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Radiofrequency Ablation of Liver Tumors: The First Preliminary Report in Iran

Background/Objective: Radiofrequency ablation (RFA) is emerging as a new therapeutic technique for unresectable hepatic malignancies. We report our experience with the use of this method for the first time in Iran.

Patients and Methods: Eighteen patients with primary or metastatic hepatic malignancies, which were considered not suitable for surgical resection, were included in our study. RFA was performed via the percutaneous ultrasound-guided method, under general anesthesia, by an interventional radiologist. Patients were followed prospectively with contrast-enhanced CT or ultrasonography, and tumor marker serum levels 1, 3 and 6 months after RFA.

Results: RFA was used to treat 26 tumors (diameters of 12-70 mm). These tumors included hepatocellular carcinoma in three cases and metastatic carcinoma in 23 cases. Three patients had complications: two bilomas and one abscess in the right lobe. At follow-ups, tumor recurred at the site of RFA in four tumors, all of which were over 4 cm in diameter.

Conclusion: RFA is a procedure with the potential to be safe and effective for treating unresectable liver tumors.

Keywords: radiofrequency, catheter ablation, liver tumors

Introduction

Hepatocellular carcinoma (HCC) is one of the most common solid tumors in the world.¹ Moreover, the liver is second only to lymph nodes as a common site of metastasis from other solid cancers, especially in patients with colorectal carcinoma.²

Surgical resection of primary and metastatic liver tumors remains the gold standard of therapy.³ Unfortunately, resection is possible in only 20% of these patients at the time of their presentation.⁴ Difficulties related to surgical resection are those of the site, size, number of tumors, and vicinity to vascular and biliary structures, extrahepatic involvement, poor general condition and poor liver function.^{5,6} Thus, for patients with primary or metastatic hepatic malignancies who are not candidates of surgical resection, new procedures must be explored to control and potentially cure these tumors.

Radiofrequency ablation (RFA) is a novel technique for treatment of hepatic tumors not amenable to resection. RFA destroys tumor by generating heat within a lesion. During RFA, a high-frequency alternating current (AC) causes thermal coagulation and protein denaturation. The procedure is carried out using a needle electrode connected to a radiofrequency generator.

The purpose of this study was to report our experience with the use of radiofrequency ablation in the treatment of primary and secondary liver tumors in Iran.

Patients and Methods

We performed this prospective study from July 2003 to August 2004. All

patients had histologically confirmed primary or metastatic liver tumors and were eligible for treatment using an RFA protocol, in Noor Medical Imaging Center in Tehran. Informed consent was obtained from all cases at the time of enrollment.

Our reference population was patients with liver tumors (primary or secondary), and our cases were selected according to the following inclusion criteria:

1) Patients deemed to have unresectable liver tumors (surgeons opinion); 2) No evidence of extrahepatic disease, clinically or radiographically; 3) Distance from great vessels more than 1 cm; 4) Less than four hepatic tumors; 5) Mass size smaller than 70 mm. Cases who refused the follow-up or who died were excluded from this study.

RFA was performed via the percutaneous ultrasound-guided method, under general anesthesia, by an interventional radiologist. We used prophylactic antibiotic (Cefalotin 1g /single dose) in cases with severe cirrhosis, infections, immunosuppression and biliary pathologies such as ductal ectasia or previous biliary bypass. The patients were monitored continuously during and after the procedure using ultrasonography.

RFA was performed using Cool tip electrodes (Valley Lab, Burlington, MA). We used the cluster needle for lesions over 3 cm in diameter and single needle for lesions smaller than 3 cm. In each case, a 1-cm margin of normal hepatic parenchyma surrounding the lesion was ablated. Lesions not to be ablated with an adequate margin underwent multiple overlapping fields. During and immediately after the procedure, all patients underwent a control ultrasound study to assess the ablated site and to monitor complications. The patients were discharged on the same day if no immediate complication occurred.

Follow-up was done using contrast enhanced CT or ultrasound and measuring tumor marker levels (AFP, CEA or CA19-9) at 1, 3 and 6 months after RFA.

Decrease in size and tumor marker level indicated effectiveness, and an increase in size with enhancement was considered as relapse.

Results

A total of 29 patients were treated by RFA during the study period; 7 patients who were lost to follow-

up and 4 patients who died were excluded. Among the 18 remaining cases, 12 patients were female (67%) and 6 patients were male (33%).

A total of 26 tumors were ablated in these patients. One half of our cases were 50 years of age or older, and the mean age of 50.9 ± 13.9 years (19-71 years). RFA was used to treat a single tumor in 11 patients (61%), two tumors in 6 patients (33%) and three tumors in one patient (6%).

The primary cancer diagnoses in these patients are shown in Table 1.

Table 1. Primary cancer diagnosis in 18 patients treated with radiofrequency ablation

Diagnosis	No. of patients (%)
Colorectal adenocarcinoma	12
Breast carcinoma	4
Hepatocellular carcinoma	3
Pancreatic carcinoma	1
Gastric carcinoma	1
Esophageal carcinoma	1
Metastasis from unknown primary	4

History of liver surgery was positive only in one case.

Among the 26 tumors on which RFA was performed, 17 masses were in the right, and 9 masses were in the left liver lobe.

The diameter of tumor was 12 to 70 mm. All of five tumors < 2 cm in diameter were colorectal metastases. Eleven tumors were 2 to 4 cm in diameter, two of which were HCC. Others were metastatic (3 colorectal, 3 breast, 1 pancreas and 1 stomach). Among 10 tumors greater than 4 cm in diameter, one case was HCC and 9 tumors were metastatic (4 colorectal, 1 breast, 1 esophagus and 3 unknown primary tumors).

RFA time in our cases was approximately 12 minutes. Ultrasonography showed hyperechogenicity in all ablated tumors immediately after the procedure, which is consistent with a successful procedure.

In lesions smaller than 3.5 cm in diameter, we saw 100% tumor destruction. For lesions measuring 3.5-5 cm, approximately 75% of these lesions were treated completely with RF ablation, and less than 50% of tumors measuring greater than 5 cm were completely ablated.

There were one major and two minor complications after RFA. Biloma was seen in two patients (a 54-year-old man with HCC and a 45-year-old woman

with colon metastasis), and one patient with HCC (71 years old) developed liver abscess in the right lobe. All of these lesions were 2–4 cm in diameter. These complications were seen in the third month following the procedure. The liver abscess was treated by percutaneous drainage without any further complication. The bilomas did not require any additional treatment and the patient was asymptomatic. No other complications occurred in the 26 treated lesions.

Follow-ups were available for 23 lesions after one month, 9 lesions after three months, and 3 lesions after 6 months, using CT or ultrasound. Tumors had recurred at the site of RFA in four of the 26 treated tumors, all of which were originally over 4 cm in diameter (maximum size: 7.2 cm).

A serum tumor marker (AFP, CEA or CA19-9) was measured in 8 patients before the procedure. Five patients had elevated tumor marker levels before RFA. After RFA, serum tumor markers significantly declined in four of the five patients, and none had local recurrence.

The reason for mortality among our patients is not well known, but is not documented to be the result of an RFA complication.

Discussion

Hepatocellular carcinoma (HCC) and hepatic metastases from solid tumors are major causes of cancer-related mortality and morbidity.¹ Without specific therapy; these tumors have a very poor prognosis, with median survival rates of 0.9 to 12.8 months and 6 to 10 months, respectively.^{7,8} Resection of primary or metastatic hepatic lesions in some patients is curative but unfortunately, less than 10–20% of these patients are candidates for surgical resection.^{9,10} The other patients may be candidates for local ablative approaches (percutaneous ethanol injection, interstitial laser photocoagulation, cryosurgical ablation, or radiofrequency ablation), hepatic directed techniques (hepatic artery ligation, hepatic artery infusion chemotherapy or transcatheter arterial chemoembolization), or systemic chemotherapy.

Radiofrequency ablation is a relatively new technology that is capable of destroying tumor cells by thermally induced coagulation necrosis. RFA is safe and effective for treatment of liver tumors in patients

who cannot take the surgical therapy. It has some advantages compared with the other percutaneous procedures: the procedure time is shorter than percutaneous ethanol injection, and is safer and demonstrates lower complications than cryotherapy.^{11,12}

The local recurrence rate in our patients was 15%. Hong chi et al. reported 16.7% recurrence after a median follow-up of 10 month—they had 21 primary HCC, 12 colorectal liver metastasis and 3 other metastatic tumors.¹³ Curley et al. reported 123 primary and metastatic liver tumors treated with RF. In a median follow-up of 15 months, they observed 3 recurrences in 169 treated lesions but metastatic tumors had developed at other sites in 34 cases (27.6%).¹⁴ As our median follow-up was less than the above-mentioned studies, we cannot compare our results with these studies. Similar to our study, many studies have reported that recurrence rate is higher in larger tumor sizes, especially in primary tumor size over 4 cm.^{15,16} Besides the primary tumor size, this could be due to the nature of tumor.

Our results showed that the size of the tumor to be treated is an important factor in determining whether complete local therapy can be achieved and these results are comparable with Goldberg's results (Table 2).¹⁶

Table 2. Comparisons of success rate between Goldberg's study and our results according to size

Tumor Size	< 2.5 cm	2.5-3.5 cm	3.5- 5 cm	>5 cm
Goldberg	90 %	70-90 %	50-70 %	<50%
Our results	100 %	100 %	75 %	<50 %

We think that if there is no evidence of new metastasis, tumor markers level is a suitable indicator of success rate. Although decrease in size is an important factor in success rate, but no enhancement of tumors after CT-scan with contrast is more important.

Major complications due to hepatic RFA include hemorrhage, hydrothorax, pneumothorax, ascites, abscess formation, visceral and diaphragmatic injury, hepatic and renal insufficiency, skin burns and death.¹⁵ We had one major complication in our study. Prevalence of all complications was 11.5% that is similar to some other reports. For example, Chan et al. (who performed RFA on 67 primary and secondary liver tumors) mentioned a complication rate of

14.9% (P value=0.67). The complication rate is lower in some other reports, for example, Chen et al. reported 14 complications (2.5%) among 338 liver tumors following 565 RF procedures (p value=0.034).¹⁷⁻²² Our complications were clinically lower than some other reports (p value=0.1).²³ These differences could be partly due to the large diversity in the sample size between these studies. Larger sample sizes could be more reliable for estimating complication rates.

Limitations of this study are its small sample size and short follow-up interval. If more patients undergo therapy and continue to be monitored for recurrence, we will be better able to assess long-term survival rates and overall efficacy of RFA.

Another limitation was that we could not follow up our patients with contrast-enhanced CT scan; in fact, some of our patients were followed by ultrasonography. Following up of all patients with contrast-enhanced, CT-scan can yield more accurate results on the tumor relapse.

Finally, regarding acceptable local destruction and low complications, it seems that RFA could be considered for treating unresectable primary and secondary liver tumors. In this regard, its safety and efficacy (in association with disease free survival, overall survival and quality of life) can be assessed in future studies with a larger sample size and longer follow-ups.

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