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Original Article

Radiofrequency ablation of hepatocellular cancer: Complication and residual tumor rates

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Abstract

Aim: To investigate the feasibility, technical success and complication rates of RF ablation in hepatocellular carcinoma (HCC).

Material and Methods: 34 patients (26 male, 8 female) with HCC who underwent percutaneous RF ablation were analyzed, retrospectively. In order to diagnose HCC, using criteria defined by American Association for the Study of Liver Diseases guidelines and the inclusion criteria were determined according to Barcelona criteria. Ultrasound (n=24) or CT (n=10) were used as guideline imaging method for ablation. All ablation procedures were performed with a monopolar ablation device. The successful procedure was defined as the tolerance of patient and completion of the RF ablation with normal vital sing. Technical success was defined as the lack of residual tumor on the follow-up imaging at one month. Residual tumor and complication rate were recorded in each patient.

Results: The procedure was successfully performed in all patients (100%). There was a residual tumor in just one subcapsular localized lesion (2.9%). The technical success rate was 97.%. As a major complication in 2 patients (5.9%), pneumothorax was detected. There was no procedure-related mortality.

Conclusions: RF ablation was a safe and an effective treatment for HCC, with high technical success rates and low complication rates.

Keywords: Hepatocellular Carcinoma; Radiofrequency Ablation Treatment; Complication rate; Technical Success Rate.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth most common cancer type in the world and the second most common reason of death due to cancer (1). Liver transplantation or resection is the only curative treatmentfor HCC. However, multifocal distribution, insufficient hepatic reserve, extra-hepatic disease and comorbidities decrease the chance of surgical treatments (2). Surgical resection could be performed in only 9%-27% of patients with HCC (3). Thus, minimally invasive local ablative treatments with lower morbidity and complication rates are becoming more important. Radiofrequency ablation (RF), one of the local ablative treatment modalities for HCC, can be performed percutaneously, laparoscopically and intra-operatively according to tumor localization and patient status (4). During RF ablation high-frequency alternating current electrodes are utilized. The increased heat produced by those electrodes within the tumor causescoagulation necrosis (5).The heat increase and the prevention of increased heat within the tumor are essential for tumoral necrosis. And an important disadvantage of RF ablation is the insufficient heat increase and insufficient duration of that heat increase in large or subcapsular tumors (5).

RF ablation is superior to surgery in terms of lower morbidity and lower complication rates. In addition, surgical resection and RF ablation had similar overall survival and disease-free survival rates in the treatment of early stage HCC (<2 cm) (6). Thus, RF ablation is an alternative treatment option to surgery for early stage HCCs and it can assist in curative treatment and can be used as a bridging option for transplantation (7).

In the current study; we aimed to investigate the feasibility, technical success, complication rates and safety of RF ablation in HCC.

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MATERIALS AND METHODS

One author reviewed all patients' medical records on hospital data systems and picture archiving communication systems (PACS), retrospectively.

Patients

Between March 2011 and December 2014, written informed consent was obtained from all patients prior to treatment.Thirty fourpatients (26 males, 8 females) with HCC who underwent percutaneous RF ablation were analyzed. Diagnosis of HCCs was established based on criteria defined by American Association for the Study of Liver Diseases guidelines (8). Single tumor smaller or equal to5cm, 3 tumors smaller or equal to 3 cm, HCCs without major vascular invasion and patients withChild-Pugh class A or B cirrhosis were the inclusion criteriaaccording to Barcelona criteria (8). The exclusion criteria were life expectancy less than 6 months, HCCs with major vascular invasion, refractory coagulopathy, tumor size greater than 5 cm and patients with extrahepatic metastasis. This retrospective study was approved by the institutional ethics committee.

Pre-ablation assessment

All patients were evaluated with complete blood count and coagulation parameters before the procedure. Anti-aggregant and anti-coagulant agents were interrupted at least 3 days before the RF ablation. Patients with platelet count less than 50000/mm^3 and INR values above 1.5 were not performed RF ablation.Prophylactic antibiotics were not used in any patient. For lesion detection, contrast-enhanced CT or MR was utilized. According to lesion localization, the imaging modality used during RF ablation was selected.

Ablation

RF ablation was performed under ultrasound (Toshiba Xario™, iStyle™, 2010, JAPAN) guidance with 3.5 MHz convex probes or CT (GE, LightSpeed Ultra 8 Slice, 2002, USA) guidance (CT parameters were 50 mAs, 120 kV, 1.25 – 0.625 mm slice thickness). Ablation was performed by an experienced radiologist. For sedoanalgesia fentanyl citrate (1 mg/kg) and midazolam hydrochloride (0.010-0.030 mg/kg) were given intravenously.

In all patients, 14 gauges 15 cm expandable RF ablation device (StarBurst® XL RFA, RITA Medical Systems, Angiodynamics Inc, USA) and radiofrequency generator (RITA model 1500X) were used. For adequate ablation, target tissue temperature was adjusted to 105°C. In order to ablate optimally, a peritumoral normal parenchymal necrosis of 0.5-1 cm was aimed. The necrosed tissue volume during RF ablation is geometrically the volume between the 0.5 cm proximal to the end of the trocar and the 0.5 cm distal to the central electrode.Thus, the ablation electrode was placed more proximally avoiding central placement. Active electrode tip length was determined according to the tumor dimensions. If the tumor was smaller than 2 cm or between 2 to3 cm or 3 to 4 cm or 4 to 5 cm an active tip of 2 cm, 3 cm, 4 cm, and 5 cm was used, respectively. In all patients tract ablation (generator power setting with 60 W and target temperature 60°C) with 0.5 cm intervals was performed to avoid tumor seeding and to control local hemostasis.

Assessment of Procedure Feasibility and Technical Success

The successful procedure was defined as the completion of the RF ablation procedure and the patient's tolerance. The RF ablation procedure was terminated when 105 degrees Celsius achieved which is necessary for tumoral necrosis in each active electrode and this was described as a complete RF ablation.The patient's tolerance was defined as the absence of1) decreased oxygen saturation, 2) tachycardia, 3) severe pain despite sedoanalgesia during RF ablation procedureTechnical success was defined as the lack of residual tumor on the follow-up CT or MR at one month. All follow-up CT or MRIs were obtained dynamically following intravenous contrast material and all images were compared with the pre-procedural ones.Therapeutic response was evaluated according to the Working Group on Image-Guided Tumor Ablation (9) criteria as; (a) lack of enhancement in the ablation zone except for peri-ablational reactive enhancement (b) smooth ablation zone margins, (c) the dimensions of the ablation cavity greater than the pre-procedural tumor dimensions.

Complications

Complications were defined according to the Working Group on Image-Guided Tumor Ablation criteria[9]. Major complications were defined as situations causing extended morbidity and minor complications were defined as the all other entities.

Statistical Analysis

Statistical analyses were assessed with SPSS (Statistical Package For Social Sciences for Windows v.15.0, SPSS Inc. Chicago, IL). Categorical variables were evaluated with Pearson's Ki-Square testand Fisher's Exact Test. P<0.05 was defined as statistically significant.

RESULTS

The results were summarized in Table 1a and 1b.

Table 1 a. Patients' characteristics

Characteristics	Value
Age (year)	
Mean (y) / ± SD	66.18±8.50
Median (y)	67
Range (y)	47-80
Sex	
Male	26 (76.5 %)
Female	8 (23.5 %)
Etiology of cirrhosis	
Hepatitis B	21 (61.9 %)
Hepatitis C	8 (23.5 %)
Hepatitis B and Delta	3 (8.8 %)
Alcoholism	1 (2.9 %)
Autoimmune hepatitis	1 (2.9 %)

*US: Ultrasound, **CT: Computed Tomography

Table 1 b. Lesions' characteristics	
Tumor size	
Mean (cm) / SD	2.44±0.74
Median (cm)	2.45
Range (cm)	1-4.20
No. of tumors	
≥2 cm	28 (82.4 %)
< 2cm	6 (17.6 %)
Tumor localization	
Segment 2	4 (11.8 %)
Segment 4	7 (20.6 %)
Segment 5	5 (14.7 %)
Segment 6	7 (20.6 %)
Segment 7	5 (14.7 %)
Segment 8	6 (17.6 %)
Guidance modality	
Guidance modality	
US*	24 (70.6 %)
CT**	10 (29.4 %)
No. of residual tumor	1(2.9%)
No. of pneumothorax	2 (5.9 %)
***US: Ultrasound, **CT: Computed Tomography**	

Patients

Thirty fourpatients with HCC with a mean age of 66.18±8.50 years (range 47 to 80 years). Twenty four (70.6%) HCC lesions were ablated under ultrasound guidance and 10 (29.4%) lesions were ablated under CT guidance in a single session. There was no additional session and all of the procedures were performed percutaneously. The mean tumor diameter was 2.44±0.74 cm (range 1.00 to 4.20 cm).

Procedure Feasibility and Technical Success

RF ablation procedure was completed in all patients (100%). All of the patients tolerated the procedure without a deterioration in vital signs. Technical success was 97.1%. There was a residual tumor in just one patient (2.9%) and regarded as insufficient ablation (Figure 1).

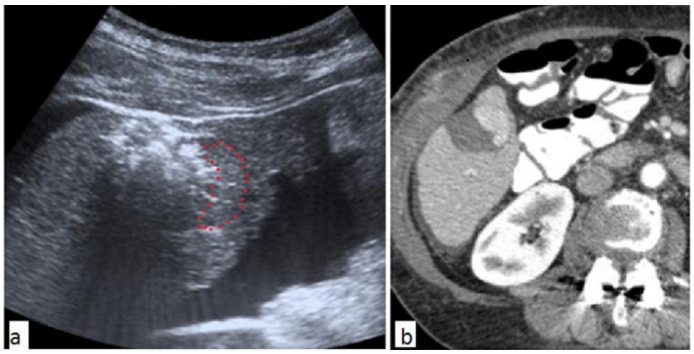

Figure 1. a. US image shows that the tips of an expandable electrode within the subcapsular lesion. There is no active electrode in the dotted field and gas bubbles which is the indicator of the ablation. **b.** Same patient as in (a) 1 month after ablation, abdomen contrast-enhanced CT, arterial phase, nodular rim enhancement indicates residual tumor present.

That patient had a subcapsular HCC located on segment 5 and the tumor diameter was 3.5 cm. Also, there was massive ascites. When the procedure images were evaluated retrospectively, it was detected that the RF active tips were not extending into the residual tumor part. There were also no gas bubblesaround the residual tumor sitewhich is the indicator of the tissue burning.

Complications

There was no procedure-related mortality. As a major complication in 2 patients (5.9%), pneumothorax was detected.Both patients had the HCCs on the dome of the liver and CT was used for guidance.

DISCUSSION

In the current study, patients with HCC were treated by monopolar RF ablation with a high procedural success (100%), a high technical success (97.1%) and a low complication rate (5.9%). Nopatient had deterioration of vital signs during the procedure. However, Kim et al. (10) reported that 0.3% of the 1482 patients with HCC treated with RF ablation, could not complete the procedure because of the worsening vital signs. Seror et al (11) found only one patient out of 24 patients, having procedure intolerance. The high procedure tolerance rate in the current study was obviously due to the small sample size. With an increasing number of patients, the procedure intolerance rates will come closer to the literature.

In this study the residual tumor was detected in just one patient (2.9%) on 1-month-follow-up imaging. Tumor size, localization (subcapsular-nonsubcapsular) and proximity to major vessels can be listed as a reason for inadequate ablation. The tumor size and the location of the tumor may be the most important factors (12). In-vivo studies demonstrated that the more distant to the active electrode the lesser the heat increase within the tumor. Thus, in monopolar RF ablation devices only 3 to 4 cm effective ablation zone was occurred (13,14), and in a large meta-analysis, the curative effect of RF was found to be less in HCCs greater than 2 cm (15). In other words, the larger the tumor the more the insufficient ablation (16). Similarly, in the current study the medium size group (3-5 cm) had the case of inadequate ablation. Because of the lack of larger number of patients within the different-tumor-sized groups and residue tumor, statistical analysis could not be made for insufficient ablation. But tumor size was not the only reason, also the subcapsular location might be a reason for residual tumor. To avoid capsular damage and hemorrhagic complications, the RF electrodes were not placed optimally within the tumor. It can be tried that some alternative techniques including artificial pneumothorax, pleural effusion, and ascites for treating tumors located in the subcapsular location like in other high-risk located lesions might be used to increase the response to ablation therapy. However, in an article by Kang et al (17), the authors described in the subcapsular group, use of hydro-dissection for tumors in a high-risk location had a higher cumulative local tumor progression rate (34.4%) than that of nonuse (20.4%) at 5 years. Nevertheless, subcapsular

location was not an independent factor for poor prognosis in patients with HCC (17). So, although it is technically difficult to place RF electrodes accurately complete ablation by helpful alternative techniques including hydro-dissection methods when necessary is crucial for subcapsular lesions.

In this study, there was no procedure-related mortality and in the literature, it was found to be less than 1% (18). The number of tumoral lesions, tumor size, and location, interventionalist experience and the level of liver disease are the main entities causing complications. During RF ablation, hemorrhagic, infectious, biliary complications or liver failure, vascular damage, skin burn, tract seeding and pneumothorax can be observed (18). Subdiaphragmatic localization and transthoracic access are actually the independent risk factors increasing the possibility of pneumothorax (19). Although, the incidence of pneumothorax was reported as 0.3% in the literature, especially with the transthoracic access that complication rate rises to 7.7% (19,20). Also in the current study, pneumothorax rates were 5.9%. This patientswere treated with tube-thoracostomy. The possibility of requiring treatment pneumothorax should be considered in patients who were planed transthoracic ablation. For this reason, a pulmonary function test can be added to pre-procedural assessment in these patients to avoid respiratory failure caused by the pulmonary collapse. Furthermore, to decrease risk of collateral thermal injury to adjacent structures including hepatic capsule, lung, and gastrointestinal tract, some techniques for treating tumors located in the high-risk locations including artificial pneumothorax, artificial pleural effusion, artificial ascites, oblique approach under the guidance of CT-multiplanar reformation images, and CT fluoroscopy technology might be used (21-24).

There were limitations in the current study. First of all, the patient number was very small to identify predictive factors and this was restricting the statistical analysis. Secondly, only the monopolar RF ablation devices were used and multipolar devicesmay have a different number of residual tumors and complication rates.Retrospective design of the study, lack of randomization and lack of control group for comparison with surgery were the other limitations.

CONCLUSIONS

In conclusion, RF ablation was a safe and effective treatment modality for HCC, with high technical success rates and low complication rates.

Competing interests: The authors declare that they have no competing interest.
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Ethical approval: This retrospective study was approved by the institutional ethics committee.

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