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Partial Nephrectomy After Previous Radio Frequency Ablation: The National Cancer Institute Experience

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Abstract

Purpose—Development of new renal tumors or recurrence after radio frequency ablation not amendable for repeat ablation presents a difficult therapeutic dilemma. We report on the outcomes of partial nephrectomy on kidneys previously treated with radio frequency ablation.

Materials and Methods—We performed a chart review of 13 patients who underwent 16 attempted partial nephrectomies following radio frequency ablation. Hospital records and operative reports were reviewed for demographic data, perioperative data and outcomes. The outcomes of the present series were compared to historical controls of published studies in similar patient populations.

Results—No cases were converted to radical nephrectomy. Median time from radio frequency ablation to surgery was 2.75 years (range 1 to 7.1). A median of 7 tumors (range 2 to 40) were removed with a median estimated blood loss of 1,500 ml (range 500 to 3,500) and a median operative time of 7.8 hours (range 5 to 10.7). Operative notes commented on the presence of severe fibrosis in the operative field in 12 of 16 cases (75%). There was a modest but statistically significant decrease in renal function. Partial nephrectomy after radio frequency ablation had a higher reoperation rate compared to other series of primary or repeat partial nephrectomies but had the lowest rate of vascular or visceral injuries.

Conclusions—Partial nephrectomy on kidneys previously treated with radio frequency ablation is a technically challenging but feasible procedure. Residual or metachronous disease after radio frequency ablation may be salvaged with partial nephrectomy with a modest decrease in renal function. A trend toward a higher chance of reoperation and urine leak after partial nephrectomy after radio frequency ablation may be useful information for the planning and discussion of treatment decisions.

Keywords

nephrectomy; catheter ablation; treatment outcome

The incidence of renal cell carcinoma has increased during the last decade with an estimated 54,390 new cases and 13,010 deaths in 2008.[1] This trend is at least partly due to the widespread use of cross-sectional imaging with computerized tomography or magnetic

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resonance imaging leading to the detection of small asymptomatic renal masses.[2] Recently ablative techniques such as radio frequency ablation or cryoablation have become increasingly popular options for patients with small renal masses.

Although ablation may offer reasonable efficacy with less morbidity compared to partial nephrectomy, the long-term oncological outcome data are not yet available.[3,4] Short-term data on RFA or cryoablation have shown reasonable cancer control with 3-year disease-free survival similar to partial nephrectomy. Despite some advantages the recurrence of lesions or incomplete ablation remains a diagnostic and therapeutic dilemma. Some studies have shown a viable tumor in nephrectomy specimens immediately following RFA and recurrence rates have been as high as 25%. However, this is dependent on patient selection, tumor size and tumor location, and some of the studies had major flaws in histological techniques.[5,6] Nevertheless, RFA local failures require repeat or further treatment.[3,7–9]

For patients with residual disease after previous RFA, repeat ablation is frequently the first step. Unfortunately repeat ablation may be difficult or not possible in some patients due to repeat ablation failures, new tumor formation in a location not amendable to ablation, post-ablation scarring or adhesions to adjacent organs. In these patients the remaining options are observation or surgical resection. Additionally, in cases of bilateral tumors, solitary kidneys or renal insufficiency when repeat ablation is not possible, nephron sparing surgery remains the only reasonable option to avoid dialysis. To our knowledge there are limited data on the feasibility and outcomes of partial nephrectomy following ablation. We report our experience with attempted partial nephrectomy on kidneys previously treated with RFA.

MATERIALS AND METHODS

We reviewed the records of all patients who underwent attempted partial nephrectomy on a renal unit previously treated with RFA at the National Cancer Institute from 2001 to 2007. All patients were part of a National Cancer Institute institutional review board approved protocol. Patients were included in the analysis if they had an attempted partial nephrectomy performed on a kidney previously treated with RFA only. Patients were excluded from study if they had any other renal surgery before RFA on the same renal unit. The indications for surgery included suspicious enhancement or growth of the previous RFA treated lesion, development of new tumor(s) in location(s) not amendable to safe ablation or multiplicity of tumors.

Preoperative and postoperative assessment included abdominal CT or magnetic resonance imaging, chest CT, routine laboratory work, 24-hour urine collection and nuclear medicine renal scans to assess differential function. eGFR was calculated using the Modification of Diet in Renal Disease equation, eGFR = 186 × (serum creatinine-1.154) × (age)−0.203, from which the result is multiplied by 0.742 for female patients and by 1.212 for black patients.

Baseline demographic data were collected on all patients. Operative reports and hospital discharge summaries were reviewed for intraoperative and perioperative outcomes. Specific attention was given to intraoperative complications, indications of difficult dissection around the previous RFA site in the operative note and renal ischemia time. Perioperative outcomes were assessed by estimated blood loss, transfusion requirements, visceral or vascular injuries, prolonged urinary leak, renal loss, reoperation, cardiovascular events and the need for hemodialysis. The pathology report was reviewed with specific attention to the post-RFA lesion pathology (if specified). Renal functional outcomes were assessed by comparing preoperative and postoperative (at 3 months) creatinine measurements, eGFR, 24-hour urine collection, and differential renal function using nuclear renal scans. The 2-tailed Student t test was performed to compare functional data with $p < 0.05$ considered statistically significant.

Perioperative outcomes of partial nephrectomies of the present series were compared to previously published studies describing outcomes of partial nephrectomy in patients with hereditary or multifocal kidney cancer. Table 1 was constructed after the pertinent data were extracted from the published studies.[10–12]

RESULTS

We identified 13 patients who underwent a total of 16 attempted partial nephrectomies following 18 RFA treatments. Partial nephrectomy was performed in all patients. A total of 15 partial nephrectomies were performed via open approach and 1 case was performed laparoscopically. All open partial nephrectomies were approached via a flank incision. Of the 16 partial nephrectomies 13 were performed due to suspected RFA failure and 3 were performed due to new lesions in the previously ablated kidney. Of the 13 cases suspected to be RFA failures 8 had evidence of increasing ablated lesion size while 5 had persistent ablated lesion enhancement on followup CT.

In terms of the clinical characteristics of the 13 patients median time from RFA to surgery was 2.75 years with a median resected tumor size of 3.2 cm (range 2.0 to 6.0). Median patient age was 34.5 years (range 17 to 64) and median BMI was 28 (range 21 to 40). All patients were white, 8 of 13 were men, 63% of procedures were right kidney and 13 of 18 RFAs were percutaneous with the remainder performed laparoscopically.

In terms of perioperative outcomes from the post-RFA partial nephrectomies a median of 7 tumors were removed with a median operative time of 7.8 hours and a median estimated blood loss of 1,500 ml. Of the 16 cases 12 (75%) used cold ischemia with a median renal hilum clamping time of 27 minutes (range 24 to 62). Of the cases 50% required intraoperative or postoperative blood transfusion with a median of 4 units (range 1 to 8) transfused.

Of the 16 operative reports 12 (75%) indicated a difficult dissection surrounding the previously ablated tumor. Five cases (31%) were complicated by intraoperative pleural injury. One case was complicated by intraoperative ureteral transection requiring ureteroureterostomy. Three cases (19%) were complicated by postoperative urine leak, defined as an increased creatinine in the drain at discharge home. Two cases of urine leak resolved spontaneously and 1 required postoperative ureteral stent placement. There were 2 patients requiring return to the operating room, the previously mentioned patient for ureteral stenting and the other with postoperative hemorrhage refractory to transfusion requiring reoperation to control bleeding. Three more patients had rhabdomyolysis, atrial fibrillation and deep venous thrombosis, respectively.

Renal functional outcomes are presented in table 2. There was a statistically significant increase in serum creatinine ($p = 0.003$) and decrease in creatinine clearance ($p = 0.0017$) after post-RFA partial nephrectomy. In addition, there was a statistically significant decrease in split function on the operated kidney ($p = 0.0171$). However, importantly there was no loss of renal units or need for postoperative hemodialysis in any of the patients.

In table 1 the outcomes of the present series are compared with previously published National Cancer Institute partial nephrectomy series to evaluate complication rates among similar cohorts of patients with hereditable renal cancer syndromes or multifocal renal lesions. We found that post-RFA partial nephrectomy carries a higher risk of urine leak than primary partial nephrectomy (19% vs 5%). Post-RFA NSS also had a higher reoperation rate than primary and repeat partial nephrectomy. However, there were no visceral (except for ureteral transaction) or vascular injuries in the present series and no renal units were lost.

Final pathology reports were reviewed in all 16 cases and evidence of recurrent RCC was noted in 7. Of the 13 cases performed due to suspicion of RFA failure, 6 had evidence of persistent RCC noted on final pathology reports. Preoperatively 4 of these lesions had evidence of increasing size on preoperative CT while 2 had persistent enhancement on pre-operative imaging. Of the 3 patients undergoing partial nephrectomy due to a distinct new lesion in the same kidney, 1 post-RFA lesion had some mild enhancement on preoperative CT and had evidence of persistent RCC on the final pathology report. The pathology reports of those tumors that did not have evidence of RCC after prior ablation only noted fibrosis and necrosis in the area of the ablated tumor without specific mention of increased tissue inflammation. Resected tissue was not stained with nicotinamide adenine dinucleotide phosphate for the presence of viable RCC as previously described.[5] Because these partial nephrectomies were performed in the setting of bilateral multifocal disease, we attempted to minimize the resection of normal parenchyma by performing a resection immediately adjacent to tumor pseudocapsule as described by Herring et al.[10] Therefore, only gross and not pathological examination of the surgical margins was performed.

DISCUSSION

It is now becoming evident that as ablative therapies are increasingly used, many urologists may face a complex problem of treating patients who have undergone ablation who may require surgery for recurrence or new tumors. In fact, some patients who underwent ablation as the primary intervention (because of a solitary kidney, bilateral renal masses or renal insufficiency) may become even more challenging to treat on the need for secondary intervention. In fact, these patients may still end up needing surgery despite avoiding surgery initially. However, no reliable prospective or well controlled data exist at this time regarding outcomes of cryoablation or RFA vs partial nephrectomy in terms of operative complexity, patient selection bias, rapidly evolving technologies, widely variable surgical and interventional techniques, and variable followup methodologies.

As ablative therapies gain prevalence for the treatment of small, asymptomatic renal lesions and longer term outcomes become available, the frequency of post-ablative intervention and surgery will only increase. In fact, a recent large meta-analysis by Kunkle et al demonstrated that compared to partial nephrectomy series there is an increased risk of local recurrence after cryoablation and RFA.[13] Many of these cases of recurrence require additional treatments and repeat ablation is used most commonly.[14]

However, there are a few scenarios in which repeat ablation is not possible or advisable and surgical extirpation may be the most reasonable next step. Such scenarios include repeated ablation failures, tumor growth after ablation, large tumor size, disease progression, hilar location of a new tumor and proximity of heat sensitive structures. In addition, percutaneous RFA is frequently facilitated by hydrodissection of surrounding structures to access the lesion of interest. Distortion of a normal renal and ureteral anatomy due to scarring or adhesions of the kidney to the surrounding viscera from previous ablation may preclude adequate percutaneous hydrodissection necessary for undergoing repeat ablation. Another possibility may simply include the unwillingness of the patient to undergo the same treatment modality that has failed once already.

We describe our experience with post-RFA renal surgery. Of 16 partial nephrectomies 13 were performed primarily for suspicion of an enhancing or enlarging lesion after radio frequency ablation, while the 3 remaining partial nephrectomies were performed for separate tumor formation following RFA, not for RFA failure. All patients undergoing partial nephrectomy had hereditary renal cell carcinoma, 11 patients having von Hippel-Lindau disease and 2 with hereditary papillary renal cell carcinoma.

There were 7 tumors that had the presence of RCC from the RFA site on the final pathology reports. These tumors were described as necrotic and hemorrhagic RCC with large areas of fibrosis. While these reports may confirm pathological persistence or RCC recurrence following RFA, it is important to appreciate that the present study describes the feasibility of NSS following RFA ablation but it is not designed to address RFA efficacy. Additionally, these RFA failures may not truly reflect the outcomes of modern RFA technology since all of these patients were treated by a first generation lower energy system early in the RFA experience.[15] Finally we only examined the final pathology reports and did not perform nicotinamide adenine dinucleotide phosphate vitality staining to determine the actual tumor viability.

Of importance, preoperative CT characteristics did not allow the accurate separation of those lesions with RCC from those with fibrosis or necrosis only. Neither increase in size nor enhancement could reliably predict the presence of RCC. In fact, 4 of 8 lesions with an increase in size had RCC on final report, while 3 of 5 lesions that enhanced had evidence of RCC. These findings may further call into question the reliability of CT for post-RFA surveillance.

The median age of 34.5 years reflects the earlier presentation of RCC in patients with these familial disorders. Many of our patients are indeed younger (but not always healthier) than the usual patients with kidney cancer undergoing ablative therapy.[14] Patients in our cohort are predisposed to formation of multiple metachronous bilateral renal tumors.[16] It has been our practice to observe the renal lesions until they reach 3 cm in the largest dimension and maximize the longevity of the renal units by performing nephron sparing renal surgery with removal of multiple tumors.[10,17–19] At our institution we frequently perform surgeries on previously operated kidneys. Therefore, we have an opportunity to compare the complexities of surgeries performed after prior operations with those performed after RFA.[11,12]

Similar to our results for repeat or salvage (3 or more partial nephrectomies on the same renal unit) renal surgeries, post-RFA partial nephrectomies were associated with significant scarring as reported in 75% of operative dictations. These results are in contrast to the findings of Nguyen et al in which review of surgical dictations did not indicate excessive perinephric scar tissue or increased technical difficulty in post-RFA surgeries.[6] In fact, nearly a third of our post-RFA cases had pleural injuries with 1 requiring a chest tube placement, and overall 6 of 16 (38%) and 7 of 16 (44%) had intraoperative or postoperative complications, respectively. Our higher rate of complications may be explained by longer cases, greater numbers of tumors removed and uniform attempts to perform partial nephrectomy rather than convert to total nephrectomy. However, the role of surgical team experience or variability was not specifically studied. Our post-RFA surgical complication rates may potentially be higher because a proportion of our patients had RFA performed laparoscopically whereas all RFA treatments by Nguyen et al were performed percutaneously.[6] Although it would be difficult to compare the degree of scarring and fibrosis due to RFA or cryoablation, from a percutaneous or laparoscopic approach it becomes evident that both ablative modalities can produce substantial local reaction and fibrosis, making subsequent intervention challenging. Indeed in the study by Nguyen et al partial nephrectomy was performed in only 2 of 10 patients who underwent attempted extirpation of post-ablative recurrence. One successful NSS surgery was done in the post-RFA group and 1 was successfully completed in the post-cryoablation group.

Partial nephrectomy usually offers a dialysis-free quality of life and avoidance of renal transplantation. All patients in our cohort had a contralateral kidney in place with tumors that already required or would require intervention at some point. Despite the fact that there was a statistically significant decrease in renal function, the absolute decrease was modest so that most would probably not consider it clinically significant. Nevertheless, the relative differential function of the operated kidney did decrease from a median of 50.6% to 43.6% measured by renal nuclear scans. Others have also reported some renal functional loss after partial nephrectomy.[20]

To our knowledge there have been only a few previous case reports detailing the feasibility and difficulties of surgery in the post-ablation case. However, based on our experience these surgeries are technically challenging and complicated by severe fibrosis surrounding the previously ablated lesion. These challenges may have resulted in difficult dissections due to distortion of normal anatomical planes and a high rate of pleural injury in our series. In addition, there was a relatively high rate of postoperative urinary leak due to injury to the collecting system even compared with similar patients undergoing extirpation of multiple lesions.[10–12] A lower rate of vascular and visceral complications in the post-RFA group may be explained by the fact that post-RFA surgeries were performed on patients who had only 1 to 2 lesions treated with RFA compared to redo or salvage partial nephrectomies performed after resection of numerous lesions during initial surgery (median 15, range 1 to 51) (table 1).

Additionally, a lower rate of vascular injury compared to the salvage partial nephrectomy group may be due to an easier hilar dissection in the post-RFA group. This may be explained by the fact that most lesions treated with RFA are located peripherally, minimizing the need for hilar dissection and, thus, minimizing hilar fibrosis.

In the present series we describe our experience in performing partial nephrectomy on kidneys previously treated with radio frequency ablation to provide a framework for decision making when counseling patients considering ablation. Although the majority of preselected patients in the community do end up disease-free with no need for subsequent interventions, the possible need for subsequent treatment must be considered (whether repeat ablation or surgical excision). This could be even more important for patients with lesions located on the anterior surface and upper pole of the kidney, considering the chance of severe adhesions to nearby viscera. Patients need to be informed of the potential increased surgical risks from having had prior RFA, including pleural injury, urinary leak and reoperation.

There are a few lessons that we have learned from this experience. While post-RFA surgeries are difficult, they are feasible and allow all renal units to be successfully saved without any need for postoperative dialysis. Despite anticipated difficulties the nephron sparing goal is paramount and should be attempted in all patients whenever feasible. In addition, the location of lesions should be carefully evaluated when planning ablation procedures in the first place. The anterior and hilar location of the tumor, as well as proximity to the ureter, should indicate extra caution when ablation is planned. This approach could help prevent complications during potential subsequent surgery in these patients. Since we have not been placing anti-adhesive materials when performing laparoscopic RFA we cannot comment on usefulness. Also in this small cohort CT did not allow us to accurately separate those patients with residual RCC from those with post-RFA fibrosis. Therefore, one may consider a role for biopsy in following post-RFA patients. Finally physicians recommending ablative therapy for patients with multifocal bilateral tumors should be aware of the potential future surgical challenges as new tumors may form in locations not amenable to repeat ablation.

Limitations of the study include its retrospective nature, small numbers, patient selection bias, variability of surgical teams inherent to longitudinal studies and limited cohort of patients. Comparison to historical controls and literature alone may be of limited value. The study may be confounded by lack of control for operator experience, learning or surgical volumes. Yet despite the small numbers, this may be the largest reported series of partial nephrectomy after ablative technologies. Despite these limitations we believe that this series may serve as a useful resource for urological surgeons in patient counseling before ablation or when faced with patients previously treated with RFA who are now in need of nephron sparing surgery.

CONCLUSIONS

Patients faced with radiological recurrence of RCC after RFA may have the option to proceed with observation, repeat ablation, radical nephrectomy or partial nephrectomy. Our series reveals that partial nephrectomy on kidneys previously treated with RFA is a technically challenging but feasible procedure with complication rates higher than those reported in the literature. These findings may be useful for physicians and patients in making treatment decisions when faced with such a clinical dilemma.

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Abbreviations and Acronyms

CT	computerized tomography
eGFR	estimated glomerular filtration rate
GFR	glomerular filtration rate
NSS	nephron sparing surgery
RCC	renal cell carcinoma
RFA	radio frequency ablation

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Table 1

Comparison of perioperative outcomes among present series and published studies

	Herring et al[10]	Johnson et al[11]	Bratslavsky et al[12]	Present Series
Partial nephrectomy type	Primary	Repeat	Salvage	Post-RFA
No. pts	50	47	11	13
No. partial nephrectomies	65	51	13	16
Median tumors removed (range)	15 (1–51)	7 (1–55)	5 (1–27)	7 (2–40)
Median ml estimated blood loss (range)	2,885 (150–23,000)	1,800 (50–21,500)	2,100 (200–12,000)	1,500 (500–3,500)
No. transfusion requirement (%)	Not applicable	38 (75)	10 (77)	8 (50)
Median units transfused (range)	4 (0–34)	2 (0–31)	4.5 (0–18)	4 (1–8)
No. intraop complications (%):				
Visceral or vascular injury	5 (8)	2 (4)	6 (46)	0
Ureteral injury	0	1	0	1 (6)
Pleural injury	3 (5)	Not applicable	Not applicable	5 (31)
No. postop complications (%):				
Prolonged urine leak	3 (5)	8 (15)	2 (15)	3 (19)
Permanent hemodialysis	0	3 (6)	2 (15)	0
Renal unit loss	3 (5)	3 (6)	3 (23)	0
Rhabdomyolysis	0	0	1 (8)	1 (6)
Reoperation	2 (3)	2 (4)	4 (36)	2 (13)
Cardiovascular events	1 (1)	1 (2)	0	2 (13)

Table 2

Renal functional outcomes

	No. Pts	Preop	Postop	p Value
Median mg/dl serum creatinine (range)	15	1 (0.6–1.2)	1.1 (0.8–1.3)	0.003
Median ml/min/1.73m^2 GFR (range)	15	91 (64–138)	81 (57–99)	0.0017
Median % differential function of operated unit (range)	14	50.6 (34–60)	43.6 (27–60)	0.0171