Actas Urológicas Españolas

www.elsevier.es/actasuro

Original – Renal cancer

Radiofrequency ablation as an alternative treatment for organ confined renal tumor

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ARTICLE INFORMATION

Article history:
Received 29 March, 2010
Accepted 17 June, 2010

Keywords:
Renal tumor
Radiofrequency
Minimally invasive ablative techniques

A B S T R A C T

Introduction: We report our early clinical experience associated with radiofrequency (RF) ablation in patients with renal cell carcinoma (RCC) and evaluate the efficacy, tolerability and complicactions.

Material and methods: Retrospective review of patients treated in our hospital with kidney ecoguide RF. All of them diagnosed with renal tumor and not candidates for surgery because of bilateral tumor, significant comorbidity or refusal to surgical treatment. We used an Amitech® 220 Watts generator with an electrode tip of 3 cm, needles with a straight tip and a hooked tip. Controls were performed with axial tomography at 24h, 7 days, 1, 3 and 6 months and every 6 months thereafter.

Results: 11 tumors were found in 9 patients. The mean age was 76 years (63–85 years). The average tumor size was 3.5cm (2.2–5.8cm). In 2 tumors prior chemoembolization was needed. In a further two a new RF session was needed. In 9 tumors treatment was considered effective. Mean follow-up was 17.5 months (3–52 months). One patient had local recurrence at 14 months and needed a laparoscopic radical nephrectomy and two patients developed lung metastases 41.5 months after RF. There were no clinically relevant complications.

Conclusions: In our experience, we believe that RF is considered an alternative treatment for renal tumors with clinical stage T1 or T2 very symptomatic in patients in whom surgery is not possible, with acceptable results in the medium term, a good tolerance, reduced consumption of hospital resources and low complication rate.

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0210-4806/$ - see front matter

Ablación con radiofrecuencia como alternativa de tratamiento para el tumor renal localizado

Palabras clave:
Tumor renal
Radiofrecuencia
Tratamiento mínimamente invasivo

RESUMEN

Introducción: Presentamos nuestra serie inicial de tumores renales tratados mediante radiofrecuencia (RF) continua percutánea y evaluamos la eficacia, la tolerabilidad y las complicaciones de la técnica.

Material y métodos: Revisión retrospectiva de los pacientes tratados en nuestro hospital con RF renal ecoguiada. Todos diagnosticados de tumor renal y no candidatos a cirugía por tumor bilateral, comorbilidad importante o rechazo al tratamiento quirúrgico. Utilizamos un generador Amitech® de 220W con una punta de electrodo de 3 cm, agujas de punta recta y en gancho. Los controles fueron realizados mediante una tomografía computarizada toracoabdominopélvica a las 24 h, a los 7 días, al mes, a los 3 meses y a los 6 meses, y cada 6 meses después.

Resultados: Se hallaron 11 tumores en 9 pacientes. La media de edad fue de 76 años (63–85). La media de tamaño tumoral fue de 3,5 cm (2,2–5,8). En 2 tumores se necesitó de quimioembolización previa y en otros dos se necesitó una nueva sesión de RF. Hubo 9 tumores con tratamiento considerado como eficaz. La media de seguimiento fue de 17,5 meses (3–52). Un paciente tuvo persistencia de enfermedad a los 3 meses con necesidad de nefrectomía radical laparoscópica y otros dos tuvieron metástasis pulmonares a los 26,5 meses de media. No hubo complicaciones relevantes clínicamente.

Conclusiones: En nuestra experiencia, estimamos que la RF es un tratamiento considerado como una alternativa para los tumores renales de estadio clínico T1 o T2 muy sintomáticos, en pacientes en los que no es posible la cirugía, con unos resultados aceptables a medio plazo, una buena tolerancia, un escaso consumo de recursos hospitalarios y un bajo índice de complicaciones.

Introduction

Renal carcinoma is the third leading genitourinary tumor and accounts for 2% of all adult cancers. It is estimated that 54,390 new cases of the disease will occur next year, causing 13,010 deaths/year. Renal carcinoma is the most lethal of all genitourinary tumors, and adenocarcinoma is its most prevalent type (85%).

Annual incidence has increased by 130% since 1960. Such increase appears to be due to widespread use of imaging techniques such as ultrasound examination and computed tomography (CT).

Data from the United States Surveillance, Epidemiology, and End Results review show that 54% of renal tumors are organ-confined, 20% are locally advanced, and 25% of patients have disseminated disease at the time of diagnosis. Approximately 50% of patients with localized disease will develop metastasis, and 5 and 10-year cancer-specific survival rates are 65% and 56% respectively.[1]

Partial or radical nephrectomy for stage T1a localized disease (4 cm or less in size) achieves 5-year cancer-specific survival rates higher than 95%.[2-4]

A meta-analysis reviewing clinically localized tumors found an overall mean growth rate of 0.28 cm/year. Although growth rates greatly vary depending on the report, only 1% of lesions seen evolved to metastatic cancer after a median follow-up of almost 3 years.[5]

Clinical guidelines of the European Association of Urology advise conservative surgery for organ-confined tumors, provided their size and location allow for it. There are currently other minimally invasive treatments alternative to surgery for this disease.[5]

Percutaneous radiofrequency (RF) thermal ablation is a procedure where high frequency energy is used to induce cell death. RF conduction causes molecular friction, heat, denaturing , and coagulation, with the resultant tissue necrosis. RF has been used for treating solid organ tumors, mainly in the liver, since 1990.[6-9]

RF is an outpatient procedure requiring no general or regional anesthesia and inducing minimum morbidity.[10-12]

It was introduced in urology in 1997 for the treatment of renal tumors in patients with chronic renal disease, and is currently considered as an alternative treatment for organ-confined renal tumors in patients not amenable to surgery.[13-15]

Our initial series of patients with stage T1 and/or T2 renal tumors treated by percutaneous RF is reported.

Materials and methods

Patient selection and inclusion criteria

Retrospective review of patients with renal tumors treated with continuous RF at Hospital General de Castellón.

All patients were diagnosed with renal tumors based on imaging studies (US/CT and abdominal CT). Percutaneous fine needle biopsy was also performed in selected patients (in whom radiographic diagnosis was doubtful).

Patient inclusion criteria were significant comorbidity with high anesthetic or surgical risk, refusal of surgery, and presence of bilateral RCC.

Prothrombin time, partial thromboplastin time, complete blood count, and serum creatinine levels were assessed before and after RF in all patients.

The procedure was performed after general and specific informed consents were signed by the patients.

Tumor localization to program RF was performed using the following scheme:[12,13] the kidney was divided in a cephalocaudal direction into three thirds, each of which was in turn divided into four areas (posteromedial, posterolateral, anteromedial, and anterolateral). The position of each tumor on each of these 12 areas was categorized using the area containing the greatest volume of each tumor. The tumor was classified as exophytic, parenchymal and/or mixed based on the above described scheme. When a tumor was completely surrounded by renal parenchyma with no contact with perirenal fat, it was classified as a parenchymal tumor. Tumors where more than 25% of diameter was in contact with perirenal fat were classified as exophytic, while those contacting with renal sinus and perirenal fat were classified as mixed tumors.

Description of the procedure

Patients underwent ultrasound-guided percutaneous RF ablation under local anesthesia with 2% lidocaine combined with mild intravenous (IV) sedation and analgesia (midazolam and metamizole IV).

Patients were placed in a lateral or modified supine position depending on tumor location. They all required hospital admission. A 220 W (Amitech®) generator with a 3 cm-long electrode tip was used.

Needle tip morphology was selected by the specialist based on tumor size and location.

Ablation was performed for the time period recommended by the manufacturer (4-6 min pulses).

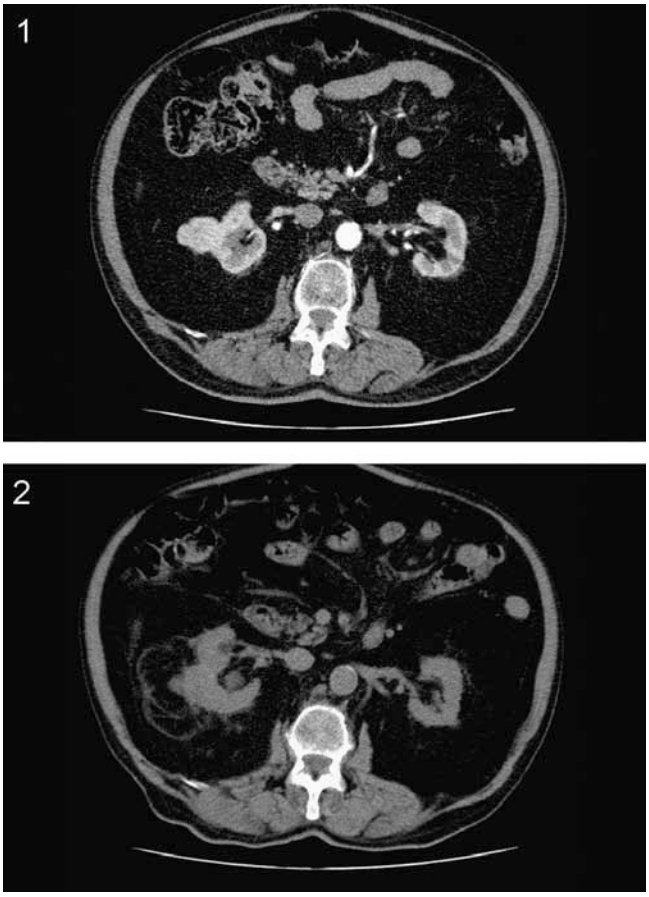
Tissue temperature was monitored throughout the process to prevent the temperature from falling below 50ºC at any time.

Patient follow-up

A contrast CT was performed 24 h, 7 days, and one, three and six months after the procedure (figs 1-3) and every six months thereafter to assess procedure performance and its efficacy, complications, and the need for repeat RF (depending on CT images one month after the procedure).

Assessment of treatment efficacy

The efficacy rate of the technique was defined as the percentage of tumor successfully eradicated after the initial procedure or in periods of additional sessions one month after treatment. Efficacy in the ablation area was defined as the decrease in contrast uptake in the area shown by radiographic images soon after ablation as compared to its radiological state before treatment (i.e. <20 HU for CT)



Figures 1 and 2 – Pretreatment image at 7 days and at 3 months respectively.

Figure 3 – Decreased contrast uptake as compared to pretreatment image.

(fig. 3). Perilesional contrast uptake with a thin line, in concentric circles in the CT with IV contrast after treatment, was considered to be indicative of a benign condition, and radiographic improvement was defined as an irregular, eccentric, scattered, or nodule contrast uptake.

Analysis of the procedure

Patient characteristics, procedure time, process temperature, ablation time, hospital stay, analgesia requirements after the process, and periprocedural complications in the early (first 24 h) and late postoperative period (in the next month) were recorded.

Results

From January 2005 to January 2010, 11 renal tumors were treated in 9 patients (5 female and 4 male patients). Mean patient age was 73.5 years (range, 63–85).

Six of the nine patients had significant comorbid conditions (high anesthetic risk >2), two had bilateral tumors, and one refused surgery.

All tumors biopsied were found to be renal cell adenocarcinomas.

Of the 11 tumors, eight were exophytic, two parenchymal, and one mixed (table 1).

Mean tumor size was 3.5 cm (2.2-5.8 cm).

Mean operating time was 78 min (range, 32-85), and RF duration was 12 min in all patients.

A total of 18 22G needles with a length of 100.5 mm and a 5-mm active tip (Amitech®), 10 with a straight tip and 8 with a hooked tip, were used. Mean temperature was 53.2°C (range, 50.2–56.3).

Four patients experienced a mean increase in serum creatinine levels of 1.3 mg/dL (range, 0.6–2.2) as compared to pretreatment levels, but values normalized within 48 h. Creatinine levels remained elevated in a single patient due to a preexisting chronic renal disease. No changes occurred in all other test parameters, except for one case.

Mean follow-up time was 17.5 months (range, 3–52).

During the follow-up period, nine tumors (efficacy rate = 81.8%) were found to be successfully treated, seven of them by a single ablation session, while two tumors in two patients required an additional session based on CT images at the first month after the procedure. Prior chemoembolization was performed in two patients due to tumor size (both tumors >4 cm).

CT images taken during follow-up showed in all patients a variable reduction in the size of the initial lesion, with a mean size reduction by 2.7 cm (range, 2.2-4.5) as compared to the preoperative CT image.

Five tumors showed an increased contrast uptake which was considered benign and disappeared at 58 days on average (range, 24-72) (table 2).

A tumor showed criteria of a persistent residual lesion at three months, and laparoscopic radical nephrectomy was decided because of tumor location (close to renal pelvis). No technical difficulties due to prior RF treatment were found during surgery.

Lung metastases occurred in two patients during follow-up after a mean of 26.5 months (range, 16–37).

All patients remained at hospital for 24 h under observation and were administered scheduled IV analgesia (metamizole IV, 2 g/8 h) and prescribed oral metamizole 575 mg/6 h for 7 days upon hospital discharge.

Three patients experienced complications in the early postoperative period. One patient had self-limited gross hematuria for 24 h with a decreased hematocrit, but no transfusion was required. Non-clinically relevant renal damage occurred in two patients (table 2).

Discussion

The management of small renal tumors is constantly evolving.

Multiple treatment options are currently available, ranging from partial nephrectomy (open and/or laparoscopic) to minimally invasive procedures.[16] Percutaneous RF is a treatment option for renal tumors and patients who, because of either the characteristics of their disease (bilateral tumor) or their associated comorbidities (CRF, high surgical risk), are not amenable to conservative surgery.[17,18] As this is a percutaneous renal puncture technique, it is feasible for any urologist with a minimum experience in nephrostomy puncture.

There is agreement in the available medical literature in that tumor size is a significant predictor of treatment success. Advances in imaging procedures have allowed for a highly

Table 1 – Patient characteristics: age, indication of radiofrequency, tumor number and location

Patient	Age	ASA*	Indication	No. of tumors	Location
1	72	3	AF, PTE	1	Exophytic
2	66	2	Bilateral tumor	2	Exophytic
3	78	3	CHF	1	Parenchyma
4	81	3	HBP, DM	1	Exophytic
5	85	3	DM	1	Mixed
6	81	2	Bilateral tumor	2	Parenchymal+exophytic
7	67	2	Qx refusal	1	Exophytic
8	63	3	CHF, DM	1	Exophytic
9	69	3	COPD	1	Exophytic

ASA: American Society of Anesthesiologists; DM: diabetes mellitus; CRF: chronic renal failure; AF: atrial fibrillation; HBP: high blood pressure; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; Qx: surgery; PTE: pulmonary thromboembolism.
* Classification used by the American Society of Anesthesiologists to estimate the risk of anesthesia for different patient states.

Table 2 – Tumor size, radiofrequency sessions, additional treatments, complications, follow-up time, and disease-free time

Patient	Tumor size (cm)	Sessions	Additional treatment	Complications	Follow-up (months)	DFT
1	5.2	1	CE	Creat. elev.	15	15
2	3.3–2.8	2	No	Hematuria	42	37
3	3.0	1	No	Creat. elev.	31	31
4	3.8	1	Nephrectomy	Creat. elev.	3	3
5	2.7	1	No	Tract lesion	12	12
6	5.8–2.6	2	CE (1 tumor)	Tract lesion	19	16
7	2.2	1	No	No	15	15
8	3.6	1	No	No	15	15
9	3.3	1	No	Persist. creat. elev.	6	6

Creat. elev.: transient creatinine elevation; Persist. creat. elev. persistent creatinine elevation; CE: chemoembolization.

accurate calculation of tumor size. A largest diameter of the lesion greater than 4 cm (clinical stage > T1) may lead to a non-beneficial outcome of RF.[19]

Most tumors in our series were less than 4 cm in size, and results in terms of tumor mass reduction and lack of contrast uptake at 3, 6, and 9 months were similar to those reported in medical literature.[20] Tumor size was greater than 4 cm in only two patients (5.8 and 5.2 cm).

It has been reported that adjuvant treatments and/or several RF sessions may be used for greater tumors.[21,24] Thus, selective chemoembolization of both tumor masses was performed in those two patients, and a tumor mass reduction that was sufficient to allow for subsequent application of RF was achieved.

Tumor location is another factor to be considered. Good results are difficult to achieve with centrally located tumors because the great concentration of vessels at those kidney regions causes a greater scattering of thermal energy that decreases the extent of the coagulation generated.[15] Thus, exophytic tumors surrounded by perirenal fat respond much better to treatment because fat acts as a thermal insulator and allows for achieving higher temperatures during RF.

This phenomenon was initially reported in liver tumors and is called the "Owen effect".[22]

Percutaneous ultrasound-guided RF was performed in all patients. RF success was assessed using contrast CT of the abdomen. A regular perilesional contrast uptake was considered benign, and a benign uptake suggested an adequate physiological response to the thermal damage induced[23] (initial reactive hyperthermia and subsequent fibrosis). This finding may be seen immediately after RF and for 2-3 months after the procedure. Irregular peripheral contrast uptake represents the presence of residual tumor and, to be considered as such, should occur in the lesion margin, may show an eccentric or nodular growth, and suggests incomplete treatment.

In our series of treated patients, perilesional benign contrast uptake was identified in five tumors.

An irregular perilesional contrast uptake suggesting a persistent lesion was found in two tumors from two patients. In both, initial tumor size exceeded 4 cm (5.2 and 5.8 cm respectively). The 5.2-cm tumor was exophytic and the 5.8-cm tumor was exophytic and parenchymal, with tumor size being the limiting factor for inefficacy of the first treatment.

While RF is considered a minimally invasive procedure with a sufficiently proven safety profile, it has well documented complications,[24] such as bleeding with transfusion requirement, urinary tract damage occurring as burns, and urinomas, as well as paresthesia and self-limited hematuria.

Acute renal failure due to hypoperfusion has been reported during laparoscopic RF, but its mechanism is not known. Four patients in our series showed transiently elevated creatinine levels, which returned to baseline values within 24 h in all but one.

Our study results agree with those reported in medical literature and support percutaneous RF of small renal masses as a safe, effective, reproducible, well tolerated alternative for the treatment of stage T1 renal tumors using few hospital resources.

However, our study had some limitations. First, patient sample was clearly small as compared to another large series. However, results in terms of short and mid-term disease control widely agree with those reported in the literature. The other main criticism relates to treatment of lesions larger than 4 cm in size. Such treatments should be justified by stating that they were performed in patients not amenable to surgery because of their high surgical risk and their significant symptoms, including hematuria causing anemia. RF was therefore performed in an attempt to stabilize their condition. A significant clinical improvement was achieved in some cases, but prior additional treatment with selective chemoembolization was required.

As regards follow-up time, clinical guidelines of the European Association of Urology recommend a 10-year follow-up to assess the effectiveness of an alternative treatment to surgery, as this has shown overall survival rates of 95%.[25] Mean follow-up time in our series is 17.5 months (range, 3-52 months). It is obvious that no categorical conclusions may be drawn about the efficacy of this treatment, overall and compared to surgery. However, we think that this is an initial follow-up of some relevance that should lead to our results being considered.

Thus, our initial experience suggests that RF is a treatment to be considered as an alternative for highly symptomatic stage T1 and T2 renal tumors in patients not amenable to surgery providing acceptable short-term results which is well tolerated, uses few healthcare resources, and has a low complication rate.

Conflict of interest

The specific material (RF generator, needles, and electrode) was provided by Amitech Pharma®.

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