpern, E. F.; Goldberg, S. N. Treatment of focal liver tumors with percutaneous radio-frequency ablation: Complications encountered in a multicenter study. Radiology 226(2):441–451; 2003.
28. Pawlik, T. M.; Izzo, F.; Cohen, D. S.; Morris, J. S.; Curley, S. A. Combined resection and radiofrequency ablation for advanced hepatic malignancies: Results in 172 patients. Ann. Surg. Oncol. 10(9):1059–1069; 2003.
29. Kingham, T. P.; Tanoue, M.; Eaton, A.; Rocha, F. G.; Do, R.; Allen, P.; De Matteo, R. P.; D'Angelica, M.; Fong, Y.; Jarnagin, W. R. Patterns of recurrence after ablation of colorectal cancer liver metastases. Ann. Surg. Oncol. 19(3):834–841; 2012.
30. Brouquet, A.; Vauthey, J. N.; Badgwell, B. D.; Loyer, E. M.; Kaur, H.; Curley, S. A.; Abdalla, E. K. Hepatectomy for recurrent colorectal liver metastases after radiofrequency ablation. Br. J. Surg. 98(7):1003–1009; 2011.
31. Ramia, J. M.; López-Andujar, R.; Torras, J.; Falgueras, L.; Gonzalez, J. A.; Sanchez, B.; Figueras, J. Multicentre study of liver metastases from colorectal cancer in pathological livers. HPB (Oxford) 13(5):320–323; 2011.
32. Yamakado, K.; Inoue, Y.; Takao, M.; Takaki, H.; Nakatsuka, A.; Uraki, J.; Kashima, M.; Kusunoki, M.; Shimpo, H.; Takeda, K. Long-term results of radiofrequency ablation in colorectal lung metastases: Single center experience. Oncol. Rep. 22(4):885–891; 2009.
33. Chew, M. H.; Teo, J. Y.; Kabir, T.; Koh, P. K.; Eu, K. W.; Tang, C. L. Stage IV colorectal cancers: An analysis of factors predicting outcome and survival in 728 cases. J. Gastrointest. Surg. 16(3):603–612; 2012.