Computed Tomography Follow-up for the Detection of Hepatocellular Carcinoma Recurrence after Initial Radiofrequency Ablation: A Single-center Experience

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ABSTRACT

Purpose: Recurrence of hepatocellular carcinoma (HCC) is very common even after curative resection or ablation. This retrospective study compared the radiologic features of recurrent HCC seen by computed tomography (CT) to evaluate our empirical protocol of CT surveillance using 4-month intervals.

Materials and Methods: A total of 113 patients who were diagnosed with a first HCC recurrence after radiofrequency (RF) ablation between January 2005 and December 2006 were enrolled at a single center. Definite HCC was defined as hyperattenuation in the arterial phase with washout in the portal venous phase, and a diagnosis of naive and recurrent HCC was based on dynamic CT findings. Recurrent nodules were classified according to the enhancement patterns of previous CT images. The treatment modality for recurrent HCC and survival were evaluated.

Results: One hundred seventy-seven nodules were diagnosed as recurrent HCC: 31 (17.5%) had already been diagnosed on previous CT images as typical HCC, 72 (40.6%) had arterial hypervascularity without washout in the portal venous phase, 21 (11.9%) showed portal venous phase washout without arterial hypervascularity, and no lesions were noted in the remaining 49 (27.7%). Tumor size at recurrence was smaller than 2 cm in diameter in 98 (86.7%) cases. One hundred four patients were treated for recurrent HCC with RF ablation. The 5-year survival rate after recurrence was 49.8%. There was no significant difference in survival among groups divided by the enhancement pattern on the previous CT examination.

Conclusions : Dynamic CT in 4-month intervals is an acceptable recurrence-monitoring strategy because it detects most recurrent nodules at a stage at which RF ablation is still feasible.

ABBREVIATIONS

AFP = alpha-fetoprotein, AFP-L3 = lens culinaris agglutinin-reactive fraction of AFP, DCP = des-gamma-carboxy prothrombin, HCC = hepatocellular carcinoma, RF = radiofrequency

Hepatocellular carcinoma (HCC) is a predominant malignancy in Japan, and its incidence is currently increasing in the United States and several European countries (1–3). Percutaneous tumor ablation (PTA) HCC offers important nonsurgical options with high rates of success that can preserve liver function (4–9). Radiofrequency (RF) ablation is among the most commonly used, providing an efficient technique with a high rate of local success (10–14). Nevertheless, recurrence of HCC is common, even with effective tumor ablation (15–18). Thus periodic surveillance is mandatory to diagnose and treat recurrent HCC. There are still varying perspectives regarding ideal postintervention imaging follow-up regimens (19,20).

Hyperattenuation in the arterial phase with hypoattenu-

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ation in the portal venous phase on dynamic CT or dynamic magnetic resonance (MR) imaging is considered a definite indicator of primary HCC (21–24), and pathologic examination is not necessarily required (16–18). Although no diagnostic criteria have been established for recurrent HCC, intrahepatic recurrence is usually diagnosed using the same criteria used for diagnosing primary HCC. However the diagnosis of HCC recurrence in the liver may be confounded by false-positive and false-negative results resulting from arterioportal shunts associated with previous treatments or from changes in hepatic perfusion as the underlying liver disease progresses. Conversely, considering the high recurrence rate, some nodules without typical radiologic findings (both arterial phase hyperattenuation and portal phase washout) may be more likely to be HCC requiring treatment.

We performed dynamic CT every 4 months after the initial treatment with ultrasound (US)-guided RF ablation for HCC (12) and adopted the same diagnostic criteria used for primary HCC. Nodules without typical radiologic findings in the liver were usually followed until typical findings appeared on the next CT examination. We then examined the radiologic features of recurrent HCC nodules on the CT images before deciding on the definite diagnosis and evaluated whether our surveillance protocol for intrahepatic recurrence was acceptable for the treatment of recurrence and for survival.

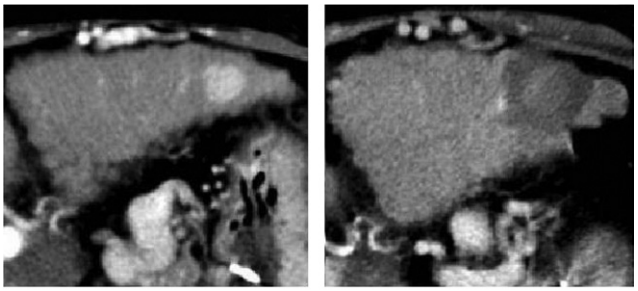
MATERIALS AND METHODS

Patients

The enrollment criteria for the current study were as follows: *(a)* patients with treatment-naive HCC treated by US-guided percutaneous RF ablation between February 1999 and December 2004, *(b)* patients in whom complete necrosis was confirmed by CT, and *(c)* first intrahepatic tumor recurrence diagnosed between January 2005 and December 2006. We excluded those who were followed by using dynamic MR imaging because of allergy to CT contrast media or impaired renal function, because the aim of this study was to evaluate CT follow-up protocol. We also excluded patients whose recurrence was considered to be local tumor progression of an initially ablated nodule. This research was approved by the ethics committee of the institution (Registration No. 2058).

Diagnosis of Primary HCC

HCC was diagnosed using dynamic CT and was defined as hyperattenuation in the arterial phase with washout in the portal venous phase based on Japanese Clinical Practice Guidelines for HCC (25). For patients diagnosed by tumor biopsy, the pathologic grade was based on Edmondson-Steiner criteria (26).



a. **b.**

Figure 1. Images before and after RF ablation (RFA). **(a)** A single HCC nodule, 13 mm in diameter, is diagnosed. **(b)** After complete ablation, the nodule is visualized at the center of the ablated area in the liver.

RF Ablation Indications and Techniques

RF ablation was the treatment of choice in patients with HCC who satisfied the following criteria: *(a)* ineligibility for surgical resection/liver transplantation or refusal of surgery, *(b)* no extrahepatic metastasis/vascular invasion, and *(c)* no other malignancies that could determine the patient's prognosis (27). Indication criteria for RF ablation were as follows: total bilirubin concentration less than or equal to 3 mg/dL, platelet count greater than or equal to $50 \times 10^3/mm^3$, and prothrombin activity greater than or equal to 50%. Patients with portal vein tumor thrombosis, refractory ascites, or extrahepatic metastasis were excluded. In general, we performed RF ablation on patients with Child-Pugh class A or B, a single tumor less than or equal to 5 cm in diameter, or three or fewer tumors less than or equal to 3 cm in diameter. However we also performed ablation when it was thought that it would be clinically effective (28) and was not being used as a bridge to transplantation.

The precise techniques of RF ablation are described elsewhere (12,27,28). Briefly, all RF ablation procedures were performed percutaneously under US guidance (Power Vision 8000, Aplio XV, or Aplio XG; Toshiba, Tokyo, Japan). After administration of sedatives and local anesthesia with pentazocine (30 mg), hydroxyzine (25 mg), and atropine (0.5 mg), a 17-gauge cooled-tip electrode (Cool-tip RF Ablation System; Covidien, Mansfield, MA) was inserted. The equipment was connected to a 500-kHz RF generator (Radionics, Burlington, MA), which produces 200 W at 50 Ω of impedance. RF energy was delivered for 6–12 minutes for each application. Percutaneous ablation was performed in more than one session when necessary.

Treatment efficacy was evaluated by dynamic CT performed 1 to 3 days after ablation. CT images were obtained after axial reconstruction with a slice thickness of 5 mm. Complete ablation was defined as hypoattenuation of the entire tumor on dynamic CT. Whenever possible, we ablated not only the tumor but also some surrounding liver parenchyma to make sure that no viable tumor cells would remain (27). We confirmed complete ablation in all slices on which a target nodule was visualized (**Fig 1**). In the case of incomplete ablation, patients underwent