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Cryoablation or Radiofrequency Ablation of the Small Renal Mass: A Meta-analysis

David A. Kunkle, MD and **Robert G. Uzzo, MD**
Department of Urologic Oncology Fox Chase Cancer Center Temple University School of Medicine

Abstract

Background: The incidence of renal cell carcinoma(RCC) is rising due to incidental detection of small renal masses(SRMs). While surgical resection remains the standard of care, cryoablation and radiofrequency ablation(RFA) have emerged as minimally-invasive treatment alternatives. We performed a comparative meta-analysis evaluating cryoablation and RFA as primary treatment for SRMs.

Methods: A MEDLINE search was performed reviewing world literature for clinically-localized renal masses treated by cryoablation or RFA.

Results: 47 studies representing 1375 kidney lesions treated by cryoablation or RFA were analyzed. No differences were detected between ablation modalities with regard to mean patient age(P=0.17), tumor size(P=0.12), or duration of follow-up(P=0.53). Pretreatment biopsy was performed more often for cryoablated lesions(82.3%) than RFA(62.2%)(P<0.0001). Unknown pathology occurred at a significantly higher rate for SRMs undergoing RFA(40.4%) versus cryoablation(24.5%)(P<0.0001). Repeat ablation was performed more often following RFA(8.5% versus 1.3%, P<0.0001) and rates of local tumor progression were significantly higher for RFA(12.9% versus 5.2%, P<0.0001) compared to cryoablation. The higher incidence of local tumor progression was found to be significantly correlated with treatment by RFA in the univariate(P=0.001) multivariate regression analysis(P=0.003). Metastasis was reported less frequently for cryoablation (1.0%) versus RFA(2.5%)(P=0.06). Cryoablation was usually performed laparoscopically(65%) whereas 94% of RFA lesions were aproached percutaneously.

Conclusions: Ablation of SRMs is a viable strategy based on short-term oncologic outcomes. While extended oncologic efficacy remains to be established for ablation modalities, these data suggest that cryoablation results in fewer retreatments, improved local tumor control, and may be associated with a lower risk of metastatic progression compared to RFA.

Keywords

kidney; kidney neoplasms; cryoablation; radiofrequency ablation

Cancer of the kidney is the third most common cancer of the urinary tract, accounting for 3.5% of all malignancies.1 With an estimated 51,190 new cases occurring in 2007 and 12,890 deaths attributable to the disease, renal cell carcinoma (RCC) is the most lethal of all genitourinary tumors.1

Robert G. Uzzo, MD Department of Urologic Oncology Fox Chase Cancer Center 333 Cottman Avenue Philadelphia, PA 19111 Tel. (215) 728-3501 Fax (215) 214-1734 Email: Robert.Uzzo@fccc.edu.

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The clinical diagnosis of RCC is radiographic and effective imaging of the kidneys can be achieved by ultrasound, CT, or MRI.2 Due to increased utilization of diagnostic imaging for evaluation of patients with abdominal symptomotology, incidentally discovered small renal masses (SRMs) are being diagnosed with greater frequency 3 and may account for up to 66% of RCC diagnoses.4 Thus an increased incidence of RCC over the last three decades has been associated with stage migration 3 and a concurrent rise in rates of surgical intervention.5 Unfortunately, despite earlier diagnosis and treatment, cancer specific (CSS) and overall survival have not significantly improved.5

Surgical resection remains the standard of care for clinically localized RCC due to the favorable prognosis associated with surgery and the relative ineffectiveness of systemic therapy. Patients undergoing radical or partial nephrectomy for SRMs (pT1a, ≤4cm) exhibit 5-year CSS rates in excess of 95%.6, 7 Laparoscopic approaches to partial nephrectomy have demonstrated similarly favorable early results.8

Recently, minimally invasive ablative technologies have emerged as potential treatment options for clinically localized RCC. Effective renal cryoablation has been achieved by open, laparoscopic and percutaneous image-guided techniques.9 Percutaneous radiofrequency ablation (RFA) has been successfully performed under ultrasound, CT, or MRI guidance.10 While these newer nephron-sparing techniques appear promising, the majority of published studies are single institution series with relatively few numbers of patients. To date, only one published study has quantitatively compared the efficacy and outcomes of these two ablation modalities.11

While treatment options for low stage RCC have expanded in recent years, their proper application and affect on the biology of the SRM is yet to be fully defined. The purpose of this study is to analyze the combined published data regarding ablation as primary treatment of SRMs. Here, we review the published literature and perform a comparative meta-analysis evaluating cryoablation and RFA for the management of enhancing renal masses.

MATERIALS AND METHODS

Data Sources

A MEDLINE search was performed through October 2007 using the National Center for Biotechnology Information PubMed Internet site to review the world literature regarding the treatment of suspected renal malignancies by means of renal cryoablation or RFA.

Study Selection

This meta-analysis was limited to series analyzing clinically localized sporadic renal tumors that were managed by open, laparoscopic, and percutaneous cryoablation or RFA. Series consisting of only patients with hereditary or metastatic RCC were excluded. Data taken from series reporting ablation of both sporadic and hereditary renal lesions was censored to include only those sporadic RCC. Additionally, series that were purely technical and did not assess tumor recurrence or other oncologic endpoints were excluded. Prospective and retrospective series were included in the study, although single case reports were excluded. Multi-institutional series as well as single-institution experiences were analyzed, provided that other inclusion criteria were met. In the case of multiple series from an institution or overlapping patient cohorts with potentially redundant data, only the most recent series or that with the largest study population was selected in order to avoid double counting of subjects. In total, 47 studies from 45 institutions met inclusion criteria and were analyzed.

Data Analysis

Mean data pertaining to patient age, tumor size, and length of follow-up were extracted from published series. The incidence with which pre-ablation biopsy was performed was determined from each series and the results collated. Pathologic data were categorized as histologically confirmed RCC, benign lesions, or unknown/indeterminate histology. Oncologic outcomes evaluated included local tumor progression or distant metastases. For both cryoablation and RFA, local tumor progression was defined as radiographic or pathologic evidence of residual disease following initial treatment, regardless of time to recurrence in accordance with the recommendations of the Working Group on Image-Guided Tumor Ablation.12 In addition, data regarding tumors undergoing repeat ablation sessions was extracted for analysis.

Differences in mean patient age, tumor size, and follow-up were weighted by differences in study sample size and analyzed using the Mann-Whitney test. Data for each series could not be weighted by inverse standard errors, which might have increased the efficiency of analysis, since over 40% of the studies did not include variances or standard errors with their descriptive statistics. Many authors reported ranges instead of variances as a measure of variability.

Differences in malignancy rates and pathologic reporting between ablation modalities were investigated using Fisher's exact test. Rate of pre-ablation biopsy, use of repeat ablation, incidence of local tumor progression, and development of metastatic disease were similarly analyzed by means of Fisher's exact test. We further investigated models of local and metastatic tumor progression using univariate and multivariate linear regression analyses. The multivariate analysis included data pertaining to treatment modality, sample size in each study, incidence of histologically confirmed RCC, incidence of unknown/indeterminate pathology, mean patient age, mean tumor size, and mean follow-up time as covariates.

RESULTS

Forty seven series representing 1375 renal tumors treated at 45 institutions met inclusion criteria and were analyzed. Institutions contributing published data are listed in table 1. Table 2 depicts patient and tumor characteristics for included studies.

Patient and Tumor Characteristics

Mean patient age weighted by sample size for all ablated lesions was 67.2 years. Mean tumor size for all renal lesions undergoing ablation was 2.64 cm, and mean duration of reported follow-up after ablation was 18.7 months. No statistically significant differences were seen between ablation modalities with regard to patient age (P=0.17), tumor size (P=0.12), or duration of post-ablation follow-up (P=0.53). Reported approaches to renal cryoablation included laparoscopy (64.8%), percutaneous (23.2%), and open surgery (12.0%). Percutaneous renal tumor RFA was described for 93.7% of lesions, with laparoscopy being utilized for 6.3% (figure 1).

Pathological Data

While 82.3% (494/600) of lesions treated by cryoablation underwent a pre-ablation biopsy, only 62.2% (482/775) of those managed by RFA were biopsied (P<0.0001). Available pathological data was classified according to malignant, benign, and unknown/indeterminate histology for each ablation modality (figure 2). Overall, 53.9% of all ablated lesions were pathologically confirmed RCC while 12.7% were benign lesions and 33.5% had unknown or indeterminate pathology. Unknown or indeterminate pathology was reported for 24.5% (147/600) of lesions managed by cryoablation and 40.4% (313/775) of those treated by

RFA, a statistically significant difference (P<0.0001). The incidence of malignancy among only those reported lesions with known histology was determined for cryoablation (325/453, 71.7%) and RFA (416/462, 90.0%; P<0.0001).

Local Tumor Progression and Metastasis

Local tumor progression was reported in 5.2% (31/600) of lesions following renal cryoablation and 12.9% (100/775) after RFA, and this difference was determined to be highly significant, (P<0.0001). Of 600 cryoablated lesions, 8 (1.3%) subsequently were treated by repeat ablation; by comparison, 8.5% (66/775) of lesions treated by RFA were subjected to at least two ablation sessions (P<0.0001). Progression to metastatic disease was described in 1.0% (6/600) of lesions undergoing cryoablation and 2.5% (19/775) of those undergoing RFA (P=0.06). Overall, metastasis developed in 1.8% (25/1375) of reported lesions undergoing ablation.

Univariate and multivariate models analyzing local tumor progression and metastatic disease were performed using univariate and multivariate linear regressions (table 2). Forty-three of 47 (91%) studies included complete information and were included in the regression analysis. Incidence of local tumor progression was significantly correlated with ablation modality in the univariate (P=0.001) and multivariate (P=0.003) regression analyses. Incidence of malignant pathology, incidence of unknown pathology, mean patient age, and mean tumor size were not statistically associated with local recurrence in either the univariate or multivariate analyses. Detection of local tumor progression was marginally associated with duration of follow-up time in the multivariate analysis (P=0.076). When the regression analyses were performed evaluating the incidence of metastases, no significant differences were seen for lesions regardless of ablation modality. As depicted in table 3, the incidence of metastases was not significantly associated with any of the tested variables by univariate or multivariate regression analyses.

DISCUSSION

Surgical resection is considered the standard of care for clinically localized RCC due to the favorable prognosis associated with surgery. The 5-year CSS for patients after nephrectomy ranges from 97% and 87% for pT1a and pT1b tumors, respectively, to only 20% for pT4 disease.6 Similarly, patients undergoing partial nephrectomy demonstrate 5- and 10-year CSS of 92% and 80% across all pathologic stages and 96% and 90% for those tumors less than 4 cm.7 Early data for laparoscopic partial nephrectomy is similarly favorable, with 100% CSS reported at 3-year median follow-up.8 The importance of effective treatment for localized RCC is accentuated by the fact that systemic treatments have demonstrated limited success as treatment for metastatic disease as well as in an adjuvant setting.13, 14

Cryoablation was first applied to the SRM in 1995,15 and its mechanism of tumor destruction involves the use of rapid freeze and thaw cycles.9 Initial extracellular ice formation causes movement of intracellular water, alterations of intracellular pH, and protein denaturation.16 Ice formation also results in mechanical disruption of cell membranes.16 Hours and days following cryotherapy, delayed tissue necrosis occurs as injury to the local microvasculature causes diminished tissue perfusion and delayed cell death.16, 17 Effective renal cryoablation has been achieved by open, laparoscopic and percutaneous image-guided techniques.9 The procedure can be monitored by means of a thermocouple or ultrasound in real time to confirm extension of the ice ball beyond the margins of the renal tumor.9, 18 Our analysis of the published literature demonstrates that currently more than three-quarters of reported renal cryoablation treatments have been performed via an open or laparoscopic approach, whereas percutaneous approaches have been utilized much less frequently.

RFA of an exophytic renal mass prior to open radical nephrectomy was first described in 1997 19 with the first report of RFA as sole treatment for a renal tumor published in 1999.20 While RFA has been applied using open, laparoscopic, or percutaneous approaches under ultrasound, CT, or MRI guidance, 9, 10 current literature describes percutaneous access in approximately 94% of renal RFA cases. Tumor coagulation by RFA occurs as radiofrequency waves are converted to heat, resulting in thermal tissue damage.9 High-frequency current applied to target tissues results in ionic agitation thereby heating the tissues, resulting in denaturation of proteins and disruption of cell membranes.21 This process occurs over 4–6 minutes at temperatures above 50°C and almost immediately above 60°C.21 Since temperatures >105°C result in tissue vaporization and ineffective ablation, optimal RFA is performed at temperatures of 50–100°C throughout the tumor.21 Vascular parenchyma may, however, act as a heat sink during RFA; therefore exophytic tumors may be better ablated than central tumors in close proximity to the renal vasculature.22

In addition to their minimally invasive nature, another primary benefit of ablative therapy for renal tumors is the potential for preservation of renal function. However, to date few studies have examined the effects of kidney ablation on renal function. Gill et al examined 56 patients with 3-yr follow-up after renal cryoablation and reported preoperative and postoperative serum creatinine levels of 1.2 and 1.4 mg/dl, respectively.23 In 10 patients with a solitary kidney in this series, mean preoperative and postoperative serum creatinine was 2.2 and 2.6 mg/dl, respectively, and 13 patients with baseline renal insufficiency demonstrated levels of 3.0 and 2.7 mg/dl, respectively.23 In another series of 14 patients undergoing cryoablation in a solitary kidney, no adverse effect on renal function was noted although 3 lesions required repeat treatment for incomplete ablation.24 A series which examined the effects of RFA on 16 patients patients with a solitary kidney demonstrated a decrease in mean glomerular filtration rate from 54.2 ml/min/1.73m2 preoperatively to 47.5 ml/min/1.73m2 at last follow-up.25 Similarly, Jacobsohn et al studied 16 patients undergoing RFA in a solitary kidney and demonstrated a 13.3% change in creatinine clearance within 1 week after ablation and a 9.1% change at mean follow-up of 15.3 months with 1 patient developing chronic renal failure.26 Thus while a few studies have examined the functional impact of ablation, none have directly compared the ability of cryoablation and RFA to preserve renal function. The ability to maximally spare nephrons remains a careful balance against the possibility of insufficient tumor destruction.

Radiographic follow-up after cryoablation or RFA is currently the most common means of assessing treatment effect.12 Enhancement on post-contrast imaging is considered evidence of incompletely treated disease.27 Some centers have performed biopsy following ablation to assess for viable disease, while others have relied solely on radiographic evaluation.12, 28, 29 While the presence of grossly viable disease may be detectable on follow-up imaging immediately following ablation, microscopic disease may require a longer duration of surveillance to become apparent. This may explain recent data suggesting that viable tumor may be present on post-ablation biopsy despite lack of radiographic enhancement.23 The Working Group on Image-Guided Tumor Ablation has used the term *local tumor progression* to indicate incomplete tumor destruction regardless of time to when enduring disease becomes clinically evident.12 Therefore in our meta-analysis, we considered any lesion with evidence of local disease persistence following ablation as local tumor progression, regardless of time to reappearance. However, it should be noted that many local recurrences after ablation have been successfully retreated by subsequent ablation. Thus the ultimate rate of treatment failure after salvage ablation remains to be fully defined. Furthermore, it is likely that ablation techniques have undergone refinement with increased experience and published series therefore may not truly reflect contemporary results.

To our knowledge, only one published study has quantitatively compared the efficacy and outcomes of these two ablation modalities. In 2006, investigators at the Cleveland Clinic retrospectively compared their experience with laparoscopic cryoablation of 179 renal lesions with 81 tumors treated by RFA at that institution.11 Radiographic evidence of disease persistence was identified in 1.8% of lesions after cryoablation and 11.1% following RFA.11 Thus, rates of local tumor progression reported in this institutional series are similar to those determined herein by meta-analysis. Cancer-specific survival was 98% after cryoablation and 100% after RFA at 1-year median follow-up in this cohort.11

When comparing rates of local disease persistence among treatment modalities, it is important to consider that non-uniform criteria may have been used to define recurrence following ablation. While the majority of series utilize contrast-enhanced imaging to determine treatment effect, the definition of ablative success has been called into question by studies that have demonstrated viable tumor on post-ablation biopsy despite a lack of enhancement on imaging.29 Perhaps the true rate of local disease progression may be more accurately determined if biopsy were routinely included in post-ablation surveillance protocols.

The context in which the technical success of renal ablation is considered must include consideration of the emerging body of data regarding the observation or active surveillance of SRMs in elderly or infirmed populations. Although published series addressing the natural history of small renal tumors under active surveillance report some variability in the clinical behavior of observed SRMs (growth rates of 0.09 to 0.86cm/year), a meta-analysis of clinically localized tumors determined an overall median growth rate of 0.28cm/year for observed lesions across multiple published series.2 Moreover, it has been reported that 26-33% of enhancing renal masses demonstrate zero net growth when observed over a median of 29 months.30 Notably, only 1% of lesions reported in the active surveillance literature have demonstrated progression to metastatic disease in the absence of treatment.2 This information raises the possibility of an overtreatment bias for SRMs and suggests that treatment may not impact the biologic potential of many lesions.31 Thus, the indolent nature of certain SRM's must be considered when analyzing the treatment efficacy of ablative technologies.

In this meta-analysis, we demonstrate that cryoablation and RFA are technically viable approaches to the management of the SRM. However, our data depict that lesions treated by cryoablation report a significantly lower incidence of local tumor progression following initial treatment – an association that remained significant on univariate and multivariate analyses. While the incidence of progression to metastatic disease was low regardless of ablation modality, lesions treated by RFA exhibited a greater incidence of metastatic progression although the difference was only marginally significant and not apparent on regression analysis. It is not evident from these data whether this difference in ability to produce complete tumor destruction is a function of inherent differences in the ablation technologies themselves, or rather if the laparoscopic approach more frequently used for cryoablation provides a greater propensity for effective tumor treatment than percutaneous approaches. Indeed, lesions treated by cryoablation were most often approached laparoscopically (65%) whereas 94% of lesions treated by RFA were aproached percutaneously. This information further reflects the fact that urologists have preferentially utilized cryoablation technology while renal RFA has chiefly been performed in the setting of interventional radiology suites.

Minimally invasive ablation treatment options have generally been selectively performed on older patients with smaller tumors; thus a selection bias may potentially confound data related to their usage. In addition, series of lesions undergoing ablation tend to include

shorter post-treatment follow-up when compared to published series of tumors managed by surgical excision or active surveillance.[2, 32] Furthermore, the absence of known pathology remains a confounding factor when attempting to compare oncologic outcomes for lesions treated by cryoablation or RFA. This category of tumors with unknown pathology certainly includes a number of histologically benign lesions, thus measures of treatment efficacy may be overestimated.[9] While the weaknesses of meta-analyses are well recognized,[31, 33] these data underscore the need for long-term, prospective, randomized trials to determine the proper application and biological implications for ablation of SRMs. Furthermore, this study emphasizes the importance of thorough consideration of all treatment options for patients with SRMs including proper discussion of risks, benefits, and expected outcomes after surgical excision, ablation, and active surveillance.

CONCLUSIONS

The current data illustrate that ablative technologies are viable strategies for small renal masses based on short term oncologic outcomes. However, extended oncologic efficacy remains to be established for ablation modalities. Among ablation modalities our data suggests that cryoablation may result in significantly lower rates of local tumor progression compared to RFA, although no statistical differences were detected in the incidence of progression to metastatic disease.

REFERENCES

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. CA Cancer J Clin. Jan-Feb; 2007 57(1):43–66. [PubMed: 17237035]
2. Chawla SN, Crispen PL, Hanlon AL, Greenberg RE, Chen DY, Uzzo RG. The natural history of observed enhancing renal masses: meta-analysis and review of the world literature. J Urol. Feb; 2006 175(2):425–431. [PubMed: 16406965]
3. Jayson M, Sanders H. Increased incidence of serendipitously discovered renal cell carcinoma. Urology. Feb; 1998 51(2):203–205. [PubMed: 9495698]
4. Volpe A, Panzarella T, Rendon RA, Haider MA, Kondylis FI, Jewett MA. The natural history of incidentally detected small renal masses. Cancer. Feb 15; 2004 100(4):738–745. [PubMed: 14770429]
5. Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK. Rising incidence of small renal masses: a need to reassess treatment effect. J Natl Cancer Inst. Sep 20; 2006 98(18):1331–1334. [PubMed: 16985252]
6. Frank I, Blute ML, Leibovich BC, Cheville JC, Lohse CM, Zincke H. Independent validation of the 2002 American Joint Committee on cancer primary tumor classification for renal cell carcinoma using a large, single institution cohort. J Urol. Jun; 2005 173(6):1889–1892. [PubMed: 15879769]
7. Hafez KS, Fergany AF, Novick AC. Nephron sparing surgery for localized renal cell carcinoma: impact of tumor size on patient survival, tumor recurrence and TNM staging. J Urol. Dec; 1999 162(6):1930–1933. [PubMed: 10569540]
8. Moinzadeh A, Gill IS, Finelli A, Kaouk J, Desai M. Laparoscopic partial nephrectomy: 3-year followup. J Urol. Feb; 2006 175(2):459–462. [PubMed: 16406971]
9. Aron M, Gill IS. Minimally invasive nephron-sparing surgery (MINSS) for renal tumours. Part II: probe ablative therapy. Eur Urol. Feb; 2007 51(2):348–357. [PubMed: 17084513]
10. Mahnken AH, Gunther RW, Tacke J. Radiofrequency ablation of renal tumors. Eur Radiol. Aug; 2004 14(8):1449–1455. [PubMed: 15150668]
11. Hegarty NJ, Gill IS, Desai MM, Remer EM, O'Malley CM, Kaouk JH. Probe-ablative nephron-sparing surgery: cryoablation versus radiofrequency ablation. Urology. Jul; 2006 68(1 Suppl):7–13. [PubMed: 16857454]
12. Matin SF, Ahrar K, Cadeddu JA, et al. Residual and recurrent disease following renal energy ablative therapy: a multi-institutional study. J Urol. Nov; 2006 176(5):1973–1977. [PubMed: 17070224]

13. Negrier S, Escudier B, Lasset C, et al. Recombinant human interleukin-2, recombinant human interferon alfa-2a, or both in metastatic renal-cell carcinoma. Groupe Francais d'Immunotherapie. N Engl J Med. Apr 30; 1998 338(18):1272–1278. [PubMed: 9562581]
14. Kunkle DA, Haas NB, Uzzo RG. Adjuvant therapy for high-risk renal cell carcinoma patients. Curr Urol Rep. Jan; 2007 8(1):19–30. [PubMed: 17239313]
15. Uchida M, Imaide Y, Sugimoto K, Uehara H, Watanabe H. Percutaneous cryosurgery for renal tumours. Br J Urol. Feb; 1995 75(2):132–136. [PubMed: 7850315]
16. Hoffmann NE, Bischof JC. The cryobiology of cryosurgical injury. Urology. Aug; 2002 60(2 Suppl 1):40–49. [PubMed: 12206847]
17. Gill IS, Novick AC. Renal cryosurgery. Urology. Aug; 1999 54(2):215–219. [PubMed: 10443713]
18. Onik GM, Reyes G, Cohen JK, Porterfield B. Ultrasound characteristics of renal cryosurgery. Urology. Aug; 1993 42(2):212–215. [PubMed: 8367932]
19. Zlotta AR, Wildschutz T, Raviv G, et al. Radiofrequency interstitial tumor ablation (RITA) is a possible new modality for treatment of renal cancer: ex vivo and in vivo experience. J Endourol. Aug; 1997 11(4):251–258. [PubMed: 9376843]
20. McGovern FJ, Wood BJ, Goldberg SN, Mueller PR. Radio frequency ablation of renal cell carcinoma via image guided needle electrodes. J Urol. Feb; 1999 161(2):599–600. [PubMed: 9915457]
21. Goldberg SN, Gazelle GS, Mueller PR. Thermal ablation therapy for focal malignancy: a unified approach to underlying principles, techniques, and diagnostic imaging guidance. AJR Am J Roentgenol. Feb; 2000 174(2):323–331. [PubMed: 10658699]
22. Zagoria RJ, Hawkins AD, Clark PE, et al. Percutaneous CT-guided radiofrequency ablation of renal neoplasms: factors influencing success. AJR Am J Roentgenol. Jul; 2004 183(1):201–207. [PubMed: 15208139]
23. Gill IS, Remer EM, Hasan WA, et al. Renal cryoablation: outcome at 3 years. J Urol. Jun; 2005 173(6):1903–1907. [PubMed: 15879772]
24. Shingleton WB, Sewell PE Jr. Cryoablation of renal tumours in patients with solitary kidneys. BJU Int. Aug; 2003 92(3):237–239. [PubMed: 12887474]
25. Raman JD, Thomas J, Lucas SM, et al. Radiofrequency ablation for T1a tumors in a solitary kidney: promising intermediate oncologic and renal function outcomes. Can J Urol. Apr; 2008 15(2):3980–3985. [PubMed: 18405445]
26. Jacobsohn KM, Ahrar K, Wood CG, Matin SF. Is radiofrequency ablation safe for solitary kidneys? Urology. May; 2007 69(5):819–823. discussion 823. [PubMed: 17482911]
27. Goldberg SN, Grassi CJ, Cardella JF, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria. Radiology. Jun; 2005 235(3):728–739. [PubMed: 15845798]
28. Campbell SC, Novick AC, Herts B, et al. Prospective evaluation of fine needle aspiration of small, solid renal masses: accuracy and morbidity. Urology. Jul; 1997 50(1):25–29. [PubMed: 9218014]
29. Weight CJ, Kaouk JH, Hegarty NJ, et al. Correlation of radiographic imaging and histopathology following cryoablation and radio frequency ablation for renal tumors. J Urol. Apr; 2008 179(4): 1277–1281. [PubMed: 18280507]
30. Kunkle DA, Crispen PL, Chen DY, Greenberg RE, Uzzo RG. Enhancing renal masses with zero net growth during active surveillance. J Urol. Mar; 2007 177(3):849–854. [PubMed: 17296355]
31. Kunkle DA, Egleston BL, Uzzo RG. Excise, ablate or observe: the small renal mass dilemma--a meta-analysis and review. J Urol. Apr; 2008 179(4):1227–1233. [PubMed: 18280512]
32. Herr HW. Partial nephrectomy for unilateral renal carcinoma and a normal contralateral kidney: 10-year followup. J Urol. Jan; 1999 161(1):33–34. [PubMed: 10037361]
33. LeLorier J, Gregoire G, Benhaddad A, Lapierre J, Derderian F. Discrepancies between meta-analyses and subsequent large randomized, controlled trials. N Engl J Med. Aug 21; 1997 337(8): 536–542. [PubMed: 9262498]
34. Silverman SG, Tuncali K, vanSonnenberg E, et al. Renal tumors: MR imaging-guided percutaneous cryotherapy--initial experience in 23 patients. Radiology. Aug; 2005 236(2):716–724. [PubMed: 16040927]

35. Colon I, Fuchs GJ. Early experience with laparoscopic cryoablation in patients with small renal tumors and severe comorbidities. J Endourol. Aug; 2003 17(6):415–423. [PubMed: 12965070]
36. Weld KJ, Figenshau RS, Venkatesh R, et al. Laparoscopic cryoablation for small renal masses: three-year follow-up. Urology. Mar; 2007 69(3):448–451. [PubMed: 17382142]
37. Hruby G, Reisiger K, Venkatesh R, Yan Y, Landman J. Comparison of laparoscopic partial nephrectomy and laparoscopic cryoablation for renal hilar tumors. Urology. Jan; 2006 67(1):50–54. [PubMed: 16413331]
38. Davol PE, Fulmer BR, Rukstalis DB. Long-term results of cryoablation for renal cancer and complex renal masses. Urology. Jul; 2006 68(1 Suppl):2–6. [PubMed: 16857453]
39. Rodriguez R, Chan DY, Bishoff JT, et al. Renal ablative cryosurgery in selected patients with peripheral renal masses. Urology. Jan; 2000 55(1):25–30. [PubMed: 10654889]
40. Gupta A, Allaf ME, Kavoussi LR, et al. Computerized tomography guided percutaneous renal cryoablation with the patient under conscious sedation: initial clinical experience. J Urol. Feb; 2006 175(2):447–452. [PubMed: 16406968]
41. Atwell TD, Farrell MA, Callstrom MR, et al. Percutaneous cryoablation of 40 solid renal tumors with US guidance and CT monitoring: initial experience. Radiology. Apr; 2007 243(1):276–283. [PubMed: 17329689]
42. Rukstalis DB, Khorsandi M, Garcia FU, Hoenig DM, Cohen JK. Clinical experience with open renal cryoablation. Urology. Jan; 2001 57(1):34–39. [PubMed: 11164139]
43. O'Malley RL, Berger AD, Kanofsky JA, Phillips CK, Stifelman M, Taneja SS. A matched-cohort comparison of laparoscopic cryoablation and laparoscopic partial nephrectomy for treating renal masses. BJU Int. Feb; 2007 99(2):395–398. [PubMed: 17092288]
44. Nadler RB, Kim SC, Rubenstein JN, Yap RL, Campbell SC, User HM. Laparoscopic renal cryosurgery: the Northwestern experience. J Urol. Oct; 2003 170(4 Pt 1):1121–1125. [PubMed: 14501705]
45. Cestari A, Guazzoni G, dell'Acqua V, et al. Laparoscopic cryoablation of solid renal masses: intermediate term followup. J Urol. Oct; 2004 172(4 Pt 1):1267–1270. [PubMed: 15371821]
46. Schwartz BF, Rewcastle JC, Powell T, Whelan C, Manny T Jr. Vestal JC. Cryoablation of small peripheral renal masses: a retrospective analysis. Urology. Jul; 2006 68(1 Suppl):14–18. [PubMed: 16857455]
47. Lee DI, McGinnis DE, Feld R, Strup SE. Retroperitoneal laparoscopic cryoablation of small renal tumors: intermediate results. Urology. Jan; 2003 61(1):83–88. [PubMed: 12559272]
48. Miki K, Shimomura T, Yamada H, et al. Percutaneous cryoablation of renal cell carcinoma guided by horizontal open magnetic resonance imaging. Int J Urol. Jul; 2006 13(7):880–884. [PubMed: 16882047]
49. Wyler SF, Sulser T, Ruszat R, et al. Intermediate-term results of retroperitoneoscopy-assisted cryotherapy for small renal tumours using multiple ultrathin cryoprobes. Eur Urol. Apr; 2007 51(4):971–979. [PubMed: 17084515]
50. Gore JL, Kim HL, Schulam P. Initial experience with laparoscopically assisted percutaneous cryotherapy of renal tumors. J Endourol. May; 2005 19(4):480–483. [PubMed: 15910261]
51. Shingleton WB, Sewell PE Jr. Percutaneous renal tumor cryoablation with magnetic resonance imaging guidance. J Urol. Mar; 2001 165(3):773–776. [PubMed: 11176465]
52. Bassignani MJ, Moore Y, Watson L, Theodorescu D. Pilot experience with real-time ultrasound guided percutaneous renal mass cryoablation. J Urol. Apr; 2004 171(4):1620–1623. [PubMed: 15017235]
53. Bandi G, Wen CC, Hedican SP, Moon TD, Lee FT Jr. Nakada SY. Cryoablation of small renal masses: assessment of the outcome at one institution. BJU Int. Oct; 2007 100(4):798–801. [PubMed: 17822460]
54. Lund L, Jonler M, Svolgaard N, Svolgaard PB, Petersen JB. [Laparoscopy-assisted cryoablation of small kidney tumours]. Ugeskr Laeger. Feb 5; 2007 169(6):517–520. [PubMed: 17303034]
55. Mahnken AH, Rohde D, Brkovic D, Gunther RW, Tacke JA. Percutaneous radiofrequency ablation of renal cell carcinoma: preliminary results. Acta Radiol. Apr; 2005 46(2):208–214. [PubMed: 15902899]

56. Mayo-Smith WW, Dupuy DE, Parikh PM, Pezzullo JA, Cronan JJ. Imaging-guided percutaneous radiofrequency ablation of solid renal masses: techniques and outcomes of 38 treatment sessions in 32 consecutive patients. AJR Am J Roentgenol. Jun; 2003 180(6):1503–1508. [PubMed: 12760909]
57. Lewin JS, Nour SG, Connell CF, et al. Phase II clinical trial of interactive MR imaging-guided interstitial radiofrequency thermal ablation of primary kidney tumors: initial experience. Radiology. Sep; 2004 232(3):835–845. [PubMed: 15333798]
58. Weizer AZ, Raj GV, O'Connell M, Robertson CN, Nelson RC, Polascik TJ. Complications after percutaneous radiofrequency ablation of renal tumors. Urology. Dec; 2005 66(6):1176–1180. [PubMed: 16360436]
59. Boss A, Clasen S, Kuczyk M, et al. Magnetic resonance-guided percutaneous radiofrequency ablation of renal cell carcinomas: a pilot clinical study. Invest Radiol. Sep; 2005 40(9):583–590. [PubMed: 16118551]
60. Memarsadeghi M, Schmook T, Remzi M, et al. Percutaneous radiofrequency ablation of renal tumors: midterm results in 16 patients. Eur J Radiol. Aug; 2006 59(2):183–189. [PubMed: 16725292]
61. Roy-Choudhury SH, Cast JE, Cooksey G, Puri S, Breen DJ. Early experience with percutaneous radiofrequency ablation of small solid renal masses. AJR Am J Roentgenol. Apr; 2003 180(4): 1055–1061. [PubMed: 12646454]
62. de Baere T, Kuoch V, Smayra T, et al. Radio frequency ablation of renal cell carcinoma: preliminary clinical experience. J Urol. May; 2002 167(5):1961–1964. [PubMed: 11956417]
63. Varkarakis IM, Allaf ME, Inagaki T, et al. Percutaneous radio frequency ablation of renal masses: results at a 2-year mean followup. J Urol. Aug; 2005 174(2):456–460. [PubMed: 16006864]
64. Karashima T, Inoue K, Shimamoto T, Yamasaki I, Kamada M, Shuin T. [Conservative therapy by percutaneous radiofrequency ablation of renal cell carcinomas--therapeutic experiments of four patients with seven renal tumors--]. Hinyokika Kiyo. Apr; 2006 52(4):241–247. [PubMed: 16686349]
65. Ukimura O, Kawauchi A, Fujito A, et al. Radio-frequency ablation of renal cell carcinoma in patients who were at significant risk. Int J Urol. Dec; 2004 11(12):1051–1057. [PubMed: 15663674]
66. Uribe PS, Costabile RA, Peterson AC. Progression of renal tumors after laparoscopic radiofrequency ablation. Urology. Nov; 2006 68(5):968–971. [PubMed: 17095053]
67. McDougal WS, Gervais DA, McGovern FJ, Mueller PR. Long-term followup of patients with renal cell carcinoma treated with radio frequency ablation with curative intent. J Urol. Jul; 2005 174(1):61–63. [PubMed: 15947578]
68. Farrell MA, Charboneau WJ, DiMarco DS, et al. Imaging-guided radiofrequency ablation of solid renal tumors. AJR Am J Roentgenol. Jun; 2003 180(6):1509–1513. [PubMed: 12760910]
69. Ahrar K, Matin S, Wood CG, et al. Percutaneous radiofrequency ablation of renal tumors: technique, complications, and outcomes. J Vasc Interv Radiol. May; 2005 16(5):679–688. [PubMed: 15872323]
70. Salagierski M, Salagierski M, Salagierska-Barwinska A, Sosnowski M. Percutaneous ultrasound-guided radiofrequency ablation for kidney tumors in patients with surgical risk. Int J Urol. Nov; 2006 13(11):1375–1379. [PubMed: 17083386]
71. Chiou YY, Hwang JI, Chou YH, Wang JH, Chiang JH, Chang CY. Percutaneous radiofrequency ablation of renal cell carcinoma. J Chin Med Assoc. May; 2005 68(5):221–225. [PubMed: 15909727]
72. Clark TW, Malkowicz B, Stavropoulos SW, et al. Radiofrequency ablation of small renal cell carcinomas using multitined expandable electrodes: preliminary experience. J Vasc Interv Radiol. Mar; 2006 17(3):513–519. [PubMed: 16567676]
73. Matsumoto ED, Johnson DB, Ogan K, et al. Short-term efficacy of temperature-based radiofrequency ablation of small renal tumors. Urology. May; 2005 65(5):877–881. [PubMed: 15882715]

74. Veltri A, Calvo A, Tosetti I, et al. Experiences in US-guided percutaneous radiofrequency ablation of 44 renal tumors in 31 patients: analysis of predictors for complications and technical success. Cardiovasc Intervent Radiol. Sep-Oct; 2006 29(5):811–818. [PubMed: 16832595]

75. Zagoria RJ, Traver MA, Werle DM, Perini M, Hayasaka S, Clark PE. Oncologic efficacy of CT-guided percutaneous radiofrequency ablation of renal cell carcinomas. AJR Am J Roentgenol. Aug; 2007 189(2):429–436. [PubMed: 17646471]

76. Sabharwal R, Vladica P. Renal tumors: technical success and early clinical experience with radiofrequency ablation of 18 tumors. Cardiovasc Intervent Radiol. Mar-Apr; 2006 29(2):202–209. [PubMed: 16447001]

77. Arzola J, Baughman SM, Hernandez J, Bishoff JT. Computed tomography-guided, resistance-based, percutaneous radiofrequency ablation of renal malignancies under conscious sedation at two years of follow-up. Urology. Nov; 2006 68(5):983–987. [PubMed: 17095059]

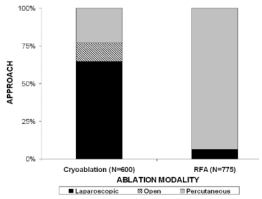

Figure 1.
Reported approaches to kidney tumor ablation.

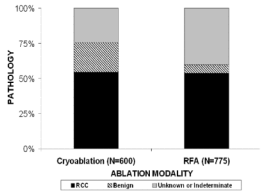

Figure 2.
Pathologic data for renal lesions treated by cryoablation and RFA.

Table 1

Institutions with published series of renal tumor ablation included in meta-analysis listed by ablation modality.

Institutions with Published Results of Renal Tumor Cryoablation	
Brigham and Women's Hospital, Boston, MA 34	Thomas Jefferson University, Philadelphia, PA 47
Cedars-Sinai Medical Center, Los Angeles, CA 35	Jikei University School of Medicine, Tokyo, Japan 48
Cleveland Clinic, Cleveland, OH 23	University Hospital, Basel, Switzerland 49
Columbia University, New York, NY 36, 37	University of California, Irvine, CA 36
Geisinger Medical Center, Danville, PA 38	University of California, Los Angeles, CA 50
Johns Hopkins University, Baltimore, MD 39, 40	University of Massachusetts, Amherst, MA 34
Mayo Clinic, Rochester, MN 41	University of Mississippi, Jackson, MS 51
MCP-Hahneman, Philadelphia, PA 42	University of Virginia, Charlottesville, VA 52
New York University, New York, NY 43	University of Wisconsin, Madison, WI 53
Northwestern University, Chicago, IL 44	Viborg Sygehus, Viborg, Denmark 54
San Raffaele Hospital, Milan, Italy 45	Washington University, St Louis, MO 36
Southern Illinois University, Springfield, IL 46	
Institutions with Published Results of Renal Tumor Radiofrequency Ablation	
Aachen University of Technology, Aachen, Germany 55	Massachusetts General Hospital, Boston, MA 67
Brown University, Providence, RI 56	Mayo Clinic, Rochester, MN 68
Case Western Reserve, Cleveland, OH 57	MD Anderson Cancer Center, Houston, TX 69
Cleveland Clinic, Cleveland, OH 11	Medical University of Lodz, Lodz, Poland 70
Duke University, Durham, NC 58	Taipei Veterans General Hospital, Taipei, Taiwan 71
Eberhard-Karls University, Tubingen, Germany 59	University of Pennsylvania, Philadelphia, PA 72
General Hospital of Vienna, Vienna, Austria 60	University of Texas Southwestern, Dallas, TX 73
Hull and East Yorkshire Hospitals, Kingston Upon Hull, United Kingdom 61	University of Turin, Turin, Italy 74
	Wake Forest University, Winston-Salem, NC 22, 75
Institut Gustave Roussy, Villejuif, France 62	Westmead Hospital, NSW, Australia 76
Johns Hopkins University, Baltimore, MD 63	Wilford Hall Medical Center, Lackland Air Force Base, San Antonio, TX 77
Kochi University, Kochi, Japan 64	
Kyoto Prefectural University Medicine, Kyoto, Japan 65	
Madigan Army Medical Center, Tacoma, WA 66	

Table 2

Patient/tumor characteristics and outcomes according to ablation modality. RCC = renal cell carcinoma, RFA = radiofrequency ablation.

	All Ablated Lesions	Cryoablation	RFA	*P* Value
No. Series	47	22	25	-
No. Institutions	45	23	24	-
No. Lesions	1375	600	775	-
Mean Patient Age, years	67.2	66.3	67.8	0.17
Mean Tumor Size, cm	2.64	2.58	2.69	0.12
Rate of Pre-ablation Biopsy	71.0%	82.3%	62.2%	<0.0001
Mean Duration of Follow-up, months	18.7	22.5	15.8	0.53
Incidence of Unknown or Indeterminate Pathology	33.5%	24.5%	40.4%	<0.0001
Incidence of RCC with Known Pathology	81.0	71.7%	90.0%	<0.0001
Rate of Repeat Ablation	5.3%	1.3%	8.5%	<0.0001
Rate of Local Tumor Progression	9.5%	5.2%	12.9%	<0.0001
Rate of Metastatic Progression	1.8%	1.0%	2.5%	0.06

Table 3

Multiple linear regression analysis for incidence of local tumor progression or development of metastatic disease. 42 studies had complete information available for the multivariable analyses. RCC = renal cell carcinoma.

	P Value			
	Local Tumor Progression		Metastatic Progression	
Variable	Univariate	Multivariate	Univariate	Multivariate
Ablation Modality	0.001	0.003	0.11	0.17
Sample Size of Study	0.12	0.08	0.31	0.35
Incidence of Histologically-confirmed RCC	0.81	0.96	0.69	0.70
Incidence of Unknown or Indeterminate Pathology	0.34	0.79	0.94	0.70
Mean Patient Age	0.38	0.65	0.75	0.78
Mean Tumor Size	0.11	0.36	0.42	0.71
Mean Follow-up Time	0.52	0.08	0.37	0.18