

Laparoscopic and Image-guided Radiofrequency Ablation of Renal Tumors: Patient Selection and Outcomes

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Abstract Multiple modalities exist for the management of small renal tumors, including active surveillance, extirpation (radical nephrectomy and partial nephrectomy), and ablative therapies. Radiofrequency ablation (RFA) is an alternative to extirpative surgery for renal tumors. This article presents the current literature on RFA for renal tumors. We reviewed 28 RFA series in the English literature from 2003 to 2010 to assess patient selection, biopsy, renal outcomes, and oncologic outcomes.

Keywords Radiofrequency · Ablation · Kidney · Renal mass · Renal tumor · Percutaneous · Laparoscopic · Minimally-invasive · Nephron-sparing

Introduction

In 2010, the American Cancer Society estimated the incidence of kidney and renal pelvis cancer to be 58,240 [1]. With the implementation of computerized tomography and ultrasound, there has been an increase in incidental renal masses with presentation at a lower stage and grade [2, 3]. Current American Urological Association (AUA) guidelines for clinical T1a and T1b renal masses include radical (RN) or partial nephrectomy (PN) except in the case of clinical patients with T1b with major comorbidities or increased surgical risk where RN is the only standard [4••]. Thermal ablation is recommended only for clinical T1a disease in patients with significant comorbidities or

increased surgical risk and remains an option for healthy patients with clinical T1a and all patients with clinical T1b disease [4••].

Radiofrequency ablation (RFA) is a thermal therapy implemented by placing an electrode into the target tissue. Most RFA systems in commercial use utilize monopolar circuitry, where one or more grounding pads are required on the skin. Once the generator is activated, the current passed through the tissue causes ionic agitation resulting in heat generation. The temperature is highest at the metal–tissue interface in the center where the electrode is located. Heat is generated by the current passing through the tissues directly, resulting in heat dissipation due to tissue resistance, and is transferred via conduction to surrounding tissue in a radiant fashion. Heat resulting from direct heating and conduction causes coagulative necrosis at 40°C to 60°C [5]. Real-time peripheral thermometry is an excellent adjunct because it improves monitoring of ablation end points but is not universally applied [6].

RFA is a technology currently used in the treatment of small renal tumors [6–9, 10••]. Advantages are the minimally invasive approach and decreased morbidity of the operation. Complications, although rare and usually minor, do occur [11]. Intraoperative complications that may occur include pneumothorax, perinephric hematoma, renal capsular tear, spleen or liver lacerations, and skin burns. Postoperative complications include genitofemoral neuralgia, acute urinary retention, hydronephrosis, hematoma, urinoma, ureteropelvic junction obstruction, and hematuria. RFA carries an increased risk of local recurrence as defined as the need for a secondary intervention when compared to surgical excision [12], potential for difficult surgical salvage if the tumor progresses [13, 14], and possible skin burns secondary to the grounding pad [15]. Larger tumors or those with irregular shape also have an increased risk of

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recurrence in RFA [16]. Oncologic efficacy has been demonstrated in comparative series [8, 17].

RFA offers comparable outcomes compared to PN when considering multiple ablation outcomes [8, 17]. Additionally, RFA affords a markedly reduced risk and complication profile compared to PN [8] and has been shown to reduce the risk of overall nephron loss when compared to other modalities [18••, 19]. RFA, when used in treating renal tumors, typically is performed as an outpatient procedure, requires no vascular occlusion, and has lower blood loss than PN [8]. Assessment of patient selection, intraoperative biopsy, oncologic outcomes, renal functional outcomes, and differences in laparoscopic and percutaneous approaches are discussed in this article, which reviews these key points in assessment of RFA in the treatment of renal masses.

Methods

Utilizing PubMed, a review of the English literature was performed using search queries for “renal,” “renal mass,” “renal tumor,” “kidney,” “ablation,” “RFA,” “biopsy,” “GFR,” “creatinine,” and “outcomes.” Of the resulting manuscripts, case reports, series updated in more recent reports (ie, intermediate follow-up and then longer follow-up for the same patient series), and nonhuman studies were excluded. Included series reported on RFA of renal tumors and were not review articles. This resulted in 28 manuscripts published between 2003 and 2010.

Patient Selection

Key factors in the selection of patients for RFA are patient comorbidities, tumor location and size, and, of course, patient and surgeon preference. AUA guidelines recommend thermal ablation for patients with T1a disease with significant comorbidities [4••]. This definition is not exclusive because RFA still remains an option in patients with T1b disease or healthy patients [4••]. Therefore, RFA is a preference for poor surgical candidates, but not exclusive of healthy patients.

Tumor Size

The upper size limit of RFA has not been established. Most published RFA series report extensive experience in renal tumors less than 4 cm, and larger tumors in select patients may be successfully ablated [6, 10••]. Theoretically, a tumor of any size could be ablated with the application of multiple RFA probes, repositioning of probes, and peripheral thermometry to ensure overlap of ablation zones;

however, as tumor size increases beyond T1 disease, the ability to safely spare nephrons is compromised, risk of damage to the collecting system is increased, and alternatives such as PN or RN become more attractive.

Tumor Location

Tumor location is an additional selection criterion for RFA. First, any tumor must be accessible either directly (Fig. 1a) or via organ manipulation (Fig. 1b). Any tumor without a direct needle trajectory path may provide great difficulty during the operation. Tumors adjacent to bowel, liver, ureter, or other vital organs require adequate planning. Tumors with anterior location can be distanced from bowel via laparoscopic manipulation, or through injection of water or an isotonic nonconducting fluid to allow bowel spacing when a percutaneous approach is used [20]. Proximity to

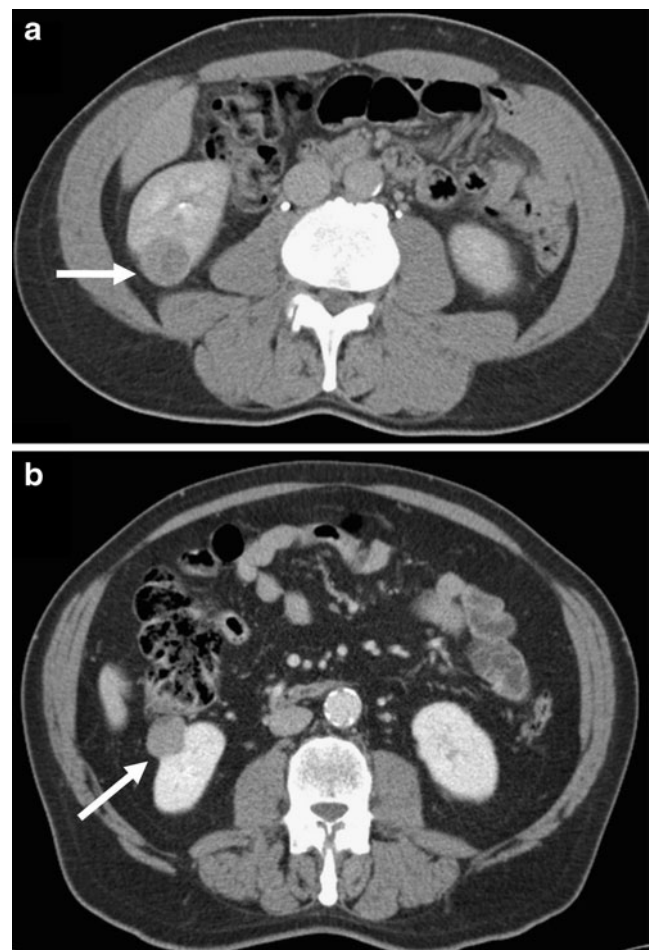


Fig. 1 Surgical approach. Preoperative CT scans are shown for two tumors. **a** CT scan of a posteriorly located tumor selected to undergo percutaneous RFA because of its posterior location and percutaneous accessibility. **b** CT scan of an anteriorly located tumor in close proximity to bowel is shown. This is an example of a tumor selected for laparoscopic RFA because of its anterior location and adjacent organs. *CT* computed tomography, *RFA* radiofrequency ablation

liver typically presents a minor obstacle because laparoscopic techniques for liver retraction can be used as well as a transhepatic approach in percutaneous procedures. Tumors adjacent to ureter require strict temperature monitoring because avoiding damage requires low temperatures. Of note, if the ureter cannot be adequately separated from the tumor, then it may be impossible to achieve simultaneous adequate tumor coagulative temperatures and protective ureteral temperatures.

The renal collecting system will act as both a thermal convection system and an electrical conductor dissipating the generated electric field causing heat sinks. Therefore, it should be understood that tumors near or abutting the collecting system may limit the extension of the ablation zone. Large vessels cause a similar convection effect and should be factored into decision making. Cystic masses create a similar challenge. The high fluid content of the cystic mass may affect conduction of heat and current flow to the surrounding tissue. If the mass is predominantly cystic, fluid may be aspirated intraoperatively before ablation. Aside from incomplete ablation secondary to changes in the electrical and thermal fields, cystic masses may rupture during the procedure. The tissue and fluid in a cystic mass are in a confined space. The phase change of the fluid from liquid to expanding vapor (gas phase) causes increased pressure and eventually may lead to cyst rupture. This phase change occurs at 100°C in water, and likely at a higher temperature in cystic fluid due to salt and protein content. In theory, all tissues reaching this high temperature are nonviable, and non-concerning when “spilling” occurs after cyst rupture. However, it is impossible to verify that all spilled cells reached above 60°C in this scenario and caution should be heeded. It is not our policy to purposefully ablate cystic tumors. The ability to place the RFA probe in the desired position is largely reliant on the physician’s experience. For inexperienced persons, tumor location and size become somewhat limiting and may affect patient selection.

In addition to the consideration of the factors mentioned above, ideal candidates for RFA are patients having bilateral renal tumors, patients with Von Hippel–Lindau disease with multiple tumors, patients with a solitary kidney or renal insufficiency, patients with local recurrences post-PN, patients preferring RFA over extirpative techniques, and patients deemed high-risk for surgical complications. An absolute contraindication to RFA is uncontrolled bleeding diathesis. However, patients on anticoagulation are only relatively contraindicated if corrected before surgery. RFA provides hemostasis in its application. All of the factors mentioned above must be weighed in decision making along with the patient’s preference. Careful patient selection helps to ensure safe and effective RFA procedures.

Tumors Biopsy

Patients post-RFA of renal tumors undergo radiographic follow-up [4••]. Intraoperative biopsy results may help determine frequency of postoperative imaging. Although the role of renal biopsy remains controversial, it has gained favorability, with high diagnostic success reported. Its role in RFA is well described in the literature [21]. Some RFA series have reported preoperative radiographic characteristics to diagnose renal cell carcinoma (RCC) in renal tumors without conclusive biopsy [22]. Radiographic appearance on preoperative CT scan does appear to correlate with tumor diagnosis [23], but this does not replace the role of biopsy. For the purposes of this manuscript, biopsy-proven renal cancers are included in the interpretation of results (Table 1).

Most experts recommend tumor biopsy before ablation [24]. Diagnostic yield of biopsy before focal therapy in the kidney has ranged from 66% to 96% [10••, 21, 25–27]. To increase biopsy yield, fine-needle aspiration in place of biopsy should be avoided in solid renal tumors, greater than 1 core biopsy should be performed, and biopsies should be performed before ablation [21]. In RFA, as opposed to other ablation techniques, multiple biopsies may be taken without fear of bleeding because RFA provides a hemostatic effect during ablation.

Outcomes

A review of the literature was performed for RFA of renal tumors. Most ablations are performed in patients with small renal masses (SRM; <4 cm). Mean tumor sizes in RFA series range from 1.7 to 3.8 cm [26, 28–36]. About 80% of resected SRMs are malignant [37]; however, biopsy results in RFA series have shown RCC in 48% to 91% of studies [6, 10••, 26, 29], with some series reporting exclusively malignant tumors [36, 38].

The AUA guidelines based upon data from the Working Group on Image-Guided Tumor Ablation [39] report failure as any persistent or recurrent disease [4••], and success as lack of recurrence after initial ablation, and not after performing multiple ablations. There is inconsistency in reporting with some authors reporting as any radiographic evidence of persistent enhancement at any time after the initial therapy, whereas other series report recurrence as patients having evidence of disease greater than 3 months postoperatively and exclude patients re-ablated in the first 3 months. This creates a nonuniform system for measuring outcomes. For the literature reviewed, the success after one ablation session, cancer-specific success after one ablation session, and the success after multiple ablation sessions were recorded or calculated based on the results. These results were not initially reported by all authors, but the values for

Table 1 Selected radiofrequency ablation series

Study	Tumors, n (pts)	Biopsy-proven RCC, %	Nondiagnostic biopsy, n (%)	Surgical approach	Mean tumor diameter, cm	Recurrence-free after 1 ablation, %	Cancer-specific recurrence-free after 1 ablation, %	Recurrence-free after 2 or more ablations, %	Mean follow-up, mo
Lewin et al. [41]	10 (10)	N/A	N/A	PC	2.3	100	100	N/A	25
Varkarakis et al. [26]	56 (46)	48.2	N/A	PC	2.2	83.9	67	96.4	27.5
Gervais et al. [29]	100 (85)	90.9	N/A	PC	3.2	67	N/A	90.9	27.6
Matsumoto et al. [25]	109 (91)	68	4 (3.7)	PC/Lap/Open	2.4	98	97.3	99	19.4
Ahrrar et al. [44]	30 (29)	N/A	N/A	PC	3.5	96	N/A	N/A	10
Mahnken et al. [38]	15 (14)	100	N/A	PC	3.0	100	100	100	13.9
Salagierski et al. [30]	45 (42)	N/A	N/A	PC	3.8	93.3	N/A	100	14
Park et al. [42]	94 (78)	77	5 (6)	PC/Lap	2.4	94.6	92.3	96.8	38
Arzola et al. [45]	27 (23)	N/A	7 (26)	PC	2.7	80	N/A	90	24
Breen et al. [32]	105 (97)	N/A	N/A	PC	3.2	79	N/A	90.5	16.7
Carey et al. [6]	37 (36)	83.8	4 (10.8)	PC/Lap	3–5	94.6	93.5	97.3	11.3
Zagoria et al. [36]	125 (104)	100	N/A	PC	2.7	87.2	87.2	92.8	13.8
Stern et al. [17]	40 (40)	81	3 (8.1)	PC/Lap	2.4	92.5	N/A	95	30
Lucas et al. [19]	86 (86)	57	N/A	PC/Lap	2.3	96.5	94	N/A	40
Levinson et al. [43]	31 (31)	51.6	6 (19.4)	PC	2.1	90.3	81.3	100	61.6
Wingo et al. [9]	41 (39)	77	6 (14)	PC/Lap	2.7	90.2	87.5	100	29
Veltri et al. [33]	87 (68)	N/A	N/A	PC	2.9	86.2	92	89.7	24.4
Schirmang et al. [34]	106 (101)	N/A	N/A	PC	2.6	94	N/A	92	25
Gupta et al. [28]	163 (151)	70	12 (7.4)	PC	2.3	97	94.5	97	19.6
Hoffmann et al. [46]	13 (10)	N/A	N/A	PC	2.7	100	100	N/A	N/A
Turna et al. [40]	36 (29)	82.8	1 (3.4)	PC	2.6	55.2	45.8	N/A	14
Pirasteh et al. [49]	41 (41)	N/A	N/A	PC	2.2	90.2	N/A	N/A	N/A
Raman et al. [18••]	53 (47)	76	8 (15)	PC/Lap	2.7	96	95	100	18.1
Tracy et al. [10••]	243 (208)	79	11 (5)	PC/Lap/Open	2.4	93	90	96.3	27
Takaki et al. [22]	51 (51)	N/A	N/A	PC	2.4	82.4	N/A	100	34
Pettus et al. [47]	62 (62)	68	14 (23)	PC	1.9	N/A	N/A	N/A	N/A

Lap laparoscopic, N/A not available, PC percutaneous, pts patients, RCC renal cell carcinoma

each publication were calculated if the data was available in the manuscript. For example, an author may report a success rate of x , but mentioned in the manuscript that this included patients undergoing multiple ablation sessions. The number of radiographic failures may be mentioned and this was used to calculate the single ablation success rate y . Table 1 lists the “success rates” after one ablation and after multiple ablations for the papers reviewed using Working Group on Image-Guided Tumor Ablation criteria [39]. The term “incomplete ablation” is unclear. It has been used to categorize patients receiving RFA with radiographic failure early in the postoperative course [10••]. This term is not used for patients with a failure after a longer follow-up period. Incomplete ablations should be considered treatment failure because radiographic failure at the ablation site most likely resulted from viable cells postablation regardless of the postoperative interval.

RFA success was reported as 55% to 100% after a single RFA session [6, 10••, 26, 28–36, 40]. In patients with RCC, cancer-specific success after a single RFA session has been reported as 45% to 100% [25, 26, 38, 40–42]. The mean weighted follow-up of 27 of the 28 studies reported in this review was 23.8 months. The largest case series to date by Tracy et al. [10••] reported 243 tumors treated openly, laparoscopically, and percutaneously. Success after one session was reported in 227 of 243 (93%) of tumors treated with a mean follow-up of 27 months (range 1.5–90 months). They reported nine local recurrences, excluding seven tumors deemed “incomplete ablations.” With the nine reported recurrences, they showed a 5-year recurrence-free survival of 93% (cancer-specific: 90%). Levinson et al. [43] similarly had long-term mean follow-up of 5 years (61 months) in 31 patients undergoing percutaneous RFA. They reported a success rate of 90.3% after one session, and a cancer-specific 81.3% success rate after one session.

Several series reported re-ablation (RA) rates to help judge their success of RFA. This method of reporting is

inferior to monitoring for recurrence when assessing outcomes of RFA because many of the RFA papers have different RA criteria. Additionally, the patients largely influence their treatment decisions after discovering a recurrence and may elect to have active surveillance, PN, or RN in place of an RA. Therefore, RA rate is not a uniform measure of RFA success unless all the patients are committed to having RFA treatment of recurrences.

Renal Preservation

Renal functional outcomes were reported in ten of 28 studies reviewed [19, 22, 31, 38, 40, 43–47]. There was no clear method of reporting outcomes with either glomerular filtration rate (GFR) or creatinine change documented. Renal outcomes from individual studies are shown in Table 2. RFA appears to have very little effect on increasing creatinine [31, 38, 40, 43–46], decreasing GFR [19, 22, 40], or changing classification of chronic kidney disease [18••]. RFA has an excellent nephron-sparing effect when used in the treatment of renal tumors. This is likely influenced by most ablations being performed in patients with bilateral kidneys, but studies performed in solitary kidneys [18••, 40, 43, 46] show very minimal changes in renal function. Of note, some studies were performed using peripheral thermometry to monitor ablations [6, 9]. Theoretically, this should help prevent damage of healthy renal tissue by accurately monitoring the borders of the targeted lesion. Tumors treated with RFA also are typically T1a, and likely influence the outcomes because smaller portions of the kidney are ablated.

Intent to Treat: Does the Approach Matter?

When comparing outcomes of laparoscopic and percutaneous RFA, a meta-analysis performed by Hui et al. [48]

Table 2 Series reporting renal functional outcomes

Study	Tumors, n (pts)	Mean follow-up, mo	Renal functional change
Ahrar et al. [44]	30 (29)	10	Cr: +0.24 mg/dL
Mahnken et al. [38]	15 (14)	13.9	Cr: +0.06 mg/dL
Hegarty et al. [31]	81 (72)	12	No change in Cr
Arzola et al. [45]	27 (23)	24	Cr: +0.12 mg/mL
Lucas et al. [19]	86 (86)	40	GFR for preop <60: 1.7; < 45: +3
Levinson et al. [43]	31 (31)	61.6	Cr: +0.14 @ last FU
Hoffmann et al. [46]	13 (10)	N/A	Cr: +11 mmol/L; CrCl:–8 mL/min
Tuma et al. [40]	36 (29)	14	69% of pts decreased GFR; 55% of pts increase Cr
Raman et al. [18••]	53 (47)	18.1	GFR: 11.4 @ last FU
Takaki et al. [22]	51 (51)	34	GFR: 0 @ 1 wk;–3.2 @ last FU
Pettus et al. [47]	62 (62)	N/A	GFR: +3 @ 1 mo; +2 @ 1 y

Cr creatinine, CrCL creatinine clearance, FU follow-up, GFR glomerular filtration rate, N/A not available, pts patients

comparing percutaneous and surgical approaches for renal tumor ablation contained 21 percutaneous and 3 “surgical” RFA series. This meta-analysis included cryoablation series, and reported no difference in oncologic outcomes if RA was allowed. However, a “primary effectiveness” (single session) of 87% (95% CI, 82–91%) was achieved for percutaneous ablation compared to 94% (95% CI, 92–96%) for surgical approach. “Secondary effectiveness” (multiple sessions) was 92% (95% CI, 90–95%) for percutaneous ablation and 95% (95% CI, 93–97%) for surgical approach. Also of note, the mean tumor size was 2.8 cm and 2.5 cm for the percutaneous and surgical groups, respectively, but with no statistical difference. This may have influenced the decreased primary success of percutaneous approach, along with a higher percentage of the percutaneous tumors being RCC, and a difference in the imaging modality used for targeting [48]. A prospective study with exclusively RFA patients would be more substantial.

Percutaneous RFA is performed both by surgeons and interventionalists, while laparoscopic RFA is performed solely by surgeons. Biopsy is not performed in some percutaneous series [49]. Surgeons likely have a more aggressive approach to treating renal cancer and perform every ablation under the assumption that the lesion is cancerous. Not performing a biopsy suggests that an author may not be concerned with the diagnosis, and may be performing unnecessary operations. The AUA guidelines for T1 renal masses [4••] state that the percutaneous surgical approach produced higher “incomplete ablation” rates than laparoscopic approach in their review. This advantage of laparoscopic approach over percutaneous approach is likely resultant of surgeons’ intent-to-treat principle in the laparoscopic group and unlikely due to actual differences in approach. This has not been clearly defined. When choosing an approach, it should be based on the safety of the procedure as well as the ability to access the tumor via that approach.

Conclusions

RFA is selectively used in patients with clinical T1a renal tumors with significant comorbidities. Our review of the current RFA series shows that RFA may be used in T1b tumors, and is not limited to unhealthy patients. The renal preservation is excellent and oncologic outcomes appear to be fairly durable, understanding there are no long-term efficacy studies and the inherent limitations of the existing predominantly retrospective data. RFA appears to be a feasible option in the treatment of renal masses and should be considered an option when appropriate.

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