

# Local Recurrence of Renal Cancer After Surgery: Prime Time for Percutaneous Thermal Ablation?

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## Abstract

**Purpose** The purpose of the study was to retrospectively assess the safety and efficacy of radiofrequency thermal ablation (RFA) for retroperitoneal relapse following surgery for renal cell carcinoma (RCC).

**Patients and Methods** After open radical nephrectomy or nephron-sparing surgery, eight patients with no evidence of distant metastases were treated for retroperitoneal relapse of RCC with RFA. A total of 16 lesions were ablated. Technical success, tumor response, follow-up duration, and complications were retrospectively analyzed.

**Results** Disease progression after surgery occurred within a mean time of 57 months (range 9–120). Recurrent tumor size varied from 5 to 34 mm. Five patients previously underwent surgical resection of retroperitoneal recurrent

lesions. Six patients were treated with percutaneous approach, while two with recurrent nodes located on the anterior pancreatic surface underwent laparotomic RFA approach. All lesions were completely ablated and patients were followed up with CT at 30 days, after 3 and every 6 months. There was no residual enhancement after a mean follow-up of 12 months (range 7–17). Both patients treated with laparotomic approach had a grade 2 complication according to the Clavien–Dindo classification.

**Conclusions** In our small series, RFA after relapse of surgically removed RCC was safe and effective. Percutaneous and laparotomic thermal ablation should be assessed as first line loco-regional treatment on a larger patient group.

**Keywords** Radiofrequency thermal ablation · Renal cell carcinoma · Retroperitoneal relapse

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## Introduction

Renal cell carcinoma (RCC) is the most common primary malignancy of the kidney. This tumor accounts for 2 % of all cancer diagnoses in humans [1]. Moreover, due to the increasing use of magnetic resonance, computed tomography (CT), and ultrasound (US), a growing detection rate of incidental renal neoplasms has been described [2].

Minimally invasive therapies have been used increasingly in the care of patients with renal tumors. In patients previously unfit for surgery, image guided ablation has changed the treatment paradigm and now favors the treatment of tumors less than 3 cm [3].

However the real challenge is often represented by metastatic disease. Currently, the development of new drugs has led to improved prognosis of RCC by means of

targeted therapies and immunotherapies. However, 20–25 % of the patients are refractory to treatment and most patients will acquire drug resistance during their therapy [4]. Moreover, the role of surgery in such patients remains at least controversial.

A quite rare form of metastatic disease is the local recurrence in the renal fossa or elsewhere in retroperitoneum. Even if rare, these lesions must be seriously considered as indicators of a poor prognosis. Up until now surgery has been the only curative solution before or after systemic treatment [5]. To our knowledge, loco-regional treatment has not been previously described for this kind of metastatic disease from RCC. Thus, our aim is to describe a preliminary experience in RFA for retroperitoneal relapse after renal surgery in a small cohort of patients. Safety and efficacy are retrospectively evaluated.

## Materials and Methods

Between May 2012 and May 2014, eight patients underwent radiofrequency thermal ablation (RFA) of 16 retroperitoneal nodes. Patient's characteristics, American Society of Anesthesiologists (ASA) score at the time of ablation, systemic treatments, previous renal surgery, and staging for the primary lesion are listed in Table 1. Patient's history was analyzed and images were completely reviewed within our multi-disciplinary team. Treatment options were discussed and a consensus achieved between a consultant Urologist, Oncologist, and Interventional Radiologist.

Selection criteria for RFA treatment were as follows: histologically verified retroperitoneal metastases from RCC, previous surgery, lesions dimension no larger than 3.5 cm, no other metastatic site elsewhere after a staging with a contrast media CT scan (HiSpeed Advantage; GE Medical Systems).

All patients were seen by Interventional Radiologist in the outpatient consultation room and a full explanation of the procedure was given with particular attention to the

pros and cons and the need for long-term imaging follow-up. Thus, a formal written informed consent was obtained. A week before the treatment all patients were referred to our pre-assessment department for a complete check of their general clinical condition by an anesthesiologist. A final ASA score was recorded.

All procedures were performed as inpatients in the Interventional Radiology or Abdominal Surgery departments under general anesthesia. Discharge was considered after a clinical evaluation and CT scan performed within 24 h after procedure to exclude complications. Post procedure instructions were provided including a 1 month CT scan and a following outpatient consultation.

The patient's database was assessed for immediate and late technical success, follow-up length, disease relapse, and complications. Technical success was defined as the complete nodule devascularization at postoperative CT scan. Follow-up was considered in months from our treatment. Complications were classified according to the Society of Interventional Radiology (SIR) Standards of Practice into "minor" and "major" [6]. For the two laparotomic thermal ablations the Clavien–Dindo classification of surgical complications was used [7].

Our Ethical Committee approved this review study, all the procedures were in accordance with the ethical standards of the institutional research committee and informed consent was waived by the Ethical Board for the database consultation.

## RFA Procedure

In six patients, utilizing general anesthesia, the procedure was performed percutaneously in the angio-suite utilizing the most favorable position for a direct needle approach to the retroperitoneal lesion. In two other patients with pancreatic nodes, a laparotomic approach was preferred because of either a difficult location or the need for treating all lesions in one session, respectively. In the two laparotomic procedures, a high-frequency probe was used for US guidance in an intraoperative setting. A contrast media CT

**Table 1** Patient's characteristics

Patients	1	2	3	4	5	6	7	8	Mean
Age	77	63	43	54	64	63	76	63	59
Sex	M	M	M	M	F	M	M	M	
ASA	3	2	2	3	3	2	3	3	
Surgical approach	RN	RN	PN	RN	RN	PN	PN	PN	
Staging	pT1b pNx	pT3 pN0	T1a pNx	NA	NA	pT1b pNx	pT1a pNx	pT1a pNx	
Neoadjuvant treatment	\	\	\	BEV-INF	BEV-INF	Sunitinib	\	\	

RN radical nephrectomy, PN partial nephrectomy, BEV-INF Bevacizumab and Interferon alfa, ASA American Society of Anesthesiologists score

scan was performed as soon as possible after laparotomy according to the clinical circumstances.

RFA was performed with different sizes (2, 3, or 3.5 cm) umbrella-shaped multi-tines needle electrode (LeVeen CoAccess RFA needle electrode, Boston Scientific, MA, USA), selected to match the size of the tumor. The electrode was inserted at two to three different sites in the tumor on the basis of node size and shape and then connected to the generator (RF 3000, Boston Scientific); energy was applied till roll-off occurred. Roll-off was achieved two or three times before needle repositioning or removal and was considered the endpoint for complete tissue coagulation.

In all six percutaneous procedures, the RFA needle was inserted under US guidance, and its correct position was confirmed by CT (Fig. 1). If needed pneumodissection was also induced with a percutaneous 22 G needle after deploying hooks and before generating energy in order to protect adjacent bowels from heat damage (Fig. 2). After RFA, all patients were observed overnight and discharged the following day if clinically stable. Prior to discharge a cell blood count and contrast CT were performed to rule out an unapparent complication.

All procedures were performed by four Interventional Radiologists with more than 15 years of experience in thermal ablation procedures. Once discharged, all patients were evaluated both clinically and with CT on regular basis at 30 days, 3 months, and every 6 months after treatment.

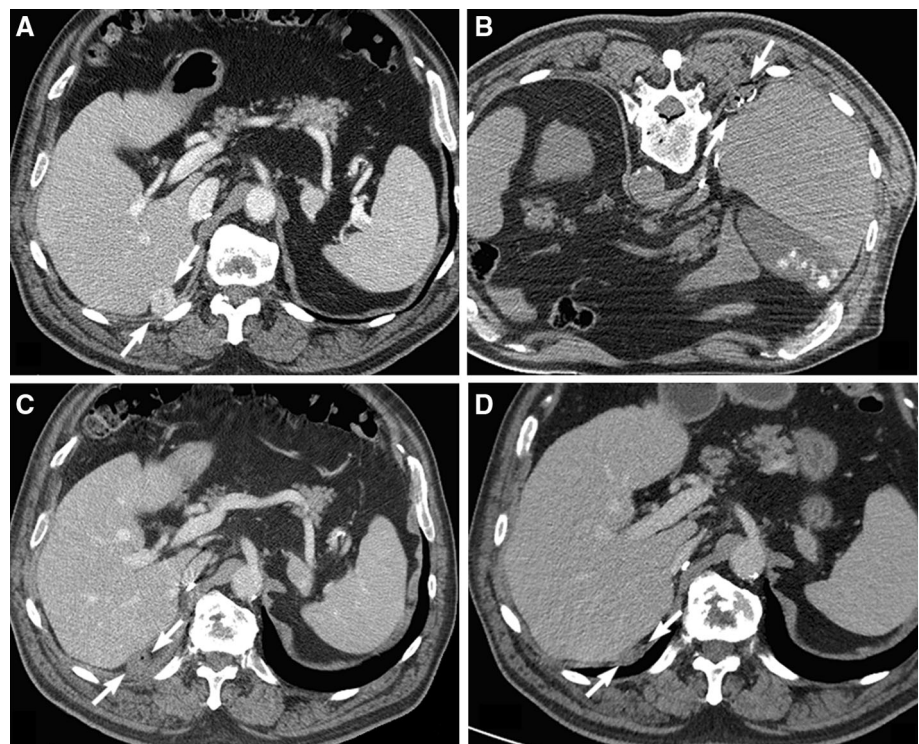
## Results

A total of seven male and one female (mean age of 59 years) underwent RFA of recurrent RCC after surgery. All patients had previous renal surgery (partial or radical nephrectomy) with a mean relapse time of 57 months. Details are summarized in Table 2.

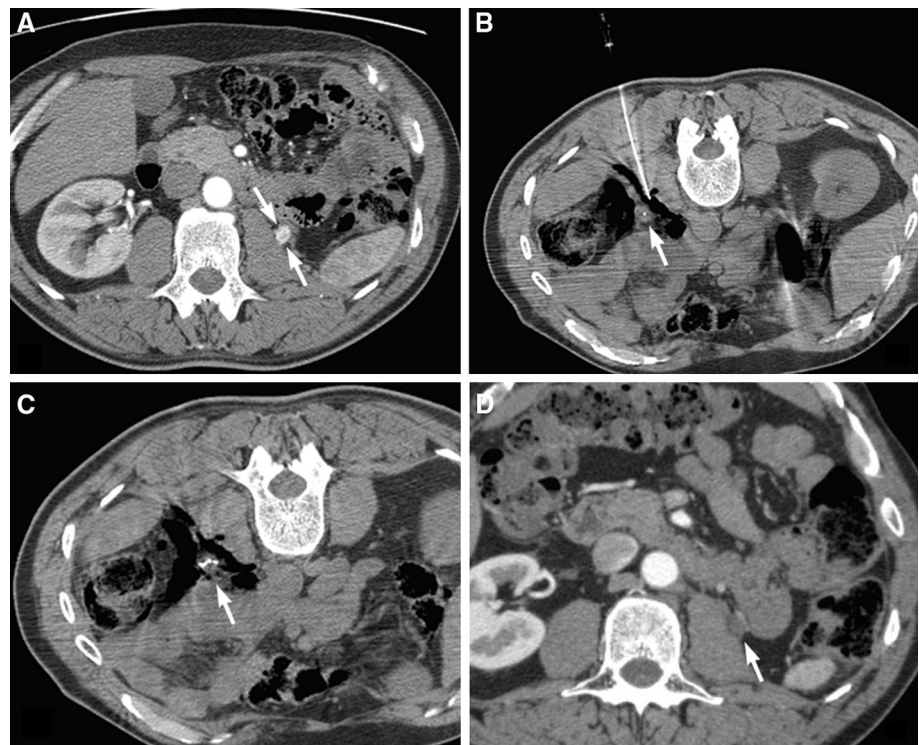
All 16 nodes were completely ablated with no evidence of residual enhancement at post treatment CT and at the last CT examination. With a mean follow-up of 12 months (range 7–17), five patients are free from disease, one is progressing after 15 months for a single relapsed node not suitable for further percutaneous approach (patient 3, Table 2); the two last patients had lung metastases 10 and 13 months after RFA treatments with, respectively, stable disease and partial response after systemic treatment (patients 5 and 6, Table 2). All patients but three received immunotherapy (interferon, bevacizumab, and sunitinib) before or after RFA. All patients are alive at the time of manuscript submission.

Complications were observed in 2/8 (25 %) occurring only in laparotomic treatments. The first patient underwent ablation of five lesions placed on the anterior pancreas surface; one was closely linked to the hepatic hilum and a plastic biliary stent was endoscopically placed before the ablation in order to avoid biliary obstruction in case of main duct thermal damage. A retroperitoneal fluid collection located in the sovramesocolic area was treated

**Fig. 1** A single recurrence 78 months after radical nephrectomy for RCC (pT1b pNx) in the right subfrenic space. The nodal lesion (arrows) is represented before treatment (A), during radiofrequency with needle hooks deployed (B), the day after the treatment with some residual air bubble inside (C) and 12 months after with a residual scar (D)



**Fig. 2** A single nodal recurrence (arrows), 9 months after radical nephrectomy for RCC (pT3 pN0) in the left renal fossa before treatment (A), during treatment after a careful pneumodissection (B), with hooks deployed inside the nodal lesion (C) and 6 months after with a complete devascularization (D)



**Table 2** Details of the previous patient's history, RFA procedure and follow-up

Patients	1	2	3	4	5	6	7	8	Mean
Time to relapse (months)	78	9	120	60	36	42	60	49	56.75
Lesion number	1	1	2	1	5	3	2	1	
Tumor size (mm)	23	12	13–14	20	12–7–15–5–13	26–30–34	11–12	17	16.5
Tumor location	Subfrenic space	Renal fossa	Renal fossa	Pancreas	Pancreas	Renal fossa	Renal fossa	Renal fossa	
Approach	P	P	P	L	L	P	P	P	
Pneumodissection	N	Y	N	\	\	Y	N	N	
Operative duration (min)	105	70	50	331	270	150	50	80	135
Hospital stay (days)	2	3	3	15	18	3	2	2	6
Peri-operative complications	\	\	\	Collection	Fistula	\	\	\	
Complication (SIR-C/CD)	\	\	\	2 s CD	2 s CD	\	\	\	
Follow-up (months)	12	7	17	12	15	16	7	7	11.7
Technical success	Y	Y	Y	Y	Y	Y	Y	Y	
Local progression free survival	12	7	15	12	15	16	7	7	11.3
Systemic treatment	\	Sunitinib	Sunitinib	BEV-INF	BEV-INF	Sunitinib	\	\	
Type (AD/NEO)	\	AD	AD	NEO	NEO\AD	NEO\AD	\	\	
Progression-free survival	12	7	15	12	10	13	7	7	
Laparotomic surgery for relapse	\	Y	Y	Y	Y	Y	\	\	

P percutaneous, L laparotomic, CD Clavien–Dindo classification, SIR-C Society of Interventional Radiology Classification System for Complications by Outcome, AD adjuvant, NEO neoadjuvant



conservatively. The second patient had a laparotomic approach in order to restore a symptomatic laparocoele as consequence of the previous renal surgery with a surgical mesh misplacement and a subsequent abdominal fistula without surgical reintervention. Both complications are grade 2 following the Clavien–Dindo classification.

## Discussion

This study is focused on RFA for loco-regional recurrence after surgery for RCC. We merely reported feasibility, safety, and progression-free survival (local and systemic) in a small population, but so far no previous description has been reported in literature.

To our knowledge, the largest retrospective analysis for loco-regional recurrence after nephrectomy is from Itano et al. [8]: they analyzed 1737 cases after nephrectomy finding 1.8 % of loco-regional recurrence. The risk of local recurrence was associated with primary tumor stage and even if rare such event seemed to be related with a poor prognosis with a 5-year survival of 51 % for those who underwent surgical treatment and 13 % for those who underwent medical treatment only.

Until now the only loco-regional curative treatment option for such patients has been either open or laparoscopic surgery. El Hajj et al. [9] described their experience of nine patients treated by a pure laparoscopic approach for local recurrence of a renal tumor. They showed that the laparoscopic approach is a safe and feasible alternative treatment option for selected cases with low morbidity. They concluded that surgical removal of isolated local recurrence remains the only possibility of cure in patients with RCC. More recently RFA for small renal masses is becoming a standard for primary malignancies and a randomized trial versus surgery has been claimed [10]. The only clinical experience published dealing with percutaneous treatment of local recurrence after surgery for RCC is from Bang et al. [11]: they analyzed complications, local tumor recurrences, overall survival, and of cost-effectiveness for multisite cryoablation of oligometastatic RCC. This paper has several differences with our study: a palliation intent is assessed, patients with local recurrence are a sub population even with systemic disease, nodes up to 7 cm are enrolled, and cryoablation is used as opposed to RFA. However, advantages of a non invasive treatment such as short hospitalization and low morbidity are emphasized and comparable to those of our six patients treated percutaneously.

In our opinion, patient selection should play a key role in order to achieve a better clinical outcome. Our patients were selected with the intent to achieve a radical result, with a single session ablation of the nodes sized up to

3.5 cm in maximum diameter. This may be the reason explaining a survival of 100 % with 62 % (5/8) of disease-free patients in our series, even considering a short follow-up. Therefore in any case of RCC local recurrence after surgery smaller than 3.5 cm, we strongly suggest this procedure because of the lower morbidity versus open and laparoscopic surgery.

One important consideration is the surgical risk of tumor rupture as source of local relapse: no clear evidence from literature is available, but tumor recurrence in the renal fossa after pT1 RCC was described [12] as well as in our series (4/8 patients had pT1 RCC). There are not enough data to confirm this hypothesis; however, it could be reasonable to treat such patients with thermal ablation *ab initio* instead of resection, in order to reduce the risk of local relapse. Indeed once again the need for a randomized prospective trial is reminded [10].

There are some important limitations in our paper: first the patient population is small. Second and more important we retrospectively consulted our database collecting a heterogeneous group of patients.

In conclusion this study, despite the limitations, underline the feasibility and the potential curative role of RFA for small isolated RCC local recurrence after surgery. Such treatment option should be always considered as first line loco-regional therapy in patients with this uncommon clinical condition and assessed on a larger patient group.

**Conflict of interest** Lorenzo Monfardini, Gianluca Maria Varano, Riccardo Foà, Paolo Della Vigna, Guido Bonomo, and Franco Orsi declare that they have no conflicts of interest including financial support, relationship, or any other professional and/or personal interest.

**Statement of Informed Consent** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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