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ORIGINAL ARTICLE

Percutaneous imaging-guided radiofrequency ablation of small renal cell carcinoma: techniques and outcomes of 24 treatment sessions in 18 consecutive patients

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Summary

Purpose: *To evaluate the early clinical experience associated with percutaneous imaging-guided radiofrequency ablation (RFA) in patients with renal cell carcinoma (RCC).*

Methods: *Eighteen consecutive patients with RCC were treated with percutaneous RFA sessions (24 sessions for 19 solitary RCC in 18 patients: 15 patients underwent a single RFA session, 3 had 2 sessions and one 3 sessions). Treatment indications were localized, solid renal mass <4.5 cm, comorbidities precluding surgery, high operation risk, and refusal to perform surgery. During 23 sessions, RFA was performed using computed tomography (CT) guidance and in one session it was guided by ultrasonography. The average patient age was 76.8±7.6 years (range 64-89), and the average renal mass size 3.3 ±0.7 cm (range 2.0-4.5). Follow-up imaging was performed at 3- and 6-month intervals and yearly thereafter. Successful treatment was defined as lack of enhancement of the treated region on follow-up CT studies.*

Results: *RFA was technically successful in all patients. After the last imaging control, 17 of the 19 tumors were completely necrotic according to the imaging criteria (the secondary clinical success rate was 89.5%). Thirteen tumors were not visible on the first follow-up imaging control (the primary clinical success rate was 68.4% - 13 of 19). In 4 of the 6 patients residual tumors were successfully re-ablated, while in 2 patients repeated RFAs were not performed at the time of writing this report. Five patients (20.8%) developed treatment-related complications, including mild pain, large perirenal abscess, mild perirenal hematoma and transient elevation of the white blood cell count. The mean follow-up period was 25.3±16.8 months (range 1-51).*

Conclusion: *RFA is effective and safe treatment option of exophytic RCC <5 cm in diameter in patients not suitable for surgery due to serious concomitant diseases or advanced age.*

Key words: radiofrequency ablation, renal cell carcinoma, small size, treatment

Introduction

RCC is frequently discovered incidentally in asymptomatic patients due to increasing use of imaging techniques [1]. Previous studies have found that kidney tumors measuring < 4 cm in diameter are generally not associated with metastasis [2]. At the same time, recent advances have led to the use of nephron-sparing surgery techniques, such as a partial nephrectomy or laparoscopic nephrectomy in selected patients with small renal tumors [3]. The traditional surgical treatment is not ideal for treating all tumors because some patients are unable or unwilling to undergo surgery or would have limited or no functional renal tissue remaining after surgery [3,4]. There is increasing evidence that percutaneous RFA can be a curative treatment with minimal morbidity for selected patients with RCC. Percutaneous image-guided RFA offers advantages over surgical methods including minimal invasiveness, potentially lower mortality and morbidity, shorter hospital stay, and faster recovery. However, the majority of published patient series had limited follow-up, so even medium-term (>2 years) efficiency of the technique needs evaluation. The recurrence rate of tumors with complete ablation on early imaging studies is still unknown. Although the complication rate seems low, some severe thermal injures to the collecting system have been reported [4-9].

The purpose of this study was to review our 4-year experience with RCC patients submitted to RFA.

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Methods

Patients

We retrospectively reviewed all patients submitted to percutaneous imaging-guided RFA of RCC at the Clinical Institute of Radiology, University Medical Centre Ljubljana, Slovenia, between January 2006 and June 2010. Our study included 24 RFA sessions performed on 19 renal tumors in 18 patients. The diagnosis of RCC was based on fine needle biopsy results in 6 renal tumors. The remaining 13 renal tumors were diagnosed by CT, when the results were consistent with RCC. Existence of secondary deposits was evaluated by CT of the abdomen, chest CT or chest radiograph, and in some cases by radionuclide bone scanning, depending on the preference of the referring urologist. The indications for nonsurgical treatment were high surgical risk (n=13), bilateral renal cell carcinomas (n=1), solitary kidney (n=3), and presence of metastatic disease (n=1). Significant concomitant diseases contributing to high surgical risk included chronic renal insufficiency, congestive heart failure, insulin-dependent diabetes mellitus, chronic obstructive pulmonary disease, or other primary malignancy. The tumors were classified as exophytic when >25% of the tumor diameter contacted the perirenal fat, parenchymal when limited to the parenchyma, and central when the tumor extended into the renal sinus. The presence of coagulopathy disorders was excluded, and routine laboratory tests (levels of hemoglobin, hematocrit, WBC, blood urea nitrogen, and serum creatinine) were obtained before and after RFA in all cases. Informed consent for the procedure was also obtained from all patients. Review of our study by the Institutional Review Board was not made, because it was not required for retrospective studies at the University Medical Center Ljubljana.

Among our patients there were 11 men and 7 women with an average age of 76.8±7.6 years (range 64-89). Tumor size ranged from 2.0-4.5 cm, with average size of 3.3±0.7 cm. Twelve tumors (63.2%) were located in the left kidney (upper pole, n=2; lower pole, n=4; interpolar, n=5) and 7 tumors (36.8%) were in the right kidney (upper pole, n=2; lower pole, n=3; interpolar, n=2). Seventeen (94.7%) of the 19 tumors were classified as exophytic and the remainder were parenchymal. The patient characteristics are summarized in Table 1.

Treatment

We defined an ablation session as the sum of ablations used for the treatment of one tumor during one encounter. During one ablation session, more than one RFA was often used to treat a tumor, with multiple overlapping ablations used for tumors 4-4.5 cm. One patient had ablations of 2 bilateral tumors. One patient with single persistent tumor received 2 follow-up RFA sessions and 3 patients received 1 follow-up ablation session. In total, 24 RFA sessions for 19 renal tumors in 18 patients were conducted. All 24 percutaneous RFA treatments were performed by two experienced interventional radiologists under general anaesthesia. RFAs were performed

Table 1. The study patient characteristics

Patient number	*Age (years)/Sex*	*Indication*	*Kidney*	*Tumor size (mm)*	*Tumor location*	*Method for making diagnosis*	*Approach*
1	77/F	HSR	L	35	Ex	CT	CT
2	80/M	HSR	L	35	Ex	CT	CT
3	89/M	BRC	R/L	40/30	Ex	CT	CT
4	79/m	SK, C	L	45	Ex	Biopsy	US
5	64/F	SK, C	R	40	Ex	Biopsy	CT
6	83/F	SK, C	L	45	Ex	CT	CT
7	76/M	HSR	R	36	Ex	CT	CT
8	78/M	HSR, C	L	31	Ex	CT	CT
9	85/F	RS, HSR	L	30	Ex	CT	CT
10	73/M	HSR, C	L	38	Ex	CT	CT
11	79/M	HSR	L	27	Ex	CT	CT
12	60/M	C, CM	R	30	Par	Biopsy	CT
13	66/F	HSR	L	28	Ex	CT	CT
14	80/F	HSR	R	30	Par	CT	CT
15	82/M	HSR	R	30	Ex	CT	CT
16	77/F	HSR	R	40	Ex	Biopsy	CT
17	75/M	HSR	L	22	Ex	Biopsy	Combeam CT
18	75/M	HSR	L	20	Ex	Biopsy	Combeam CT

HSR: high surgical risk, CM: comorbidities, SK: single kidney, BRC: bilateral renal tumor, C: cancer, RS: refusal of surgery, Ex: exophytic, Par: parenchymal, CT: computerized tomography, US: ultrasonography, L: left, R: right by 150 W generators (RITA Medical System, AngioDynamics, UK), using expandable needle systems (RITA Medical Systems StarBurst XL, Mountainview, CA). No prophylactic antibiotics were administered. A small 17 gauge needle was inserted into the lesions with the help of CT, Combeam CT, or ultrasound guidance. At maximum deployment, the device induces an ablation sphere of 5 cm in diameter. Because the maximum size of the target tumors was 4.3 cm, the ablation protocol was always planned with the aim to destroy the visible tumor mass plus at least a 0.5 cm safety margin around the tumor. Tract ablation was performed at the end of treatment. Each treatment took about 8 min to perform.

Follow-up

After the RFA session and a brief period of observation in the postoperative anaesthesia care unit, the patients were transferred to the urology ward for overnight observation, and further care. In order to follow eventual complications, these were previously defined. Therefore, a mild perirenal hematoma was defined as bleeding area with diameter < 1 cm on imaging, and a moderate hematoma was defined as bleeding area with diameter >1 cm, but not requiring transfusion.

A follow-up ultrasound was performed one day after the procedure to assess periprocedural complications. CT was performed after 1 and 3 months to assess eventual complications and clinical effectiveness. In addition, follow-up CT was performed after 6 and 12 months, and then yearly to detect any new areas of enhancement or an increase in lesion size in the ablated tumor region. Successful treatment (complete tumor necrosis) was defined as lack of enhancement of the treated region on follow-up CT studies. Images were also reviewed for the presence of any new secondary deposits or new renal tumors. Recurrence of a tumor was defined as new CT enhancement developing after previous CT study demonstrating complete necrosis. No patient in our study has developed detectable secondary deposits after RFA of a renal tumor. No patient was lost to follow-up. The mean follow-up period was 25.3±16.8 months (range 1-51).

Results

The procedure was technically successful in all patients (100%). After the last imaging control, 17 (89.5%) of the 19 tumors were completely necrotic according to the imaging criteria (Figure 1). Over the radiologic follow-up period, 13 of 19 tumors were successfully treated with one RFA session, and 3 tumors from 3 patients re-

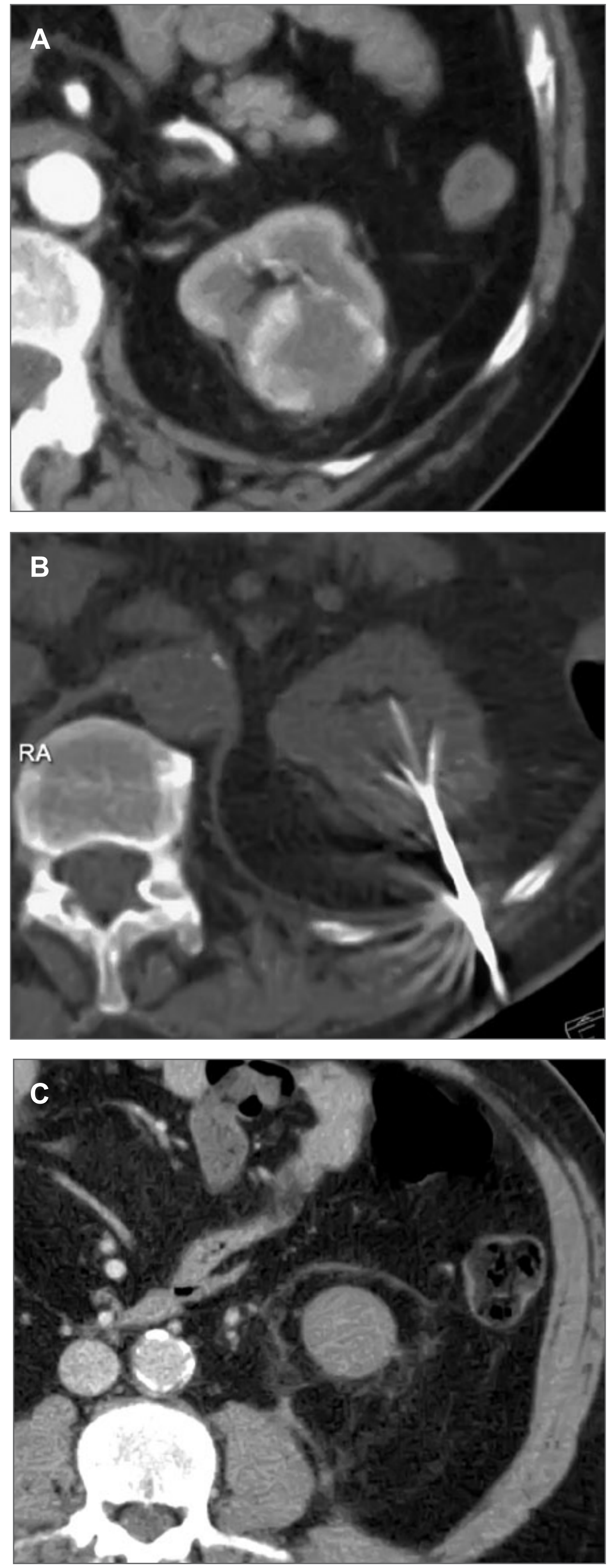

Figure 1. RFA of renal tumor. **A:** CT image of a 3-cm solid renal mass incidentally detected on ultrasound in an 81-year-old man with severe cardiovascular disease. The patient was considered to be poor candidate for surgery. Therefore, RFA was elected as minimally invasive alternative. **B:** CT image demonstrates a single RF electrode in the mass. **C:** One-year follow-up contrast-enhanced CT scan demonstrates no areas of abnormal contrast.

quired more than one session, based on their follow-up CT scan results. One tumor required 3 sessions, as a result of persistent enhancement within the tumor. Also, 6 tumors from 6 patients required change of the electrode's position during RFA, due to the large size of the tumor. Thirteen tumors were not visible on the first follow-up imaging control. Thus, the primary clinical success was 68.4% (13 of 19). In 4 of 6 patients residual tumors (3.8, 4.0, 4.2 and 4.5 cm in diameter, respectively) were successfully re-ablated. At the time of writing this report, one of the patients still has primary tumor visible (4.5 cm in diameter) with secondary pulmonary deposits, and one patient refused a second RFA. Thus, the secondary clinical success rate was 89.5% (17 of 19).

Complications recorded within the first 24 h were mild pain (n=1), large perirenal abscess (n=1) mild perirenal hematoma (n=1) and transient elevation of the WBC count (n=2). The remaining 19 ablation sessions passed without complications. The patient with large perirenal abscess required drainage and his stay in hospital was prolonged. The small perirenal hematoma resolved spontaneously. No additional complications were found on further follow-up of the patients. The length of hospital stay was < 48 h after 19 ablation sessions, 4 days for 4 ablation sessions, and 16 days for one session. Hospitalization was prolonged over 2 days only for patients with serious concomitant diseases requiring hospitalization for reasons other than ablation-related problems. No procedure-related death occurred. The RFA results are summarized in Table 2.

Table 2. RFA results

Patient number	*Number of sessions*	*Number of electrode repositions*	*Follow-up duration (months)*	*Compli-cations*	*Follow-up response*
1	1	1	51	None	CR
2	2	2	50	None	CR
3	1/1	2/1	49	None	CR
4	2	1	37	WBC	PR
5	2	1	32	None	PR
6	3	2	32	None	CR
7	1	2	29	Abscess	CR
8	1	2	28	None	CR
9	1	1	28	WBC	CR
10	1	2	28	None	CR
11	1	1	26	Hematoma	CR
12	1	2	24	None	CR
13	1	1	24	Hematoma	CR
14	1	1	7	None	CR
15	1	1	5	None	CR
16	1	1	3	None	CR
17	1	1	1	None	CR
18	1	1	1	None	CR

CR: complete response, PR: partial response, WBC: transient elevation of white blood cells

Discussion

For the past 50 years, the standard of care for RCC had been radical nephrectomy. Recently, partial nephrectomy has been shown to be equivalent to radical nephrectomy for curing small low-stage RCC, indicating that renal-sparing procedures can be curative [2,3]. However, nephrectomy is not suitable for many patients, such as those who cannot tolerate surgery because of serious concomitant diseases. Alternative treatments that spare renal parenchyma are currently being studied to provide options for those patients who are at high risk for surgical complications. The trend toward less invasive RCC treatments is at least partly due to much earlier diagnosis of RCCs in the course of the disease today.

Percutaneous RFA of malignant tumors has been developed as a feasible option for patients with primary and metastatic hepatic lesions that are not good candidates for traditional surgery [5]. This approach may have a role in the management of renal tumors, too. One report with long-term data following RFA concluded that the RFA technique was the most successful treatment of small exophytic renal tumors [6].

Tumor size and location are the two most important factors that govern whether RCCs can be treated successfully by RFA. Because heat decreases exponentially from the RF source, large tumors (>5 cm in diameter) pose significant challenge for RFA, especially because 0.5-1.0 cm "ablation margin" surrounding the tumor is also necessary. In general, RCCs that are ≤3 cm in diameter are ideal for ablation, with near-perfect success rates on post-procedural imaging [7,8]. The majority of tumors < 3 cm could be treated by RFA successfully in a single session. Tumors between 3.0-3.5 cm in diameter can also be treated successfully with confidence, but multiple RFA sessions may be required. In general, RFA of tumors > 4-5 cm is currently avoided, and patients are considered for surgical resections. In addition, even small tumors located in the more vascularized central areas of the kidney cannot be treated by RFA with certainty. Therefore, strategies that increase the success rate of tumor destruction by RFA, even for small lesions, are needed.

The location of the tumor (exophytic, parenchymal, or central) also influences the RFA results. Even large exophytic tumors are almost always treated successfully, with ≥70% requiring only a single RFA session [8-10]. Parenchymal tumors may be more difficult to treat, but RFA of centrally located tumors has the lowest success rate. The presence of central component in a tumor > 3 cm is reported to be a significant predictor of failure. Analysis of tumor location in our patients showed that many lesions (17/19) were exophytic (>25% of the tumor margin in contact with the perirenal fat). Two lesions were mixed (margins adjacent both to the renal sinus and perirenal fat), and none of the lesions in our patients was purely central (tumor abutting on the renal sinus fat and limited to the confines of the renal contour). We treated 19 of 21 tumors without consideration of cortical location of a tumor as contraindication for the treatment. Only two patients referred for renal RFA could not be treated because their exophytic lateral tumor mass was adjacent to the descending colon. Thus, we found that the majority of patients with solid renal masses are candidates for this procedure.

We usually performed a RFA using percutaneous CT guidance. At the introduction of the RFA in our institution, a percutaneous ultrasound-guided approach was performed in one patient. However, we later preferred CT guidance because the electrode is more reliably placed, and the production of gas at the ablation site does not obscure the lesion for additional treatments. Consequently, an overlapping ablation was always easily performed by re-positioning of the electrode. During one ablation session, more than one RFA was often used to treat a tumor, with multiple overlapping ablations used for larger tumors.

One advantage of RFA is the low rate of serious complications. Several studies have shown that RFA of RCCs has minimal complication rate (7-17%) [10-13]. Major complications are remarkably rare with their incidence ranging from 0-4% [13-20]. The most commonly reported major complication associated with percutaneous RFA is hemorrhage. Perirenal hematomas often look worse at imaging than at clinical examination and often resolve spontaneously without treatment. Hematuria occurs rarely, is self-limited, and resolves within 24 h of treatment [19,20]. Gross hematuria causing obstruction and requiring stenting is extremely rare. Because of the kidney's location, care must be taken to avoid thermal injury of the adjacent bowel. At least 5 mm of intervening fat should be present between bowel and the target tumor to avoid bowel necrosis [13,18,19]. Fat is an effective insulator, and 5 mm or more is thought to be adequate protection for the adjacent bowel. If bowel abuts on the tumor to be treated, sterile water can be injected to displace the bowel and allow for safe ablation of the RCC. Ablation of renal tumors adjacent to the adrenal gland can cause sudden release of vasoactive catecholamines. For ablation of these tumors, the operator should be prepared to administer α-adrenergic blocking medications. The risk of clinically significant thermal injury to liver or spleen, when ablating a RCC, is thought to be insignificant. Even in the treatment of central tumors, the development of clinically important renal sinus damage has been rarely reported [13,14]. Our study showed that after 24 treatment sessions, 5 (20.8%) patients had mild or moderate complications. Although the complication rate was higher (20.8%) in our study than that reported by others (7-17%) [10-13], this finding seems to be largely attributable to the abnormalities that are counted as complications. No long-term or clinically significant complications occurred. We did detect transient elevation of the WBC in two sessions, presumably because of demarginalization of these cells caused by the stress of the ablation procedure. Renal RFA was generally well tolerated by our patients, who required only minimal oral pain medication post-treatment.

The major reason for performing follow-up imaging after renal RFA is early detection of residual or recurrent tumor. Imaging after thermal ablation must be performed at regular intervals. Clinical factors may influence the choice of imaging (e.g. pacemaker precluding MRI or contrast agent allergy or renal insufficiency precluding CT); otherwise, within a clinical trial, the use of imaging modality should be uniform among longitudinal imaging sessions. Although the use of CT as the primary imaging modality is justified because of cost and availability issues, a substantial number of eligible patients cannot be exposed to iodine-containing contrast agents owing to pre-existing allergies or impaired renal function, with creatinine levels >2.0 mg/dL (176.8 mol/L). These patients are usually referred for contrast-enhanced MRI of the kidneys.

The endpoint for successful treatment was the absence of contrast enhancement on follow-up contrast-enhanced CT or MRI. Imaging immediately after the procedure can be difficult to interpret because peripheral inflammation may mimic the appearance of viable tumor. Lack of enhancement on imaging follow-up has generally been assumed to mean lack of viable tumor [4,11]. Any focal and nodular peripheral enhancement in the ablated lesion should be considered indicative of residual or recurrent tumor. The presence of residual disease on the follow-up scans does not necessarily indicate poor outcome for the patient, because residual tumor can be re-treated and there does not appear to be a high risk of systemic spread from residual tumor's nests. No patient in our or other published series has developed detectable secondary deposits after complete or incomplete renal tumor ablations. Hence we believe that lack of contrast enhancement on CT or MRI indicates tumor eradication, but further follow-up imaging is warranted because long-term results for renal tumor RFA ablation are lacking, and later scans should be used to detect metastatic or metachronous lesions. Although the optimal time for imaging follow-up has not been determined, we currently schedule the patient for dedicated renal contrast-enhanced CT (using 5-mm collimation) at 3- and 6-month intervals after the original RFA session. If there is no evidence of enhancement at 12 months, we then follow the patient yearly. The optimal time intervals for follow-up should be investigated in future studies.

Our study shows that RFA can be completed successfully in a high proportion of patients with small RCC. The safety profile of the procedure was also acceptable, with no mortality or life-threatening complications associated with RFA.

Despite our findings, this study had several limitations, including small patient sample size and relatively short follow-up period (25.3±16.8 months). Therefore, a long-term radiographic and clinical follow-up would be required to assess the true outcome of RFAs. In addition, histopathologic diagnosis was not confirmed in 13 renal tumors, although we know that > 90% of solid renal masses viewed on imaging studies are RCC. Finally, imaging follow-up were performed only with contrast-enhanced CT scans to determine the extent of an "unablated residual tumor".

Conclusion

RFA is effective and safe treatment option of exophytic RCC < 4.5 cm in diameter in patients not suitable for surgery due to serious concomitant diseases or advanced age.

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