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Radiofrequency ablation of intrahepatic cholangiocarcinoma: feasability, local tumor control, and long-term outcome ☆

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ABSTRACT

A retrospective analysis of patients who underwent radiofrequency ablation (RFA) of intrahepatic cholangiocarcinoma (IHCC) was performed. Seven patients with 9 tumors underwent RFA. The mean tumor size was 2.4 cm (range=1.3–3.3 cm). RFA achieved technique effectiveness and local tumor control in 89% (8/9 tumors) of the patients respectively, with a mean overall survival of 38.5 months (range=12–69 months). To conclude, RFA was effective in achieving local tumor control and may offer a therapeutic option for patients with recurrent or primary IHCC.

1. Introduction

Cholangiocarcinoma is the second most common primary hepatic malignancy following hepatocellular carcinoma and is classified as intra- or extrahepatic based on its location in the liver [1,2]. Intrahepatic cholangiocarcinoma (IHCC) has a dismal prognosis with limited treatment options and a very high rate of recurrent or metastatic disease [1,2]. Whether primary or recurrent, most patients only survive about 6 months without any treatment [2–6].

Currently, surgical resection offers the only chance for cure. However, less than 20% of patients with cholangiocarcinoma are surgical candidates [1,3,7,8]. Even for surgical candidates, recurrence rates can be as high as 52%, with 5 year postresection survival rates ranging from 8% to 44% [2,3,5–8]. Repeated surgery is limited by patients' comorbidities or by poor functional hepatic reserve. In patients with recurrence, palliative treatments such as radiation and systemic chemotherapy remain as the only options.

Image-guided percutaneous radiofrequency ablation (RFA) has an established role in minimally invasive therapy of hepatocellular carcinoma [6,9–15]. Despite its widespread use for treatment of hepatocellular carcinoma, little has been explored regarding the use of RFA to treat IHCC. The purpose of this study was to assess the technical success rate, complications, and the impact of the procedure on patient survival and long-term local tumor control.

2. Materials and methods

2.1. Patient selection

An institutional-review-board-approved, HIPPA-compliant retrospective analysis was performed with waiver of informed consent. A departmental interventional radiology database was used to identify patients who underwent image-guided percutaneous RFA of IHCC between January 1998 and June 2011. Hilar involvement of tumor was considered extrahepatic cholangiocarcinoma, and thus, these patients were not included in the study. Patients who had tumors larger than 5 cm, more than three lesions in the liver, or evidence of extrahepatic spread or vascular invasion, or those who were coagulopathic (international normalized ratio >1.5, platelet count <50,000) were not considered amenable to RFA treatment and therefore were not included in our study.

The electronic medical records were reviewed to collect patient (gender, age) and tumor (size, number) demographics as well as details regarding treatments prior to RFA. Time to recurrence after primary treatment (i.e., surgical resection) was recorded. Details of RFA, including type of imaging guidance used during the procedure, electrode type, number of overlapping ablations, and complications, were also collected.

2.2. Radiofrequency ablation treatment

All ablations were performed on an outpatient elective basis, with use of local anesthesia and intravenous procedural sedation. Patients were given preprocedure prophylactic intravenous antibiotics (ampicillin 1 g and gentamycin 80 mg) to decrease the risk of hepatic abscess formation or other infectious complications. Sedation was achieved

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with midazolam (Roche, Nutley, NJ, USA) and fentanyl citrate (Sublimaze; Taylor, Decatur, IL, USA) with continuous hemodynamic monitoring. Imaging guidance for electrode placement consisted of computed tomography (CT) or combined ultrasound and CT. Radiofrequency ablations were performed using either a 200-W generator with internally cooled single or cluster electrodes (Covidien, Boulder, CO, USA) or with a 200-W generator with extendable tines (RITA, Sunnyvale, CA, USA). Multiple overlapping ablations were performed with the goal of creating a zone of ablation that encompassed the tumor and that extended beyond the tumor margin by at least 10 mm. Complications were classified into minor and major complications according to Society of Interventional Radiology (SIR) clinical practice guidelines [16]. Complications that required additional therapy, caused prolonged hospital stay or permanent adverse sequelae, or resulted in death were considered major complications. Other complications were considered minor. A non-contrast CT scan was obtained immediately following the ablation to exclude complications such as bleeding and pneumothorax.

2.3. Follow-up assessment of local tumor control

Efficacy of post-RFA treatment was assessed with either contrast-enhanced CT (GE Medical System, Madison, WI, USA) or with gadolinium-enhanced magnetic resonance imaging (MRI) (GE Medical System, Madison, WI, USA; Siemens Medical Solutions USA Inc.). Follow-up imaging was performed at 1, 3, 6, 9 and 12 months post-RFA for the first year and every 6 months thereafter. The reporting criteria published by the SIR [17] for image-guided tumor ablation was followed for terminology used in this manuscript. Technique effectiveness was defined as complete ablation with no evidence of residual tumor on the 1-month follow-up imaging study. Primary effectiveness was defined when successful eradication of the tumor was achieved with one treatment, and secondary effectiveness was defined when eradication of the tumor required more than one treatment at different intervals. Nodular or thick irregular contrast enhancement seen along the margin of the ablation zone on imaging studies subsequent to the 1-month follow-up was considered local tumor progression. Local-tumor-progression-free survival was defined as the time from the initial RFA treatment to the time of detection of local tumor progression. Event-free survival was defined as the time interval from the initial RFA treatment to the detection of local tumor progression, new IHCC in the liver, metastatic disease, or patient death. Overall survival was defined as the period of time from the initial RFA treatment to patient death. All the time periods were measured in months. For patients who had subsequent ablations, only the initial RFA treatment was used to calculate the overall survival.

3. Results

Seven patients (three male, four female subjects; mean age=65 years; range=52–80 years) with nine IHCCs underwent image-guided percutaneous RFA. The mean tumor size was 2.4 cm (range=1.3–3.3 cm). Of the seven patients treated with RFA, six (83%) had recurrent IHCC following surgery, and one (17%) patient had primary IHCC. Five patients were treated for a single tumor, and two patients were treated for two tumors.

Prior to RFA, six patients had undergone partial hepatectomy for the primary tumor, and one patient had no surgical intervention who was deemed inoperable due to poor functional status and multiple other comorbidities. Of the six patients with recurrent IHCC, the average time of recurrence after surgery was 13 months (range=6–21 months). Details of patient, tumor, and primary treatment demographics are listed in Table 1.

Single-session RFA was performed for six out of seven (86 %) tumors. A representative case with preoperative imaging of the tumor, postoperative recurrence, subsequent ablation and postablation follow-up imaging is demonstrated in Fig. 1. One patient underwent repeat RFA for residual tumor identified on the 1-month follow-up imaging study. In seven patients, a total of nine primary ablations were performed. The two tumors were at a different location than the primary tumor and were seen on subsequent imaging surveillance after the initial RFA. These tumors were ablated within 1 month of their detection on surveillance imaging. These patients had no other tumors in the liver and had no signs of local tumor progression at the site of the initial ablation. Unenhanced CT scan was used as imaging guidance for eight out of the nine RFA treatments, and combined ultrasound/contrast-enhanced CT was used as image guidance for only one treatment. The average number of overlapping ablations was 3.2 (range=2–5). Six ablations were performed using the internally cooled cluster electrode, one ablation was performed using an internally cooled single electrode, and two ablations were performed using the electrode with deployable tines. There were no major or minor complications in the study group. We had no patients with hemorrhage, bile duct injury, or abscess formation. Technical details of the procedures, tumor size, and locations are listed in Table 2.

Table 1
Patient demographics and details of primary tumor (primary or recurrent IHCC), initial surgical treatment, and time to recurrence

Patient	Age (years)	Sex	Tumor type	Primary tumor size (cm)	Primary surgical treatment	Time to recurrence (months)
1	73	F	Recurrent	5	Partial hepatectomy	17
2	80	F	Recurrent	8	Partial hepatectomy	12
3	54	M	Recurrent	3.5	Partial hepatectomy	11
4	69	F	Recurrent	3.2	Partial hepatectomy	21
5	62	M	Primary	3.2	None	-
6	52	F	Recurrent	5.9	Partial hepatectomy	6
7	65	M	Recurrent	7.5	Partial hepatectomy	11

M, male; F, female.

The average time of post-RFA imaging follow-up was 31 months (range=1–67 months). One patient was lost to follow-up after the initial 1-month follow-up imaging. All of the tumor ablations except for one (8/9) patient treated for IHCC were technically effective demonstrated on subsequent imaging follow-up. The one tumor that had an incomplete treatment was reablated after 1 month, and the technique was secondarily effective with no residual contrast enhancement on follow-up imaging up to 49 months.

One patient with primary IHCC who was treated with RFA showed local tumor progression at the margin of the ablation zone seen at the 3-month postablation follow-up imaging study. This lesion was not reablated due to the detection of numerous other metastatic lesions seen on liver MRI. Patient then underwent systemic treatment and survived 16 months.

Except for two patients, all of our patients were followed until their demise. As previously stated, one patient was lost to follow-up after the 1-month postablation imaging, and the other patient is still alive. The event-free survival rate was 21.8 months (excluding the one patient with only 1 month of follow-up) in six of our seven patients. Five patients had evidence of new lesions, and one patient had local tumor progression. The overall mean survival rate in our patient group (excluding the patient lost to follow-up) was 38.5 months (range=12–69 months). Our 1-, 3-, and 5-year survival rates were