

DEFINING THE COMPLICATIONS OF CRYOABLATION AND RADIO FREQUENCY ABLATION OF SMALL RENAL TUMORS: A MULTI-INSTITUTIONAL REVIEW

D. BROOKE JOHNSON, STEPHEN B. SOLOMON, LI-MING SU, EDWARD D. MATSUMOTO, LOUIS R. KAVOUSSI, STEPHEN Y. NAKADA, TIMOTHY D. MOON, W. BRUCE SHINGLETON AND JEFFREY A. CADEDDU*

From the Division of Urology, University of Utah Health Sciences Center (DBJ), Salt Lake City, Utah, Brady Urological Institute, Johns Hopkins School of Medicine (SBS, L-MS, LRK), Baltimore, Maryland, University of Wisconsin Hospitals and Clinics (SYN) and University of Wisconsin and Veterans Administration Medical Center (TDM), Madison, Wisconsin, University of Mississippi Medical Center (EDM, WBS), Jackson, Mississippi, and Department of Urology, University of Texas Southwestern Medical Center (JAC), Dallas, Texas

ABSTRACT

Purpose: Ablative treatments (cryoablation or radio frequency ablation) for renal cell carcinoma aim to decrease morbidity by treating renal tumors in situ, eliminating the need for extirpation. These technologies have potential for complications previously unassociated with renal tumor treatment. We identified complications associated with percutaneous and laparoscopic ablative treatment of renal tumors.

Materials and Methods: Groups at medical centers with reported experience with ablation of renal tumors were invited to participate in this study. Each group submitted retrospective data regarding overall ablative treatment experience and associated complications. For each incident the nature of the complication, its associated morbidity, the necessity and nature of any subsequent interventions, and the final patient outcome were evaluated. Complications were divided into minor and major categories. Data were collected from groups at 4 institutions with a combined experience of 271 cases. Of these cases 139 were cryoablation and 133 were radio frequency ablation. There were 181 procedures performed percutaneously and 90 performed laparoscopically.

Results: A total of 30 complications occurred (11.1%) with 5 major (1.8%) and 25 minor (9.2%) complications, and 1 death (0.4%). Overall 26 of the 30 complications (86.7%) were directly attributable to the ablation procedure. The most common complication was pain or paraesthesia at the probe insertion site.

Conclusions: Ablation technologies appear to have a low complication profile when used to treat small renal tumors. The majority of complications are minor and require observation only. Further study and followup are necessary to determine long-term oncological efficacy.

KEY WORDS: kidney; carcinoma, renal cell; catheter ablation; cryosurgery, postoperative complications

Technological advances are changing the way renal tumors are being diagnosed and treated. Many tumors are discovered incidentally due to the increasing use of diagnostic imaging. At the same time advances in laparoscopy and minimally invasive surgery are changing the way renal tumors are treated with decreased morbidity and more rapid recovery, while striving to maintain oncological efficacy. Currently ablative treatments for renal cell carcinoma are being investigated, namely cryoablation (CA)^{1–3} and radio frequency ablation (RFA),^{4–10} which aim further to decrease morbidity by treating these tumors in situ and eliminating the need for extirpation. These novel technologies give rise to the potential for complications previously unassociated with renal tumor treatment. Although several groups have reported complications attributable to these technologies, their individual experiences are limited, so that the scope of complications associated with renal tumor ablation is unknown. We identified in a multi-institutional review complications that

are associated with percutaneous and laparoscopic ablative treatment for renal tumors.

MATERIALS AND METHODS

Groups at medical centers throughout the United States with reported experience in CA and/or RFA for renal cell carcinoma were identified and invited to participate in this study. Groups at each participating center performed ablation according to their protocols and entry criteria. Tumors greater than 5 cm in greatest diameter were rarely treated and not included in this database. Cases involving percutaneous or laparoscopic access to the target tumor were evaluated. Protocols admittedly had evolved with increasing experience with ablative therapy at each center. Other than distinguishing CA or RFA and a laparoscopic or percutaneous approach no other individual variables were evaluated. Groups at each center submitted retrospective data regarding their overall ablative treatment experience and the number of associated complications. For each complication information was gathered regarding the nature of the complication, its associated morbidity, the necessity and nature of any subsequent interventions, and the final patient outcome. In addition, information was gathered regarding

Accepted for publication April 8, 2004.

* Correspondence and requests for reprints: Department of Urology, University of Texas, Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, Texas 75390-9110 (telephone: 214-648-2888; FAX: 214-648-8786; e-mail: jeffrey.cadeddu@email.swmed.edu).

the case number in the overall ablative therapy experience at the given medical center. Case experience was divided into 3 groups representing the initial, intermediate and latest thirds.

Complications were divided into minor and major categories. Minor complications were defined as those that required no procedural intervention or blood transfusion. Major complications were defined as those that required hospital readmission, further procedural intervention or transfusion. It was also determined whether the complication was directly attributable to the procedure. Long-term oncological efficacy of the ablative treatment was not evaluated. Therefore, inadequate treatment or the need for re-treatment was not included as a complication.

Data were collected from 4 contributing institutions, namely The Johns Hopkins School of Medicine, University of Mississippi Medical Center, University of Texas Southwestern Medical Center and University of Wisconsin and Veterans Administration Medical Centers. Percutaneous CA, laparoscopic RFA, and percutaneous RFA techniques and equipment have been previously described.^{2,4-6} Laparoscopic CA equipment and the technique were used as described by Gill et al.³ Collected experience with ablative treatment for renal tumors at these institutions totaled 271 cases. Of these cases 139 were CA and 132 were RFA. Of these procedures 181 were performed percutaneously, while the remaining 90 were performed laparoscopically. Groups at 2 participating institutions performed percutaneous and laparoscopic ablation, while at 1 institution a group performed only percutaneous ablation and another performed only laparoscopic ablation.

RESULTS

Mean experience at each individual institution was 68 cases (range 21 to 92). A total of 30 complications occurred (11.1%) with 5 major (1.8% or 2 in the CA and 3 in the RFA group) and 25 minor (9.2% or 17 in the CA and 8 in the RFA group) complications, and 1 death (0.4%) in the RFA group (see table). A total of 20 complications (14.4%) occurred after CA (4 after laparoscopic and 16 after percutaneous ablation) and 10 (7.6%) occurred after RFA (6 after percutaneous and 4 after laparoscopic ablation). The reported death occurred 3 days after percutaneous RFA.

The complication rate decreased with experience with 16 (53.3%), 5 (16.6%) and 9 (30.0%) of the 30 complications occurring in the initial, intermediate and latest third of the collected experience, respectively. All 5 major complications occurred in the initial third of patients in each center experience. The death occurred in the final third of patients. The most common complication was pain or paraesthesia at the

percutaneous probe insertion site (see table). This accounted for 46.6% of all complications (14 of 30) and occurred in 5.2% of all cases (14 of 271).

Of the 30 complications 25 (83.3%) were directly attributable to the ablation procedure. Two of the remaining 5 patients had post-procedure pneumonia. A third patient had respiratory difficulty after the procedure with a negative pulmonary angiogram and no clear cause of the problem. The other 2 patients were diagnosed with a urinary tract infection after ablative treatment.

The 5 major complications included 1 case of open conversion due to inability to access the tumor laparoscopically, 1 of ileus after laparoscopic RFA that required hospital readmission, 1 episode of hemorrhage after percutaneous CA that required reoperation for control, self-limited and subclinical urine leakage through the ablated needle tract seen only on retrograde pyelogram and 1 case of ureteropelvic junction (UPJ) obstruction caused by scarring secondary to RFA tissue damage. Of these patients the first 4 recovered fully. UPJ obstruction led to loss of renal function and eventual nephrectomy.

The single death was attributed to post-procedure aspiration pneumonia in a patient with poor overall health, including a history of chronic obstructive pulmonary disease, congestive heart failure and pulmonary histoplasmosis. This death was not considered directly attributable to the ablation technique, but rather to a surgical procedure in a debilitated individual. In the subgroup of 90 laparoscopic procedures 8 complications occurred (8.9%), of which 3 were attributable to laparoscopic technique (3.3%), 4 were to the ablation procedure (4.4%) and 1 was iatrogenic (pneumonia) (see figure).

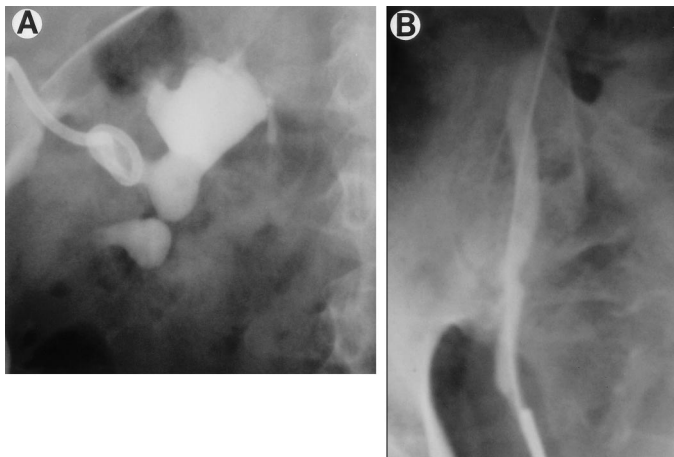
DISCUSSION

Partial nephrectomy is a proven treatment option for small renal tumors (less than 4 cm).¹¹⁻¹³ Evolving techniques seek to accomplish nephron sparing ablation with the goal of decreasing the procedure related morbidity associated with partial nephrectomy. Renal CA¹⁻³ and RFA⁵⁻¹⁰ are 2 such techniques that are currently being performed in clinical practice. CA and RFA have been used laparoscopically^{1,3,5} and via image guided^{2,4-10} techniques. Because they are novel, some complications associated with these technologies may be unique. However, procedure associated morbidity may also be anticipated because these ablative technologies draw from widely practiced percutaneous and laparoscopic renal procedures.

Parrish reported the complications associated with 1,812 percutaneous renal biopsies performed between 1953 and 1990.¹⁴ In this series the most common complication was pain more than 12 hours in duration, which occurred in 4% of

Minor and major complications of CA and RFA with outcome

Complication	Total No.	No. CA	No. RFA	No. Attributed to Technique	Outcome
Minor:					
Probe site pain or paraesthesia	14	10	4	14	Full recovery in 11 pts, persistent pain in 3
Postop urinary tract infection	2	2		0	Full recovery
Postop pneumonia infection	2	1	1	0	Full recovery
Minor hemorrhage	1	1		1	Full recovery
Elevated serum creatinine	2	1	1	2	Stable elevated serum creatinine
Wound infection	1	1		1	Full recovery
Respiratory difficulty	1	1		0	Full recovery
Pain during procedure	1		1	1	Procedure terminated
Liver burn during procedure	1		1	1	Full recovery
Major:					
Significant hemorrhage	1	1		1	Transfusion
Ileus	1		1	1	Hospital readmission with full recovery
Scarring with UPJ obstruction	1		1	1	Nephrectomy
Open conversion	1	1		1	Full recovery
Urine leakage	1		1	1	Full recovery with conservative treatment
Totals	30	19	11	25	
No. deaths	1		1	0	Death due to aspiration pneumonia



Antegrade (A) and retrograde (B) pyelograms of patient with UPJ obstruction after RFA of right renal tumor near renal hilum.

patients. Palpable hematoma was detected in 1% of patients. Prakash et al described their experience with 305 biopsies with hematuria being the most common complication, occurring in 11.8% of patients.¹⁵ Hematoma was detected in 1.6% of patients and hypotension due to blood loss occurred in 3 (1.0%).

In the current study comparable pain or paraesthesia at the probe site was the most common complication, occurring in 14 of 272 patients (5.1%). With CA since the entire probe is cooled, care must be taken to avoid cryo-injury to sensory nerves at the body surface. With RFA the active portion of the probe is positioned completely within the kidney but the probe may absorb and conduct heat from the treatment site to surrounding tissues. In addition, a final step in temperature based RFA is track ablation with the intent of decreasing bleeding and needle track seeding. This step may also damage the sensory nerves at the skin and lead to probe site pain. As such, the track ablation mode should only be activated long enough to remove the probe from the kidney and the surrounding Gerota's fascia, thereby, sparing overlying tissues.

We did not include minor hematomas, defined as those that did not cause pain or require any transfusion, intervention or further imaging, as complications in our analysis. The detection of hematoma is particularly sensitive in percutaneous procedures due to image guidance. Generally they are small and asymptomatic, and likely would have gone undetected without retroperitoneal imaging. Hemorrhage was grouped separately with 1 minor hemorrhage reported during laparoscopic CA, although no transfusion was required. This complication is generally minimized by inserting a hemostatic agent (eg fibrin glue) within the ablation tract at surgery. One episode of significant hemorrhage was reported, leading to transfusion after its discovery during percutaneous cryoablation. These incidents are most comparable to those in reports of palpable hematoma or symptomatic hypotension after percutaneous biopsy, and are similar at 0.7% (2 of 271).

The complication rate for laparoscopic urological procedures is also well defined. In a study of 2,407 urological laparoscopic procedures Fahlenkamp et al found an overall complication rate of 4.4%.¹⁶ In addition, they found a complication rate of 8.2% and 3.5% for nephrectomy/heminephrectomy and renal cyst resection, respectively. These 2 procedures most closely correlate with the laparoscopic renal ablation technique. In another study Cadeddu et al reported a laparoscopic urological surgery complication rate of 11.9%.¹⁷ In their series the rate of complications attributable to laparoscopic technique was 7%.

In our series the complication rate in the laparoscopic subgroup was similar to those of Fahlenkamp¹⁶ and Cadeddu¹⁷ et al with an 8.9% overall complication rate and a 3.3% rate of complications attributable to laparoscopic technique. Minor complications attributable to ablation consisted primarily of pain at the probe site. Regarding major complications attributable to the ablation process, 1 patient who underwent laparoscopic RFA had subclinical urine leakage through the ablated needle tract, which was seen only on retrograde pyelogram. This leakage was self-limited and resolved after a period of observation. Therefore, we recommend ultrasonographic monitoring when possible to avoid direct caliceal puncture during CA or RFA. Another patient, previously described in a case report, had UPJ obstruction after laparoscopic RFA for a 2.3 cm tumor near the hilum and renal pelvis (see figure).¹⁸ Briefly, at treatment visual inspection did not reveal any signs of direct damage to the renal pelvis or ureter. Two weeks after treatment computerized tomography (CT) showed mild right hydronephrosis and mildly delayed contrast excretion. The intent was to treat the patient conservatively with close observation but the patient was briefly lost to followup. At 6 months followup CT revealed persistent hydronephrosis and delayed contrast excretion. Antegrade and retrograde imaging showed complete obstruction and functional evaluation using nuclear renography demonstrated only 8% ipsilateral renal function. Nephrectomy was performed 11 months after initial ablative treatment. We have since altered our RFA protocol to exclude tumors that abut the renal pelvis.

The single death in this series occurred later in the ablative experience and it was not directly attributable to the ablation technique. At most centers tumor ablation is offered as a treatment option in patients with renal tumors who are not candidates for open surgery. Although this approach is rational, it may result in procedure related mortality in patients who undergo renal ablation.

Overall the complications that we identified are similar to those reported in smaller, single institution series. In their series of image guided percutaneous RFA in 32 patients Mayo-Smith et al reported 2 minor perinephric hematomas, 1 instance of presumed caliceal stricture induced by RFA and, most worrisome, 1 instance of skin metastasis at the needle puncture site.¹⁹ They also reported several instances of pain or paresthesia, which resolved spontaneously several weeks after the procedure. Farrell et al reported 4 minor complications in their series of 20 patients with a total of 35 tumors, including 3 with ipsilateral pain or paresthesia, which persisted in 1 with time. The fourth reported complication was an asymptomatic 4 cm fluid collection noted on 10-month followup CT, which they managed by observation. In their series of 20 patients who underwent cryoablation for small renal tumors Lee et al reported 1 complication, namely a pancreatic injury that required surgical reexploration.¹ Nadler et al reported 2 complications in their series of 15 patients treated with cryoablation.²⁰ One patient experienced respiratory difficulty and required re-intubation for 24 hours, while another had ileus.

Finally, there appears to be a slight learning curve associated with renal tumor ablation with more than half of the complications in this study occurring in the first third of procedures performed. This is consistent with the development of a new technique (eg renal ablation). Therefore, we anticipate that some of these complications should be avoidable in the future as CA and RFA techniques are refined and improved.

CONCLUSIONS

Percutaneous and laparoscopic renal ablation has a low complication profile when used to treat small renal tumors. The complication rate is similar to that of other laparoscopic

and percutaneous procedures. Complications stem from the approach (percutaneous or laparoscopic) as well as from ablation alone. Experience with laparoscopy and percutaneous procedures is important for preventing and managing these complications. Fortunately the majority of complications are minor and require nothing more than observation. With experience the complication rate decreases, although technique refinement may decrease the learning curve at subsequent centers initiating an ablation program. Further study and followup are necessary to determine the long-term oncological efficacy of CA and RFA for these tumors.

REFERENCES

- Lee, D. I., McGinnis, D. E., Feld, R. and Strup, S. E.: Retroperitoneal laparoscopic cryoablation of small renal tumors: intermediate results. *Urology*, **61**: 83, 2003
- Shingleton, W. B. and Sewell, P. E., Jr.: Percutaneous renal tumor cryoablation with magnetic resonance imaging guidance. *J Urol*, **165**: 773, 2001
- Gill, I. S., Novick, A. C., Meraney, A. M., Chen, R. N., Hobart, M. G., Sung, G. T. et al: Laparoscopic renal cryoablation in 32 patients. *Urology*, **56**: 748, 2000
- Su, L. M., Jarrett, T. W., Chan, D. Y., Kavoussi, L. R. and Solomon, S. B.: Percutaneous computed tomography-guided radiofrequency ablation of renal masses in high surgical risk patients: preliminary results. *Urology*, suppl., **61**: 26, 2003
- Jacomides, L., Ogan, K., Watumull, L. and Cadeddu, J. A.: Laparoscopic application of radio frequency energy enables in situ renal tumor ablation and partial nephrectomy. *J Urol*, **169**: 49, 2003
- Ogan, K., Jacomides, L., Dolmatch, B. L., Rivera, F. J., Dellaria, M. F., Josephs, S. C. and Cadeddu, J. A.: Percutaneous radiofrequency ablation of renal tumors: technique, limitations, and morbidity. *Urology*, **60**: 954, 2002
- Pavlovich, C. P., Walther, M. M., Choyke, P. L., Pautler, S. E., Chang, R., Linehan, W. M. et al: Percutaneous radio frequency ablation of small renal tumors: initial results. *J Urol*, **167**: 10, 2002
- Gervais, D. A., McGovern, F. J., Wood, B. J., Goldberg, S. N., McDougal, W. S. and Mueller, P. R.: Radio-frequency ablation of renal cell carcinoma: early clinical experience. *Radiology*, **217**: 665, 2000
- Gervais, D. A., McGovern, F. J., Arellano, R. S., McDougal, W. S. and Mueller, P. R.: Renal cell carcinoma: clinical experience and technical success with radio-frequency ablation of 42 tumors. *Radiology*, **226**: 417, 2003
- Farrell, M. A., Charboneau, W. J., DiMarco, D. S., Chow, G. K., Zincke, H., Callstrom, M. R. et al: Imaging-guided radiofrequency ablation of solid renal tumors. *AJR Am J Roentgenol*, **180**: 1509, 2003
- Beldegrun, A., Tsui, K. H., deKernion, J. B. and Smith, R. B.: Efficacy of nephron-sparing surgery for renal cell carcinoma: analysis based on the new 1997 tumor-node-metastasis staging system. *J Clin Oncol*, **17**: 2868, 1999
- Herr, H. W.: Partial nephrectomy for unilateral renal carcinoma and a normal contralateral kidney: 10-year followup. *J Urol*, **161**: 33, 1999
- Fergany, A. F., Hafez, K. S. and Novick, A. C.: Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup. *J Urol*, **163**: 442, 2000
- Parrish, A. E.: Complications of percutaneous renal biopsy: a review of 37 years' experience. *Clin Nephrol*, **38**: 135, 1992
- Prakash, J., Singh, M., Tripathi, K. and Rai, U. S.: Complications of percutaneous renal biopsy. *J Indian Med Assoc*, **92**: 395, 1994
- Fahlenkamp, D., Rassweiler, J., Fornara, P., Frede, T. and Loening, S. A.: Complications of laparoscopic procedures in urology: experience with 2,407 procedures at 4 German centers. *J Urol*, **162**: 765, 1999
- Cadeddu, J. A., Wolfe, J. S., Jr., Nakada, S., Chen, R., Shalhav, A., Bishoff, J. T. et al: Complications of laparoscopic procedures after concentrated training in urological laparoscopy. *J Urol*, **166**: 2109, 2001
- Johnson, D. B., Saboorian, M. H., Duchene, D. A., Ogan, K. and Cadeddu, J. A.: Nephrectomy after radiofrequency ablation-induced ureteropelvic junction obstruction: potential complication and long-term assessment of ablation adequacy. *Urology*, **62**: 351, 2003
- Mayo-Smith, W. W., Dupuy, D. E., Parikh, P. M., Pezzullo, J. A. and Cronan, J. J.: Imaging-guided percutaneous radiofrequency ablation of solid renal masses: techniques and outcomes of 38 treatment sessions in 32 consecutive patients. *AJR Am J Roentgenol*, **180**: 1503, 2003
- Nadler, R. B., Kim, S. C., Rubenstein, J. N., Yap, R. L., Campbell, S. C. and User, H. M.: Laparoscopic renal cryosurgery: the Northwestern experience. *J Urol*, **170**: 1121, 2003