Radiofrequency ablation of liver tumors: experience with open and percutaneous approach

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Background: Radiofrequency ablation (RFA), a thermal coagulation technique, has been used for ablation of primary and secondary liver tumors. Methods: Over a 24-month period, 41 patients, including 20 with hepatocellular cancer (HCC), 14 with liver metastases from colorectal tumors and 7 with metastases from other tumors, underwent RFA in our institution. Ablation was done using intra-operative (n=27) or percutaneous ultrasonographic (n=14) guidance. A zone of ablation larger than the size of the lesion on CT scan indicated successful RFA. Results: The mean size of lesions was 4.9 cm for HCC and 3.1 cm for metastases. Among 20 patients with HCC, 16 had complete tumor ablation and one had failure of localization. All patients with liver metastases had successful tumor ablation. There was no procedure-related death. Two patients had hemoperitoneum and one experienced skin burn. During a median follow up of 16 months, five patients with HCC and two with colorectal cancers died. One patient had tumor recurrence at the ablation site and two developed fresh solitary metastatic lesions; all three are disease-free after repeat ablation treatment. Conclusions: RFA is a safe and promising technique for the treatment of non-resectable HCC and liver metastases, in the short term. [Indian J Gastroenterol 2006;25:66-70]

Hepatocellular carcinoma (HCC) is the most common liver tumor. It comprises 1.6% of all cancers in India, and is often associated with hepatitis B virus infection and liver cirrhosis.1 Liver is also a common site of metastasis from other solid cancers, particularly colorectal cancer.2

Surgical resection of HCC and liver metastases from colorectal cancer (LMCC) can improve survival in 20% to 35% of patients.3,4 However only 5% to 15% of newly diagnosed patients with HCC or LMCC undergo potentially curative resection. In the remaining patients, difficulties in surgical resection due to size, location or number of tumors, the proximity of lesions to vascular and biliary structures, extrahepatic involvement, poor general condition of the patient and inadequate hepatic functional reserve due to co-existent cirrhosis preclude liver resection.5,6

Radiofrequency ablation (RFA) has emerged as a new modality for the treatment of such tumors. It employs a high-frequency alternating current to cause thermal coagulation and protein denaturation in tumor tissue. We report here our experience with RFA.

Methods

During a 2-year period, 41 patients with primary or secondary liver cancer (Table 1) – 20 with HCC, 14 with LMCC, 7 with liver metastasis from other tumors (neuroendocrine tumors 3, gastrointestinal stromal tumors 2, gastric carcinoma 1, ovarian carcinoma 1) – underwent RFA.

In patients with HCC, liver resection was not possible due to co-existing Child’s B cirrhosis, or close proximity of the tumor to the inferior vena cava or to the liver hilum; of these 20 patients, 16 had cirrhosis, and 9 and 3 tested positive for HBsAg and anti-hepatitis C virus antibody, respectively. Of the 14 patients with LMCC, two had previously undergone hepatectomy and had developed fresh liver metastases, and the remaining 12 had lesions located at the liver hilum, in close proximity to the hepatic veins or at the junction of the right and the left liver lobes. Five patients had multiple or bilobar liver metastases; however, RFA was used since these metastases were from neuroendocrine tumors or gastrointestinal stromal tumors. The patients with metastasis from gastric or ovarian cancer were con-
considered for RFA since they were in good health.

The diagnosis of liver tumor was confirmed by guided fine-needle aspiration or biopsy; histological proof was obtained in all patients. Wherever necessary, serum alfa-fetoprotein and carcino-embryonic antigen (CEA) levels were measured. A few patients also underwent MRI or positron emission tomography (PET) using 18FDG.

Contraindications for RFA were: lesions larger than 7 cm in size, multinodular or diffuse intrahepatic tumors (5 or more lesions), extrahepatic spread, portal vein thrombosis, Child-Pugh class C cirrhosis, refractory ascites, prothrombin activity less than 50%, or platelet count lower than 50×10^9/L.

Procedure

A 20-cm-long, 15-gauge, multi-electrode probe with expansions at 2, 3, 4 and 5 cm (Starburst XL®, RITA, California, USA; 150 W electrode) was used to deliver radiofrequency (RF) energy for lesions deep in the liver parenchyma. A short surface probe with expansions at 1, 2 and 3 cm was used for lesions located within 2 cm from the liver surface.

The operative approach (n=27) was used in patients with (i) lesions located close to the dome of diaphragm, (ii) peripherally placed tumors, (iii) lesions where percutaneous access window was not available, and (iv) prior hepatectomy. Percutaneous approach (n=14) was used for patients who were not suitable for open approach (poor operative risk or extensive cirrhosis) and those with small tumors located deep in the liver parenchyma and a favorable sonographic window.

General anaesthesia was used in all patients. In the operative approach, the lesions were identified by intraoperative ultrasonography (IOUS). Lesions larger than 4-5 cm underwent overlapping ablations. Forty patients had only one treatment session, during which one or more ablations were performed on one or more tumors. In 5 patients, the procedure was combined with metastatectomy. The patients remained in hospital for 2-3 days after percutaneous procedure and 5-9 days for open approach, unless complications necessitated a longer stay. One patient had three RFA sessions.

The success of ablation was evaluated by follow-up three-phase helical CT scan one month later. Successful treatment (complete tumor ablation) was defined as absence of a focus of enhancement within the ablated lesion or at its periphery. Failure of treatment was defined as failure of the RFA to ablate the lesion at all. Incomplete treatment was defined as failure to ablate a part of the tumor, or enhancement of a focus within or at the periphery of the lesion.

Results

RFA was performed in 41 patients for 68 nodules (Table 2). Of these, 18 received adjuvant chemotherapy including systemic chemotherapy and chemoembolization. One patient who had liver resection and simultaneous RFA for CLM at another center earlier developed a lesion at a different site.

IOUS identified additional intrahepatic lesions in three patients, but this did not change the operative procedure; these lesions were treated with RFA at the same sitting. The average hospital stay (Table 2) was longer with operative approach than percutaneous approach.

Immediate results

Complete ablation was achieved in 16 of 20 patients with HCC, and all 21 patients with liver metastases. Complete failure of RFA occurred in one patient who had undergone percutaneous RFA for multinodular HCC with gross cirrhosis; she later underwent a successful repeat percutaneous RFA.

Of the 13 patients with LMCC who had elevated serum CEA levels, these returned to normal range in all.

Complications

Three patients had complications. One patient with LMCC had superficial skin burn. Two patients with HCC and liver cirrhosis developed hemoperitoneum following percutaneous RFA, and needed surgery for control of bleeding, which was found to be from the liver surface and collaterals in the falciform ligament, respectively. There was no procedure-related mortality.

Table 2: Results of treatment with radiofrequency ablation

<table>
<thead>
<tr>
<th></th>
<th>HCC</th>
<th>LMCC</th>
<th>NCLM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of lesions</td>
<td>33</td>
<td>21</td>
<td>14</td>
<td>68</td>
</tr>
<tr>
<td>No. of</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete ablation</td>
<td>30</td>
<td>21</td>
<td>14</td>
<td>65</td>
</tr>
<tr>
<td>Incomplete ablation</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Complications</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Development of new lesions</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Hospital stay (mean; days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operative</td>
<td>6.4</td>
<td>5.0</td>
<td>5.5</td>
<td>5.6</td>
</tr>
<tr>
<td>Percutaneous</td>
<td>3.0</td>
<td>2.5</td>
<td>2.5</td>
<td>2.6</td>
</tr>
</tbody>
</table>

HCC – Hepatocellular carcinoma; LMCC – Liver metastasis from colorectal cancer; NCLM – Non-colorectal liver metastasis
Follow-up data

During a median follow up of 16 (range 12-20) months, three patients have had recurrence. One patient with HCC developed recurrence at the ablation site 10 months after RFA. Two other patients, one with HCC and another with LMCC, developed solitary lesions at distant sites 9 and 6 months later, respectively. All three patients are disease-free after repeat RFA.

Of the 20 patients with HCC, five died (liver failure 3, massive upperGI bleed 1, recurrence and liver failure 1); of the remaining 15 patients, 13 are disease-free and alive and 2 have asymptomatic recurrence. Among patients with LMCC, two died of extensive liver metastases (3 and 9 months after RFA, respectively) and the remaining 12 are alive and free of disease. In patients with metastases from tumors other than colorectal cancer, there has been no progression of disease at a median follow up of 16 months. Thus, of the 38 patients with complete tumor ablation, 34 (89%) are alive and 30 (79%) are disease-free.

Discussion

Patients with HCC carry a poor prognosis. Curative resection is possible only occasionally and most patients have unresectable tumors. Systemic chemotherapy is rarely effective, has significant toxicity, and does not improve overall patient survival significantly. Several in situ ablative techniques like percutaneous ethanol injection, cryoablation and RFA that destroy the tumor tissue have therefore been developed for potential curative or palliative use.

RFA has some advantages over the other percutaneous techniques. The time taken for RFA is shorter than that with percutaneous ethanol injection. RFA induces larger thermal lesions than those with microwave electrodes. RFA is cheaper and easier to perform than interstitial laser photocoagulation, which requires multiple fiber insertions, and is safer than cryotherapy.

RFA is best suited for tumors <5 cm in size. Using an RF current generator with 50-150 watt power output and a probe with hook electrodes of 3.5 cm diameter fully deployed, complete ablation of a 4.0-5.0 cm lesion is possible in 5-15 minutes. For larger tumors, complete ablation can be achieved by repositioning the needle electrode and creating overlapping zones of coagulative necrosis. In our study, the mean size of tumor ablated was 4.9 cm for HCC, 3.1 cm for LMCC and 2.9 cm for non-colorectal liver metastasis.

Percutaneous approach is recommended for patients who are not candidates for open approach. However, with this approach, localization of tumors may be difficult. Also, major complications like bile leak into the peritoneal cavity, intrahepatic abscesses, acute thrombosis of the portal vein, and fatal necrosis of the diaphragm have been reported following percutaneous RFA. Prior hepatobiliary surgery, especially liver resection, may be a relative contraindication for this approach, due to the risk posed by adhesions.

In our series, percutaneous approach was used in one-third of the patients. Two of these patients, both with liver cirrhosis, developed hemoperitoneum. This suggests that RFA under vision through a mini-laparotomy may be useful in patients with liver cirrhosis.

Operative approach was used in two-thirds of our patients. This approach provides greater freedom for introduction of the RF needle into the tumor, thus allowing more effective ablation, in addition to better assessment of extrahepatic and intrahepatic disease. This approach may also be safer for ablation of superficial lesions, large tumors and multiple lesions. Open RFA has been associated with a higher complete ablation rate than percutaneous RFA.

RFA may be effective for treating unresectable hepatic tumors. In a large study of 1225 malignant liver tumors in 608 patients, 63% underwent RFA at laparotomy and 37% underwent RFA via percutaneous approach. The treatment-related mortality was 0.5%, and early complications developed in 7.1%, being more frequent in patients treated with open approach and in those with liver cirrhosis. Hepatic resection is the treatment of choice for CLM; however when RFA is associated with surgery, mortality and morbidity rates are similar to that of hepatic resection for metastases.

In our study, there was no procedure-related mortality and complications developed in three (7.3%) patients. These rates are comparable to those reported in other studies. Two of these complications occurred during percutaneous RFA for HCC. One patient with LMCC had a superficial skin burn; such burns have been reported previously.

We used three-phase helical CT scan (Fig) for the evaluation of therapeutic response to RFA. In a recent report, contrast-enhanced ultrasound using sulphur hexafluoride microbubbles as contrast agent was found to be more sensitive in detecting viable tumor after RFA.
The use of RFA has been questioned by Llovet et al\textsuperscript{25} who reported neoplastic seeding in 12.5\% of patients treated for HCC. However, in three other studies, neoplastic seeding was found to be rare, being observed in only 12 of 1314, one of 226, and none of 80 cases, respectively.\textsuperscript{26,27,28}

Recurrence of tumor at the treatment margin may result from inadequate ablation. It is common for lesions located close to the large blood vessels, which act as a heat sink, preventing effective ablation;\textsuperscript{29} in one study, the local recurrence rate was 1.8\% for lesions close to large vessels.\textsuperscript{30}

Intrahepatic recurrence occurs in 40\%-60\% of patients undergoing curative resection for HCC.\textsuperscript{31} RFA has been shown to be effective for recurrent HCC in several case series.\textsuperscript{32} In our study, two patients with recurrent HCC following prior hepatectomy were successfully treated with RFA; however one patient died six months later of disease progression.

It has been reported that patients with HCC respond better to treatment with RFA than do metastatic lesions.\textsuperscript{18} However, we observed an equally good response in LMC. This may be because LMC patients did not have liver cirrhosis. However, the sample sizes for various tumors in our study was small.

Completeness of the procedure may determine the survival rate. Of 38 patients with complete tumor ablation, 34 (89\%) were still alive and 30 patients (79\%) are disease-free after a median follow-up of 20 months.

In conclusion, RFA is a promising technique to treat HCC and liver metastases that are not amenable to surgical resection. It is reasonably safe and has good short-term results. However, long-term follow-up data are needed for further evaluation of this technique.

References


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News and Notices

The International Association of Pathologists - Indian division 9th Annual CME on “Endoscopy Biopsy Correlation” will be held at T N Medical College, Mumbai, August 18 and 19, 2006.
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The 4th S R Naik Memorial Workshop on “Biomedical Research: Methods, Tools and Future” will be organized by the Department of Gastroenterology, SGPGI, Lucknow, September 23 and 24, 2006.
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