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Management and Outcomes of Tumor Recurrence After Focal Ablation Renal Therapy

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Abstract

Background and Purpose: Cryoablation (CA) and radiofrequency ablation (RFA) have emerged as viable treatment options for patients with small renal masses. Although the intermediate oncologic outcomes are comparable to those of surgery, the management of a recurrence is still controversial. This review intends to provide a comprehensive overview of management options and outcomes after failed focal ablation renal therapy. In addition, it presents how patients in whom CA and RFA fail are treated at our institution.
Methods: A systematic review of the Pub-Med database was performed to identify articles on renal CA and RFA. The keywords used were "small renal mass," "enhancing renal mass," "cryoablation," "radiofrequency ablation," "tumor recurrence," "postablation," "management," "salvage nephrectomy," "partial nephrectomy," "laparoscopy," and "active surveillance." English-language articles between 1995 and 2009 were reviewed.
Results: A total of 30 articles were included in this review; however, only 6 original articles were found that dealt specifically with the theme of this review. In the case of tumor recurrence after failed CA or RFA, viable management options include active surveillance, repeated ablation, and salvage partial/radical nephrectomy. Active surveillance up to 1 year appears to be a safe option in patients with early enhancement after CA or RFA, because the majority of the enhancements may be from postoperative inflammation. Repeated CA and RFA remain the most commonly performed procedures after a failed ablation with excellent oncologic outcomes. When significant tumor progression is present on postoperative follow-up, however, surgery is necessary. Although a partial nephrectomy would be advisable to preserve renal function, intraoperative and postoperative complications are a concern because of scarring and fibrosis from the initial ablation. For this reason, a radical nephrectomy is most commonly preferred. This could be performed through an open or a laparoscopic approach.
Conclusions: When a recurrence is suspected after CA or RFA, different options are available. This review has highlighted that active surveillance, reablation, and surgery (usually radical nephrectomy) are all viable options for the management of a failed ablative procedure.

Introduction

Kidney cancer is the third most common form of cancer in the urinary tract. The American Cancer Association estimates that 57,760 new cases of kidney cancer will be diagnosed in 2009 in the United States, which accounts for 3.91% of all new cancer incidents. With an estimated 12,920 deaths attributable to the disease, renal-cell carcinoma (RCC) is one of the most lethal genitourinary cancers.[1]

Over the last 30 years, the detection of small renal masses (SRMs) less than 4 cm has increased because of the widespread use of modern imaging technologies.[2–4] Because of earlier detection, RCC tumor size at presentation has been steadily decreasing, resulting in a concurrent stage migration.[5] SRMs now account for 48% to 66% of new RCC diagnoses, which has had significant clinical implications; physicians must now consider how to best manage low-stage kidney disease.[6]

Surgical resection remains the current standard of care for localized RCC, because outcomes have been strong with a 5-year cancer-specific survival rate of more than 95%.[7,8] It is well known, however, that SRMs are usually low-grade, slow-growing tumors with minimal metastatic potential.[9] Furthermore, they are often detected in the elderly population who have significant comorbidities.[10] For these reasons, in the last decade, SRMs have been increasingly managed through

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options that are different from surgical resection, such as active surveillance, cryoablation (CA), and radiofrequency ablation (RFA).

CA and RFA can be performed through an open, laparoscopic, or percutaneous approach. The vast majority of CAs, however, are performed laparoscopically, while the majority of RFAs are performed percutaneously.[11] At our institution, anterior and lateral tumors are generally managed with laparoscopic CA through a transperitoneal approach and posterior tumors with percutaneous RFA through a retroperitoneal approach.[12]

Five-year cancer outcomes for patients with SRMs who are treated with CA and RFA are similar because both approximate a 95% cancer-specific survival rate.[10] Although these results are similar to those of surgical resection, it is well documented that local tumor recurrence occurs more commonly after focal ablations than after radical or partial nephrectomies.[13–15] CA and RFA, however, are associated with lower morbidity for patients and fewer complications.[15–17]

This article evaluates the management and outcomes of SRMs after failed focal renal therapy by reviewing the existing literature. In addition, it also presents how failure after renal CA and RFA is managed at our institution.

Materials and Methods

A systematic review of the literature was performed. The data for this review were obtained by searching the PubMed database for articles that were published from 1995 through 2009. Three persons were involved in the data collection. The search terms used were "small renal mass," "enhancing renal mass," "cryoablation," "radiofrequency ablation," "tumor recurrence," "postablation," "management," "salvage nephrectomy," "partial nephrectomy," "laparoscopy," and "active surveillance." All articles identified were English language and full text.

Results

A total of 30 articles were considered for this review; however, only 6 original articles were found in the literature that addressed specifically the theme of this review.

Although surgical resection remains the standard of care for the management of SRMs, valid alternative options include CA and RFA, as demonstrated by the largest multiseries review of the literature on ablation-treated SRMs by Kunkle and Uzzo.[18] In this study, 94.8% of CA lesions and 87.1% of RFA lesions showed no evidence of residual or recurrent tumor after the initial ablation procedure with a mean follow-up of 18.7 months.[18] Although recurrence is relatively rare, a certain number of lesions do recur, as documented by enhancement on postoperative imaging or presence of tumor cells on biopsy findings. Consequently, it is important for surgeons to have a strong understanding on how to treat tumors after failed ablative therapy. SRMs that are not successfully managed by the initial focal renal ablation can be managed through active surveillance, repeated ablation, or salvage surgery, usually salvage nephrectomy.

Active surveillance

Successful CA and RFA procedures should show no contrast enhancement and no tumor growth at follow-up imaging. In practice, however, early postoperative scans may show increased enhancement and growth, regardless of whether a viable tumor is present.

For example, in a previously reported study of 164 laparoscopic CAs, more than 20% of patients showed peripheral enhancement at 3 months, although fewer than 5% showed enhancement at 1 year and only 1.8% of patients were eventually determined to be suspicious for a residual tumor.[19] Similarly, in another study, 16% of the patients who were treated for a SRM showed enhancement at 3 months after the CA procedure, but by 9 months, only one patient had enhancement, although a biopsy revealed no recurrent cancer.[20]

Likewise, SRMs that were managed with RFA can also demonstrate pseudoenhancement after treatment, although usually to a lesser extent than those managed with CA.[19] Furthermore, changes in the size of the renal mass immediately after RFA can also be misleading. In a study of 28 successfully treated RFA patients, follow-up imaging at 3 to 5 months showed an average increase in the size of the tumor mass of 5% and 77% for CT and MRI, respectively. However, after 1 year, the mass volume had decreased to less than the original size.[21]

Possible explanations for the observed pseudoenhancement after the ablation procedure include persistence of viable tumor cells, inflammation, and volume averaging discrepancies in imaging. In the event of early postoperative enhancement (ie, 3 months), inflammation is likely the most common scenario. Cells that were injured during the ablation procedure would be undergoing repair and apoptosis, and contrast enhancement may occur because of the increased metabolic- and vasoactivity.[22] Over time, however, this pseudo-enhancement should decrease as the ablation site contracts and scars down.

Because contrast enhancement after renal ablation does not necessarily indicate the persistence of viable tumor cells, it may be appropriate to follow enhancing renal CA and RFA lesions with active surveillance. Evidence shows that even without any treatment, SRMs have a slow growth rate of 0.2 cm per year,[23] and progression to metastatic disease is extremely rare.[18,23] Furthermore, a recent study of elderly patients over age 75 found that active surveillance did not result in any SRM-related deaths,[24] and SRM patients under active observation show similar rates of progression to metastatic disease as patients who undergo CA, RFA, or nephrectomy.[25] For these reasons, active surveillance may not be significantly disadvantageous to patients, especially because even in the worst case scenario of a recurrence, delaying treatment does not seem to alter or limit future treatment options.[26,27]

The extent of the active surveillance period is controversial, however. At our institution, active surveillance is performed in selected patients with peripheral enhancement up to 12 months after the initial ablative procedure. So far, two patients have been followed expectantly at our institution. The first patient had a solitary kidney with a 2.5 cm exophytic lesion that was treated with a laparoscopic CA. At 3 months follow-up, the lesion appeared to have a light peripheral enhancement, and a decision to follow it was taken. At 9 months, the follow-up CT scan documented no enhancement, and so far this patient has been free of disease. The second case was similar to the first; however, the pseudoenhancement persisted for 12 months and disappeared at 15 months.

Repeated ablations

Repeated ablations are the most common mode of treatment after failed CA or RFA. Between 66% and 73% of patients who show local tumor recurrence after the initial ablative procedure undergo a repeated ablation.[17,28]

A review of the literature showed that between 7.4% and 8.5% of all RFA lesions and 0.9% and 1.3% of CA lesions are reablated.[10,18] Consequently, it appears that RFA necessitates significantly more repeated ablations to achieve the same 95% cancer-specific survival rate as CA.[10] The higher RFA repeated ablation rate may arise from the nature of the procedure. As mentioned, RFA is generally performed as a percutaneous procedure and CA is generally performed as a laparoscopic procedure. Because repeated percutaneous procedures are associated with lower morbidity and risk than repeated laparoscopic procedures, physicians may be more prone to repeating RFA in the case of suspicious imaging or a possible recurrence.[10]

It is also possible that laparoscopic ablative procedures more accurately target SRMs because they allow for better probe positioning under direct vision, reducing the likelihood of tumor recurrence. For example, in a study of 337 CA patients, none of the patients who underwent a laparoscopic CA underwent reablation whereas 2.5% of those who received percutaneous CA underwent reablation.[10] The same study also found that of 283 RFA patients, none of the laparoscopic RFA patients underwent a repeated ablation in contrast to the 8.8% of percutaneous RFA patients.

The oncologic outcomes of salvage ablations are encouraging, although there is a lack of studies in the literature and most of them have a short follow-up. For example Matin and associates[28] showed that the overall incidence of local disease progression after salvage repeated ablations was 4.2% with a mean follow-up of 2 years.

At our institution, repeated laparoscopic CA is preferred for anterior and lateral tumors and repeated percutaneous RFA is preferred for posterior tumors. So far, only one patient needed a repeated ablation at our institution. This was a woman who was treated with laparoscopic CA and at 6 months follow-up, a clear enhancement was documented on CT scan. Because the tumor was posterior, a decision to perform a percutaneous RFA was taken. The procedure was performed successfully by our interventional radiologist.

Salvage nephrectomy

As mentioned, patients in whom initial CA or RFA ablation procedures fail are most commonly treated with repeated ablations. A certain number of patients in whom the initial ablation fails, however, may be poor candidates for repeated ablation because of a large tumor size or disease progression. Furthermore, a repeated ablation may have failed in some patients. For these patient categories, a salvage nephrectomy may be indicated.[17,29]

The initial CA or RFA procedure, however, can cause local tissue damage and subsequent remodeling, scarring, and fibrosis, which hinders surgical salvage attempts. The residual tumor is usually surrounded by extensive fibrosis, and the surgical procedure may often necessitate extensive lysis of these adhesions. Consequently, intraoperative and postoperative complications are higher than in virgin fields.[17] For example, in the report by Nguyen and colleagues,[17] all six post-CA patients who underwent salvage nephrectomy experienced intraoperative complications, including renal artery injury and diaphragmatic injury.

Scarring from the initial ablation procedure influences the type of salvage surgery performed.[30] Partial nephrectomy would be advisable to preserve renal function; however, it may be impractical because of extensive fibrosis, and patients more commonly undergo radical nephrectomies. For example, Nguyen and coworkers[17] demonstrated how two of four salvage partial nephrectomy attempts in postablation patients could not be completed because extensive scarring and fibrosis rendered the resection impossible. Kowalczyk and associates,[30] however, reported on a series of 16 successfully performed open partial nephrectomies in kidneys previously treated with RFA. No case was converted to a radical nephrectomy, and although this procedure had a higher reoperation rate compared with other series of primary or repeated partial nephrectomies, it was considered feasible and safe.

At our institution, a partial nephrectomy is considered in selected patients. Because partial nephrectomies on previously ablated kidneys are difficult, however, they are almost always performed through an open approach. In the case of radical nephrectomies, although some authors still prefer an open approach for difficult postablation cases, at our institution, a laparoscopic approach is considered equally safe and is generally preferred. Only one patient who underwent a percutaneous RFA that failed was subsequently treated with an open partial nephrectomy at our institution. Although the case was challenging because of extensive fibrosis, the procedure was performed successfully, and the patient recovered well. So far the patient is free of recurrence at 36 months of follow-up.

A laparoscopic radical nephrectomy was performed in a patient in whom laparoscopic CA failed at an outside institution. This was a case of 4.5 cm tumor that was considered too large and endophytic for a partial nephrectomy. The procedure was successfully performed with no complications or recurrence to date.

Conclusions

CA and RFA are effective for managing SRMs and are associated with excellent intermediate oncologic outcomes. When recurrence is suspected on follow-up imaging, however, further management approaches include active surveillance, repeated ablations, and surgical excision.

Because 3-month follow-up CT and MRI may show enhancement regardless of whether viable tumor cells are present, patients may want to have their SRMs observed for a period to determine whether there is actual disease recurrence. Because the majority of SRMs are low stage, low grade, slow growing, and rarely associated with progression to metastatic disease, active surveillance may be a valuable option in elderly patients and those who are unwilling or unable to tolerate further treatments.

If further treatments are needed because of persistent enhancement over time or the presence of viable tumor cells on biopsy, treatments such as repeated ablation and surgical resection are indicated. Because ablations are less invasive than surgical resections, CA and RFA could be repeated as long as the renal mass is still small, localized, and has not shown significant disease progression. At our institution, repeated

laparoscopic CA is preferred for anterior and lateral tumors and repeated percutaneous RFA is preferred for posterior tumors.

If repeat ablations fail or the tumor has grown and become too large for focal ablation, salvage surgery may be necessary. An open partial nephrectomy is advisable because it best preserves renal function. Extensive fibrosis and perinephric scarring from the initial ablative procedure, however, particularly in the case of CA, may make the partial nephrectomy impractical to perform. In these circumstances, laparoscopic radical nephrectomies may be necessary, keeping in mind that this might be an overtreatment, considering the natural history of SRMs.

Disclosure Statement

Dr. Belldegrun is on the Board of Directors, US HIFU. No competing financial interests exist for the other authors.

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Abbreviations Used

CA = cryoablation
RCC = renal-cell carcinoma
RFA = radiofrequency ablation
SRM = small renal mass