

Laparoscopic Cryoablation for Small Renal Masses: Three-Year Follow-up

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OBJECTIVES	To report our experience with laparoscopic renal cryoablation for patients who have completed a minimum of 3 years of follow-up.
METHODS	From July 2000 to March 2005, 81 patients underwent laparoscopic renal cryoablation for renal masses. Of these 81 patients, 31 (38%) underwent laparoscopic renal cryoablation for 36 tumors and have completed a minimal follow-up of 3 years (mean 45.7 months). The postoperative follow-up protocol consisted of serial contrast-enhanced computed tomography or magnetic resonance imaging at 1 day, 1, 3, 6, and 12 months, and yearly thereafter.
RESULTS	Twenty-seven tumors were partially exophytic, five were totally endophytic, and four were hilar tumors. The mean operative time was 2.9 hours, with a mean estimated blood loss of 97 mL. The mean renal tumor size was 2.1 cm. In early follow-up, the ablation zone was larger than the tumor but subsequently diminished to the original tumor size 6 months postoperatively. Thereafter, the ablation zone size decreased. The biopsy results revealed that 22 tumors (61%) were malignant and 14 (39%) were benign. The renal tumor 3-year cancer-specific survival rate was 100%, and no patient developed metastatic disease. One patient demonstrated return of abnormal enhancement within the cryolesion during follow-up, suggesting tumor recurrence. One patient had a hemorrhage and urinary leak after cryoablation of an endophytic tumor and was treated conservatively.
CONCLUSIONS	Renal cryoablation is safe and offers a minimally invasive nephron-sparing alternative. The oncologic adequacy of renal cryoablation requires long-term follow-up data, but the intermediate-term data seem equivalent to that achieved with extirpative therapy. UROLOGY 69: 448–451, 2007. © 2007 Elsevier Inc.

Since the proposal of radical nephrectomy by Robson *et al.*,¹ extirpative surgery has remained the reference standard treatment for renal cell carcinoma. Extirpation of the renal tumor, whether by radical or partial nephrectomy, provides histologic evidence of complete tumor removal, including margin status.

Minimally invasive cryoablation for the treatment of small renal tumors has recently become available.² The benefits of laparoscopic cryoablation over extirpative approaches in the management of small renal masses include less morbidity and a diminished surgical challenge to the surgeon relative to laparoscopic partial nephrectomy.³ However, in contrast to extirpative surgery, histologic evidence of the adequacy of tumor treatment is not available with cryoablation. Specifically, the conflu-

ence of necrosis throughout the ablation zone and margin status cannot be histologically documented after cryoablation.⁴ As such, postoperative imaging is the standard by which patient follow-up evaluation is performed.

The intermediate and long-term oncologic efficacy of renal cryoablation has not yet been established. To date, only Gill and colleagues⁵ have reported 3-year follow-up clinical data. We report on only the second large-scale study with intermediate-term follow-up after laparoscopic renal cryoablation for small renal masses.

MATERIAL AND METHODS

The institution's human studies committee approved the study. From July 2000 to March 2005, 81 patients underwent laparoscopic renal cryoablation and were prospectively enrolled in this study. Of these 81 patients, 31 (38%) have completed a minimal follow-up of 3 years (mean 45.7 months, range 36 to 63). A preoperative cross-sectional imaging study (computed tomography [CT] or magnetic resonance imaging [MRI] with and without contrast) was obtained for all patients. The indication for cryoablation was an enhancing renal mass 4 cm or less in the greatest diameter. All treatment options, including extirpative surgery, ablative therapy, and watchful waiting, were

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Table 1. Patient and tumor characteristics

Patients (n)	31
Tumors (n)	36
Age (yr)	
Mean	65.3
Range	28–90
Men (n)	16 (52)
ASA score	
Mean	2.8
Range	1–4
Comorbidities (n)	
Hypertension	20 (65)
Three or more comorbidities	15 (48)
Cardiovascular	13 (42)
Diabetes	9 (29)
Cancer other than renal	3 (10)
von Hippel-Lindau	2 (6)
Previous abdominal surgery (n)	11 (35)
Preoperative serum creatinine	
Mean	1.2
Range	0.8–2.8
Contralateral kidney (n)	
Surgically absent or nonfunctional	4 (13)
Prior partial nephrectomy	2 (7)
Multitumor cryoablation (n)	
2 Renal lesions	2 (6)
4 Renal lesions	1 (3)
Tumor size (cm)	
Mean	2.1
Range	0.5–4.0
Tumors in right kidney (n)	14 (45)
Tumor location (n)	
Exophytic	27 (75)
Endophytic	5 (14)
Hilar	4 (11)

ASA = American Society of Anesthesiologists.
Data in parentheses are percentages.

discussed with the patients. In general, the study population included elderly patients with multiple comorbidities (Table 1). The youngest patient (age 28 years) had von Hippel-Lindau disease and was treated at a single setting for four small lesions. Also, five tumors (14%) were totally endophytic and four (11%) were hilar. We defined endophytic tumors as those with no indication of abnormalities at the renal surface on laparoscopic inspection. Hilar tumors were defined as those positioned medially within 5 mm of the renal artery or vein.

A transperitoneal or retroperitoneal approach was chosen depending on tumor location, patient surgical history, and surgeon preference. Tumors anterior to a horizontal line within the coronal plane through the renal hilum were generally approached transperitoneally. Tumors posterior to this line were approached retroperitoneally. In all cases, mobilization of the kidney was performed to facilitate flexible laparoscopic ultrasonography (Aloka, Walpole, Mass) of the renal mass. For hilar tumors, the renal vasculature, pelvis, and ureter were physically retracted from the tumor and developing iceball to ensure the safety of these structures.

The renal artery and vein were not clamped. The fat over the tumor and an 18-gauge biopsy of the tumor were submitted for pathologic staging. Next, depending on the lesion's size, a cryoprobe or multiple cryoprobes were positioned in the tumor. The position of the cryoprobe tip beyond the deep margin of the lesion was confirmed by laparoscopic ultrasonography. For our initial 16 patients, a 5-mm cryoprobe (Endocare, Irvine,

Calif) was used. The subsequent patients were treated with a smaller 3.4-mm cryoprobe (Oncura, Plymouth Meeting, Pa). In all cases, a double-freeze cycle was applied, with an intervening active thaw process. Each freeze cycle was continued until the iceball extended beyond the mass with laparoscopic ultrasound guidance.

For hilar tumors, the outer edge of the iceball was allowed to contact the renal artery and/or vein but was not extended into these vessels. In all cases, if the operating surgeon considered any portion of the renal mass to be inadequately treated, an additional cryoprobe was used to ensure an adequate margin. After the second thaw allowed safe removal of the cryoprobe, hemostasis was achieved by filling the cryoablation tract with fibrin glue (Baxter, Deerfield, Ill) or FloSeal (Baxter). The mass was then inspected under low insufflation pressure to ensure adequate hemostasis.

The postoperative follow-up imaging protocol consisted of serial contrast-enhanced CT or MRI scans at 1 day, 1, 3, 6, and 12 months, and yearly thereafter. Within the limitations of measuring ablation zones, the largest diameter of the ablation zone was recorded.⁶ If the ablation zone disappeared on follow-up imaging and the renal parenchyma looked totally normal, this was also recorded. Additionally, serologic monitoring of renal function preoperatively and postoperatively was performed at each point.

Statistical analyses were performed with two-tailed *t* tests or chi-square tests for independence, as appropriate.

RESULTS

Table 2 summarizes the intraoperative data. The only intraoperative complication involved cryoablation of a 2-cm endophytic clear cell carcinoma with a 5-mm cryoprobe with an estimated blood loss of 1000 mL. Postoperatively, the patient experienced gross hematuria, developed an ileus, and required transfusion. CT revealed a small perinephric urinoma, hydronephrosis, and blood clots within the collecting system. The patient responded well to ureteral stenting.

Table 3 summarizes the ablation zone size on follow-up imaging. At 3 years after cryoablation, 42% of the lesions were undetectable, and of these lesions, 9 (60%) had been biopsy-proven malignant tumors. The malignancy rate of the tumors that were still detectable (visible but without enhancement) at 3 years on imaging studies was also 60%. Four tumors (11%) had a thin rim of enhancing tissue on the periphery of the treated area on postoperative day 1 imaging. These ablation zones showed no enhancement on subsequent imaging. Three of these tumors were exophytic, and one was hilar. Two were low-grade clear cell carcinoma and two were benign.

One patient had a radiographic suggestion of tumor recurrence during follow-up. This 56-year-old woman with an American Society of Anesthesiologists score of 3 had a hilar, 2-cm, solid enhancing tumor treated with a single cryoprobe. The biopsy finding was benign. Initially, the ablation zone increased to 3 cm in diameter and subsequently shrank to 1 cm 12 months after cryoablation. No enhancement was present until the 3-year follow-up CT, which showed a 2-cm tumor with partial

Table 2. Operative data

Estimated blood loss (mL)	
Mean	97
Range	10–1000
pRBC transfusions	1 (3)
Freeze time (min)	
First freeze	
Mean	9
Range	4–15
Second freeze	
Mean	8.5
Range	2.5–15
Operative time (min)	
Mean	177
Range	75–328
Cryoprobes per tumor (n)	
1	31 (86)
2	4 (11)
3	1 (3)
Surgical approach (n)	
Transperitoneal	22 (71)
Retroperitoneal	8 (26)
Retroperitoneal converted to open	1 (3)
Pathologic diagnosis (n)	
Malignant	22 (61)
Clear cell carcinoma	17 (77)
Papillary carcinoma	4 (18)
Chromophobe	1 (5)
Benign	14 (39)
Oncocytoma	6 (29)
Hospital stay (days)	
Mean	3
Range	1–9
Postoperative complications (n)	3 (10)
Urine leak	1 (3)
Atrial fibrillation	1 (3)
Heart failure	1 (3)

pRBC = packed red blood cell.

Data in parentheses are percentages.

enhancement. Because of the interval worsening of comorbidities, she elected to proceed only with radiographic follow-up.

One case (3%) was converted from a laparoscopic retroperitoneal approach to an open approach because of failure to progress. In this case, the tumor was surrounded by a dense, desmoplastic reaction that precluded adequate exposure, targeting, and ablation. The biopsy of this 1.8-cm tumor revealed oncocytoma. [Table 4](#) compares cryoablation of the renal tumors stratified by tumor location.

COMMENT

The lack of histologic proof of complete tumor ablation is an inherent disadvantage of all ablative technologies. However, with cryoablation, the ability to achieve real-time ultrasound imaging of the iceball appears to overcome this challenge. Combining real-time ultrasound evaluation of the iceball and a well-defined understanding of the biology of the iceball allows the surgeon to precisely target and ablate renal tissue. As such, the hallmark of successful renal cryoablation is a decreasing

Table 3. Ablation zone size on follow-up CT or MRI

	Mean Size (cm) (range)	Mean Increase or Decrease*	Lesions Undetectable (%)
Preoperative	2.1 (0.5–4)	NA	NA
Postoperative			
1 day	3.2 (1.7–5.2)	↑ 52	0
1 mo	3 (1.7–5.3)	↑ 43	0
3 mo	2.4 (1–4.2)	↑ 14	0
6 mo	2.1 (0.8–4)	↔ 0%	0
1 yr	1.7 (0–4)	↓ 19	2 (6)
2 yr	1.2 (0–3.2)	↓ 43	4 (11)
3 yr	0.6 (0–2.4)	↓ 71	15 (42)

CT = computed tomography; MRI = magnetic resonance imaging.

* Relative to preoperative tumor size.

lesion size without contrast enhancement on CT or MRI. We are unaware of any report of a local recurrence of renal cell carcinoma in which neither contrast enhancement nor lesion growth occurred. If enhancement or growth occurs, we recommend biopsy and retreatment.

In our series, we performed extensive postoperative imaging to help describe the natural history of renal cryoablation lesions. As a part of our study protocol, patients underwent contrast-enhanced CT or MRI beginning on the first postoperative day. On postoperative day 1, four ablation zones exhibited a thin rim of peripheral enhancement. Two of these tumors were proven renal cell carcinoma. Subsequent imaging in these 4 patients showed no enhancement at any point during the 3-year follow-up period. It is presumed that this immediate finding was related to a hyperemic response unrelated to residual disease. Therefore, early follow-up imaging (1 day and 1 month) may be less valuable regarding the detection of recurrence.

The data in [Table 3](#) show that the ablation zones initially increased in size by 52% on postoperative day 1 and then steadily decreased to the original tumor size by 6 months after surgery. The increased size of the ablation zone compared with the original tumor size was possibly a result of the margin of normal renal tissue purposely ablated during the procedure. The ablation zones continued to shrink on average by 71% relative to the original tumor size at the 3-year follow-up period. The rate of complete disappearance of the lesions to an undetectable size on the postoperative imaging studies did not differ between the malignant and benign lesions. We believe that initial postoperative imaging should be delayed until 6 months after cryoablation in all patients, except for those presenting with multiple tumors (eg, von Hippel-Lindau disease). If, at 6 months, the lesion shows no enhancement and the size is equal to, or less, than the original lesion, follow-up imaging can only occur on an annual basis.

Although the upper tract urothelium has been shown to be resistant to injury by cryoablation,⁷ to our knowledge, we report the only case of urinary renal leakage after cryoablation. This case was also unusual because of

Table 4. Cryoablation results stratified by tumor location

	Exophytic	Endophytic	Hilar	P Value
Tumors (n)	27	5	4	
Mean tumor size (cm ± SD)	2.2 ± 0.8 (0.5–4.0)	2 ± 0.5 (1.5–2.5)	2 ± 0.1 (1.8–2.0)	0.42
Mean estimated blood loss (mL ± SD)	78 ± 71 (10–300)	226 ± 433 (10–1000)	40 ± 20 (10–50)	0.36
Mean operative time (min ± SD)	183 ± 72 (75–328)	193 ± 79 (100–300)	128 ± 30 (100–157)	0.51
Malignant tumors (%)	18 (67)	3 (60)	1 (25)	0.62
Lesions undetectable at 3 yr (%)	13 (48)	2 (40)	1 (25)	0.86
Local recurrence (%)	0	0	1 (25)	0.08

SD = standard deviation.

Data in parentheses are ranges, unless otherwise noted.

the high blood loss and significant hemorrhage into the collecting system. Subsequent renal pelvic and ureteral clotting resulted in renal urinary obstruction. In this case, a 5-mm cryoprobe was noted to have punctured the renal collecting system on ultrasonography. The leak likely resulted from a combination of the penetrating injury to the urothelium with a large cryoprobe and the elevated intrarenal pressures due to clot obstruction. Actual necrosis of the collecting system seems unlikely, because the leak quickly resolved after stenting. This patient had successful treatment of her tumor and had a normal kidney and collecting system on follow-up CT evaluations.

Endophytic and hilar tumors treated with cryoablation are intuitively at greater risk of complications or recurrence. Despite our single intraoperative complication occurring in an endophytic tumor and our single recurrence occurring in a hilar tumor, we believe that cryoablation is well-suited for these tumors. Endophytic and hilar tumors are also the most challenging for partial nephrectomy and are associated with modest complication rates.⁸ The ability to precisely control and monitor the iceball makes cryoablation of these difficult tumors feasible. Our technique of mobilizing the renal vasculature and ureter away from hilar tumors prevents cryoinjury to these vital structures. After maximizing the safety of these structures with mobilization and physical retraction away from the target, we have allowed the outer edge of the iceball to extend up to the renal artery, vein, or pelvis to ensure adequate tumor treatment.⁹

As technology has improved and our experience has grown, we have continued to modify our technique and approach to renal cryoablation. We now routinely use 1.47-mm cryoprobes (Oncura, Plymouth Meeting, Pa) that minimize the risk of hemorrhage and urinary leak. We have found that the use of hemostatic materials is usually unnecessary with these probes. Our routine hospital stay is now 23 hours instead of the mean hospital stay in this early series of 3.3 days. Also, we are incorporating CT-guided renal cryoablation for certain tumors accessible by a percutaneous approach. The best suited approach for cryoablation of a particular tumor may be dependent on its intrarenal location. We believe that the laparoscopic approach to renal cryoablation will remain

the most suitable technique for certain renal tumors. Specifically, hilar or anterior tumors pose considerable access risks when approached percutaneously. Laparoscopic treatment of these tumors would also allow direct observation of the expanding iceball margin and physical retraction of crucial hilar structures.

CONCLUSIONS

With 3 years or longer follow-up, laparoscopic renal cryoablation appears to remain a highly efficacious treatment modality for small renal tumors. Despite an older population with significant comorbidities in this study, renal cryoablation was performed with minimal morbidity. Our findings further corroborate those of Gill and colleagues⁵ in showing that the intermediate-term success rate with cryoablation therapy is equivalent to that of extirpative therapy. Long-term follow-up of 5 years or longer is the final step needed to definitively determine the role of laparoscopic cryoablation in the treatment of small renal neoplasms.

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