

Review of the efficacy and safety of radiofrequency ablation for the treatment of small renal masses

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Abstract

Background: Small renal masses are increasingly being discovered incidentally on imaging performed for another reason. The standard of care for these masses involves excision by open or laparoscopic techniques. Recently, ablative techniques such as radiofrequency ablation (RFA) and cryoablation have taken a more prominent role in the treatment algorithm for these masses. We sought to evaluate the efficacy and safety of radiofrequency ablation in the treatment of renal tumours.

Methods: We conducted a review of the literature. There was no language restriction. We obtained studies from the following sources: the Cochrane Library, PubMed, EMBASE, LILACS and Current Controlled Trials.

Results: We identified no clinical trials in the literature. Thus we described the results from case series and retrospective studies with a reasonable sample size (number of reported patients in each study > 65). Most patients undergoing RFA had T1a disease with a mean tumour size of about 3 cm. Radiofrequency ablation was usually performed percutaneously with image guidance. Reported follow-up was short and ranged from 1 to 30 months. Most series used radiographic response as a surrogate for cancer control. The rates of local recurrence of the tumour were as high as 13.0% (average 8.5%) and were slightly higher than those associated with cryoablation and partial nephrectomy. Complications included hemorrhage, ureteral strictures and loss of a renal unit.

Conclusion: Our review demonstrates that RFA is a suitable and promising therapy in patients with small renal tumours who are considered to be poor candidates for more involved surgery. However, clinical trials with long-term data are needed to establish the oncological efficacy.

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Résumé

Contexte : De petites masses rénales sont de plus en plus souvent découvertes de façon fortuite lors d'épreuves d'imagerie commandées pour une autre raison. Les soins standard pour ces masses incluent une excision par chirurgie ouverte ou par laparoscopie. Dernièrement, des techniques comme l'ablation par radiofréquence (ARF) et la cryoablation ont pris plus d'importance dans l'algorithme de traitement. Nous examinons l'efficacité et l'innocuité de l'ablation par radiofréquence dans le traitement des tumeurs rénales.

Méthodologie : Une revue de la littérature a été effectuée, sans restriction de langue. Des articles ont été obtenus des sources suivantes : la Bibliothèque Cochrane, PUBMED, EMBASE, LILACS et Current Controlled Trials.

Résultats : Comme aucun essai clinique n'a pu être cerné dans ces bases de données, nous décrivons les résultats d'études de cas et d'analyses rétrospectives avec populations de taille raisonnable (nombre de patients pour chaque étude > 65). La vaste majorité des patients ayant subi une ARF présentaient une tumeur T1a de taille moyenne d'environ 3 cm. L'ARF était habituellement effectuée par voie percutanée et guidée par imagerie. Le suivi était court, allant de 1 à 30 mois. La plupart des études sérielles avaient recours à la réponse radiographique comme paramètre de substitution de la maîtrise du cancer. Les taux de récurrence locale de la tumeur atteignaient 13.0 % (moyenne 8.5%), et étaient en général légèrement plus élevés que les taux notés avec la cryoablation et la néphrectomie partielle. Les complications signalées étaient les suivantes : hémorragie, sténose urétérale et perte d'une unité rénale.

Conclusion : Le présent article montre que l'ARF est une technique convenable et prometteuse chez les patients porteurs de petites tumeurs rénales considérés comme de mauvais candidats pour une intervention plus lourde. Cependant, il est impératif d'effectuer des essais cliniques à long terme afin d'établir dans un avenir rapproché l'efficacité oncologique de cette technique.

Introduction

In Canada, the incidence of renal cancer is 4500 new cases per year, with 1500 patients dying of the disease.¹ Small renal masses are increasingly being discovered incidentally on imaging performed for another reason.²⁻⁴ The natural history of these incidentally discovered masses remains unclear. When surgically excised, 70%–80% are proven to be renal cell carcinomas and the rest are benign.⁵⁻⁸

When technically feasible, the standard of care for these masses has been partial nephrectomy. Local and distant oncological control has been well established with surgical excision.⁹ In the last 10 years, a minimally invasive approach with laparoscopy has largely supplanted open surgery. The question of whether in situ ablative technologies^{10,11} can replace excision for the treatment of small renal tumours remains unanswered. The reported advantages of ablative approaches over extirpative techniques include reduction

of perioperative morbidity, shorter hospital stay and faster recovery time. The main advantage of ablative techniques, however, would be to offer treatment to patients who are otherwise not candidates for invasive extirpative techniques.^{12,13}

Several ablative technologies have been investigated, including cryoablation (CA), radiofrequency ablation (RFA), microwave,¹⁴ high-intensity focused ultrasonography,^{15,16} laser interstitial thermotherapy,¹⁷ microwave thermotherapy and radio-surgery.

Radiofrequency ablation is a minimally invasive treatment for localized cancer in which a small needle attached to a device that delivers radiofrequency energy is inserted into a tumour to destroy the cancerous tissue while the patient is sedated or under general anesthesia. The procedure is usually performed percutaneously with image guidance using computed tomography (CT) or ultrasonography and the tumour is destroyed by heating to temperatures exceeding 60°C.¹⁸

Radiofrequency ablation has been licensed by Health Canada and used for many years in the treatment of cardiac abnormalities, trigeminal neuralgia and osteoid osteomas; more recently, it has been used in the treatment of neoplasms in the liver, kidney, prostate, bone and soft tissues, and other areas.¹⁹ The role of RFA in the treatment of renal neoplasms is still being investigated with several series reporting short-term outcomes.

We sought to examine the state of knowledge of RFA in the treatment of renal tumours. We reviewed the efficacy of this technology in terms of oncological control and prevention of local recurrence and metastasis. We also examined complications and safety concerns as they relate to RFA.

Methods

There was no language restriction. We obtained studies from the following sources: Cochrane Central Register of Controlled Trials (Central, The Cochrane Library, issue 3, 2008), US National Library of Medicine (PubMed; 1966–2008), Excerpta Medica database (EMBASE; 1980–2008), Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS; 1982–2008) and Current Controlled Trials to identify all studies about RFA in patients with renal cell carcinomas.

We searched the databases using a comprehensive search strategy for kidney cancer and RFA using

medical subject headings (MeSH) and key words, including an exhaustive list of synonyms (Appendix 1). We adapted the search strategy for each database to achieve more sensitivity. We also examined the bibliographic references in relevant review articles for eligible trials.

We were interested in the following clinical outcome measurements: cancer specific survival, radiographic success, tumour recurrence, local tumour progression or distant metastases, need for repeat ablation, complications, adverse events reported and renal function.

Results

Our search in the electronic databases identified 1428 titles. After screening by title and then abstract, we obtained full paper copies for 71 studies that were potentially eligible for inclusion in the review. Of these, we did not identify any randomized controlled trials. We identified several case series and retrospective studies and 1 controlled clinical trial. Thus we included the case series and retrospective studies with a reasonable sample size ($n > 65$), and the controlled clinical trial in our review.

Table 1 summarizes the characteristics of published studies on RFA. Most patients undergoing RFA had T1a disease with a mean tumour size of about 3 cm. RFA was usually carried out percutaneously with image guidance. However, if the tumour was endophytic or otherwise not accessible percutaneously, laparoscopy could be carried out to expose the kidney and the tumour. Reported follow-up was short and ranged from 1 to 30 months.

Table 2 outlines the clinical outcomes and complications reported in the RFA studies we examined. Most series used radiographic response as a surrogate for cancer control. We considered lack of contrast enhancement, decrease in size of the tumour or lack of growth on serial imaging to be signs of complete and successful ablation. The rates of local recurrence of the tumour were as high as 13.0% (average 8.5%) and were slightly higher than those associated with cryoablation and partial nephrectomy.

Although RFA is generally well tolerated with a favourable complication profile, it is not an innocuous procedure. Serious complications can occur, including hemorrhage, ureteral strictures and loss of a renal unit.

Discussion

The goal of RFA is to destroy tissue by heat using radiofrequency energy. The procedure involves

delivering an alternating electrical current at high frequency causing agitation of ions, which in turn results in heat. It has been shown that heating tissue to 55°–60°C for 5 minutes results in irreversible

Table 1. Noncontrolled, controlled and retrospective studies on radiofrequency ablation for renal tumours

Study	Design	Comparative group(s)	No. of patients	No. of tumours	Mean tumour size or range, cm	Tumour type		Type of RFA	Follow-up, mo
						Exophytic	Parenchymal, central or mixed		
Ganguli et al. ²⁰	Retrospective study	NA	66	72	2.7	47	25	Percutaneous	1
Lucas et al. ⁵	Retrospective comparative study	RN or PN	RFA 86	NR	RFA 2.34	NR		NR	RFA 22.0‡
			PN 85		PN 2.6			PN 24.0‡	
			RN 71		RN 3.16			RN 45.5‡	
Weight et al. ²¹	Retrospective comparative study	LC	RFA 88	RFA 109	RFA 2.5	NR		Percutaneous	6
			LC 176	LC 192	LC 2.4				
Wingo and Leveillee ²²	Case series	NA	131	146	1.0–5.3	41	105	Percutaneous and laparoscopic	29§
Bensalah et al. ²³	Retrospective comparative study	Laparoscopic PN	RFA 38	NR	RFA 2.3	NR		Laparoscopic	RFA 15§
			LPN 50		LPN 2.6			LPN 25§	
Breen et al. ²⁴	Case series	NA	97	105	3.2	86	19	NR	16.7§
Stern et al. ²⁵	Retrospective comparative study	Open or laparoscopic nephron-sparing surgery PN	RFA 40	NR	RFA 2.41	NR		Percutaneous and laparoscopic	RFA 30§
			PN 37		PN 2.43			PN 47§	
Zagoria et al. ^{26*}	Case series	NA	104	125	2.7	94	31	Percutaneous	13.8§
Hegarty et al. ²⁷	Retrospective comparative study	LC	RFA 72	RFA 81	RFA 2.51	NR		Percutaneous	RFA 12
			LC 161	LC 179	LC 2.56			LC 36	
Matin et al. ²⁸	Retrospective comparative study	CA	RFA 410	RFA 466	0.9–8.9	39%	61%	Percutaneous and laparoscopic	24.2§
			CA 206	CA 230					
Gervais et al. ²⁹	Retrospective study	NA	85	100	3.2	67	33	Percutaneous	28
Matsumoto et al. ^{30†}	Retrospective study	NA	91	109	2.4	NR		Percutaneous and laparoscopic	19
								Percutaneous	
Wah et al. ³¹	Controlled clinical trial	CG (biopsy of focal renal lesions)	RFA 17 CG 20	RFA 11 CG NR	3.1	NR		Percutaneous	
DiMarco et al. ³²	Case series	NA	66	91	2.0	53	38	NR	9.0§

CA = cryoablation; CG = control group; LC = laparoscopic cryoablation; LPN = laparoscopic partial nephrectomy; NA = not applicable; NR = not reported; PN = partial nephrectomy; RFA = radiofrequency ablation; RN = radical nephrectomy.

*Uzzo 2007 study is a duplicate publication of Zagoria et al.³⁴

†A 2006 study by Park has the same participants as the study by Matsumoto and colleagues.²³

‡Median.

§Mean.

cellular damage, and heating to more than 70°C causes cell death and tissue coagulation.^{33,34} Temperature-based RFA machines (e.g., RITA Medical Systems, Inc.) use temperatures as high as 105°C during treatment. One drawback to RFA is that, unlike cryoablation, it is not possible to monitor the ablated area via imaging in real time. It is therefore difficult to ensure that the entire surface area of a tumour receives the same amount of heat.

Our review demonstrates that although promising, the evidence behind RFA remains immature. Prospective and randomized trials are lacking. Reported follow-up is too short, with most studies

reporting a follow-up of 2 years or less and all studies reporting a follow-up less than 3 years. The natural history of small renal masses is not well defined, but one review demonstrated a growth rate of 0.28 cm/year with a metastatic rate of 1% after 34 months of follow-up.³⁵ This seems to indicate that the reported follow-up for most RFA series is too short to draw any meaningful conclusions about oncological efficacy.

Most RFA studies equate a successful ablation with radiological response. However, imaging changes after RFA are not always predictable. Tumours ablated with RFA do not consistently

Table 2. Clinical outcomes and complications of each included study (part 1 of 2)

Study	Outcome		Complication	
	Clinical outcome studied	Occurrence, %	Major	Minor
Ganguli et al. ²⁰	Average percentage decrease in tumour size	21	Ureteral injury; large perinephric, retroperitoneal, and pelvic hemorrhage	Second-degree burn; small perinephric or subcapsular hematomas
Lucas et al. ⁵	1) Renal function — GFR < 60 mL/min/1.73 m ²	RFA 89.47 PN 88.88 RN 100	NR	NR
	2) Local recurrence	RFA 6.97 PN 2.35 RN 0	NR	NR
Weight et al. ²¹	1) Radiographic success	RFA 85 CA 90	NR	NR
	2) No malignant cells on biopsy	RFA 65 CA 94	NR	NR
Wingo and Leveillee ²²	Successfully managed with a single RFA session	92.7 (data from endophytic tumours)	Lower extremity paresthesia	Hematuria, retention, flank bruising
Bensalah et al. ²³	1) Hospital length of stay, d	RFA 1.5 LPN 2.9	Ureteric stricture (requiring a nephrectomy) Urinary leak; delayed bleeding (requiring bladder clot evacuation and stenting)	Acute urinary retention, perirenal hematoma
	2) Recurrences	RFA 2.63 LPN 0		
Breen et al. ²⁴	1) Tumours completely treated	79.04	Moderate hydronephrosis and clyceal leak (subsequent urinoma)	Hematuria, renal hematoma
	2) Overall technical success rate	90.47		
Stern et al. ²⁵	3-year recurrence-free survival rate	RFA 93.4	UPJ obstruction (subsequently had a nephrectomy) and pneumonia Flank-site hernia	Asymptomatic lower-pole hydrocalyx and temporary probe-site numbness Ileus
		PN 95.8		

Continued on next page

regress in size. In addition, a peritumour halo may form with fat infiltration. Successfully treated tumours do usually demonstrate a lack of enhancement on CT scans.³⁰ It remains unclear whether radiological response is an adequate surrogate for cancer control. Histopathological confirmation of complete ablation is also not completely reliable owing to sampling error and the high false-negative rate of percutaneous biopsies.³⁶ Three studies performed a complete histopathological examination of tumours treated with RFA after either a radical or partial nephrectomy. Rendon and colleagues³⁷ found persistent cancer in

5%–10% of tumour volume. Matlaga and colleagues³⁸ found 2 of 10 tumours to be incompletely ablated, and Michaels and colleagues³⁹ found 4 of 5 tumours to be incompletely ablated.

Conclusion

This review demonstrates that RFA is a suitable and promising therapy in patients with small renal tumours (< 4 cm) who are considered to be poor candidates for more involved surgery. Long-term data on oncological control is lacking. Longer follow-up and more rigorous head-to-head trials

Table 2. Clinical outcomes and complications of each included study (part 2 of 2)

Study	Outcome		Complication	
	Clinical outcome studied	Occurrence, %	Major	Minor
Zagoria et al. ²⁶	Completely ablated tumour	93	Large perinephric hematoma; pneumonia; severe neuropathic pain and ureteral strictures with concomitant hydronephrosis	Small pneumothoraces, perirenal hemorrhage, apnea, tachycardia, flank pain
Hegarty et al. ²⁷	1) Radiological evidence of tumour recurrence or persistence of disease	RFA 11.1	There were no major complications	Perirenal hematoma; retroperitoneal hematoma; perirenal abscess and upper pole hydrocalicosis
		CA 1.8	Myocardial infarction; congestive heart failure and hemothorax	Urine leak; obstructed solitary kidney; pneumothorax; perirenal fluid collection and blood transfusion
Matin et al. ²⁸	Overall residual or recurrent disease	RFA 13.4	NR	NR
		CA 3.9	NR	NR
Gervais et al. ²⁹	Complete tumour necrosis by imaging criteria	90	Hemorrhage requiring RBC transfusion and stent placement; asymptomatic posterior abdominal wall enhancing mass; ureteral stricture; urinoma and ureteral injury	Hemorrhage not requiring transfusion; inflammatory track mass; skin burns and transient neuropathic pain
Matsumoto et al. ³⁰	Successful ablation of the tumour	98	Lower-pole infarct, urine leak and UPJ obstruction	Leg and arm neuropathy; pneumonia; prolonged pain; postoperative narcotic reaction and hydrocalicosis
Wah et al. ³¹	Occurrence of fever and flulike symptoms	RFA 82	Flu-like symptoms; pneumonia; pain;	Lifestyle interference with general activities and work activities
		CG NR		
DiMarco et al. ³²	Successful ablation of the tumour	95	UPJ obstruction; chronic lumbar plexopathy pain; wedge shaped renal infarct; major hemorrhage	NR

CA = cryoablation; CG = control group; GFR = glomerular filtration rate; LPN = laparoscopic partial nephrectomy; NR = not reported; PN = partial nephrectomy; RBC = red blood cells; RFA = radiofrequency ablation; RN = radical nephrectomy; UPJ = uretero-pelvic junction

are needed to determine the exact role of RFA in the treatment algorithm of small renal masses.

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Appendix 1. Summary of the bibliographic search strategies for type of clinical situation and intervention of interest

((Kidney Neoplasm) OR (Renal Neoplasms) OR (Renal Neoplasm) OR (Kidney Neoplasms) OR (Cancer of Kidney) OR (Kidney Cancers) OR (Renal Cancer) OR (Renal Cancers) OR (Cancer of the Kidney) OR (Kidney Cancer) OR (Kidney Cancers) OR (Renal masses) OR (Renal cell carcinoma)) **AND** ((Radiofrequency ablation) OR (Catheter ablation) OR (Electric Catheter Ablation) OR (Electrical Catheter Ablation) OR (Radiofrequency Catheter Ablation) OR (Transvenous Catheter Ablation) OR (Transvenous Electric Ablation) OR (Transvenous Electrical Ablation) OR (Percutaneous Catheter Ablation) OR (Percutaneous Radiofrequency ablation) OR (Radio frequency) OR Radio-frequency OR (Radiofrequency thermal ablation) OR (Minimally invasive therapy) OR (Tumor ablation) OR (CT-guided percutaneous radiofrequency ablation))

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