

## ***Clinical Science: First Prize (Tie)***

# Laparoscopic Renal Cryoablation: Efficacy and Complications for Larger Renal Masses

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### **Abstract**

**Background and Purpose:** In expanding our indications for cryoablation of renal cortical neoplasms, there was an increased morbidity with laparoscopic cryoablation. As such, we evaluated our single institution experience with laparoscopic renal cryoablation for complications and oncologic effectiveness as a function of tumor size.

**Materials and Methods:** We retrospectively evaluated our prospectively established urologic oncology database and identified 44 laparoscopic cryoablation procedures performed for the management of 51 renal masses. Measured parameters included patient age, tumor size and location, estimated blood loss, complications, and recurrences. Patients were stratified into two groups. In group 1, the patients presented with a maximum tumor diameter less than 3.0 cm. Group 2 patients had a maximum tumor diameter of 3.0 cm or larger.

**Results:** Group 1 included 30 tumors in 23 patients, and group 2 had 21 tumors in 21 patients. The mean tumor size for groups 1 and 2 were 1.8 cm (range 0.7 to 2.8 cm) and 4.0 cm (range 3.0 to 7.5 cm), respectively ( $P < 0.0001$ ). The average patient age for group 1 was 70.2 and group 2 was 77.6 years ( $P = 0.04$ ). The mean American Society of Anesthesiologists score was 1.8 and 2.1 for groups 1 and 2, respectively ( $P = 0.06$ ). There were no complications in group 1. Group 2 had 13 (62%) complications, including two mortalities. The most common complication was blood transfusions at 38%. With a mean follow-up of 9 months, there were no recurrences in group 1. With a mean follow-up of 11 months, there was a single (4.8%) recurrence in group 2. Biopsy histopathology revealed renal cell carcinoma variants in 46.7% in group 1 and 66.7% in group 2, respectively ( $P = 0.079$ ).

**Conclusion:** Renal cryoablation of renal cortical neoplasms smaller than 3.0 cm is effective and safe. Our initial experience, however, demonstrates that cryoablation of larger renal masses may be associated with increased morbidity.

### **Introduction**

SINCE THE FIRST REPORTED SERIES of probe-based renal cryoablation by Gill and colleagues,<sup>1</sup> laparoscopic cryoablation has been increasingly used for the management of small renal cortical neoplasms. Probe-based renal cryoablation is appealing for several reasons. The increasingly frequent application of CT, MRI, and ultrasonographic imaging technologies has resulted in a dramatic increase in the number of small renal cortical neoplasms that are identified.<sup>2</sup>

Published data have demonstrated that a significant number of these incidentally discovered small renal cortical neo-

plasms are ultimately determined to have benign histopathology.<sup>3,4</sup> These neoplasms have a slow and relatively predictable growth rate, with few masses smaller than 3.0 cm having ever been reported to metastasize within 3 years.<sup>5</sup> Patients who eventually undergo intervention tend to have higher tumor growth rates than those on continued observation (0.90 v 0.61 cm per year, respectively).<sup>6</sup>

There is increasing patient interest and physician acceptance of the application of minimally invasive treatment options in the management of urologic malignancies, including renal-cell carcinoma (RCC) variants.

Three-year oncologic efficacy of laparoscopic renal cryoablation for small renal masses has been established.<sup>7,8</sup> These

series and others have demonstrated that despite performing renal cryoablation on older patients with comorbidities, the patients had low morbidity based on the minimally invasive nature of renal cryoablation.<sup>9</sup> Indeed, overall complication rates with laparoscopic and percutaneous cryoablation range from 10% to 14%, respectively.<sup>1,10,11</sup> These complication rates compare favorably with rates in series of open and laparoscopic partial nephrectomy that are reported to be as high as 28%.<sup>12</sup>

Among the documented advantages of cryoablation for small renal cortical neoplasms are decreased blood loss, decreased urine leak rates, and an overall reduced morbidity, thus allowing for an expeditious recovery. While our previous experience has been very consistent with published series documenting low morbidity, we noted increased patient morbidity on expanding our indications to larger tumors. As such, we evaluated our experience with laparoscopic renal cryoablation as stratified by tumor size.

### Materials and Methods

We retrospectively evaluated our prospectively established urologic oncology database that was approved by our Institutional Review Board. Between August 2005 and May 2007, a single surgeon performed 44 laparoscopic renal cryoablation procedures on a total of 51 renal masses. Intraoperative and postoperative parameters on these patients were collected. All patients who underwent laparoscopic cryoablation were included in this study.

The indication for renal cryoablation was a localized, enhancing renal mass on preoperative CT or MRI. Each patient had an extensive discussion regarding all options including active surveillance, percutaneous or laparoscopic ablation, and open and laparoscopic approaches to extirpative surgery. Measured parameters included patient age, sex, tumor size and location, estimated blood loss (EBL), number of cryoprobes, complications, and tumor recurrences.

We classified lesions, as described by Finley and colleagues,<sup>13</sup> based on the percent of tumor that extends beyond the normal renal parenchymal contour; exophytic tumors have more than 60% of their mass outside the natural contour of the kidney. Endophytic tumors have greater than 60% of their mass within the natural border of the kidney, and mesophytic tumors have 40% to 60% of their mass in either direction.<sup>13</sup> Renal masses located within 5 mm of the renal hilum were further stratified as "hilar," because these tumors offer some additional technical challenges. In addition, we looked at renal hilar vascular clamping, EBL, complications, tumor histopathology, and recurrences.

Using a 3.0 cm cutoff, we stratified our complications and EBL with respect to the size and depth of the lesions. We further separated our lesions into two cohorts: Group 1, lesions less than 3.0 cm, and group 2, lesions of 3.0 cm or larger in diameter.

### Procedure

Posterior renal masses were approached via retroperitoneal access, and anterior renal masses were accessed via the transperitoneal approach, as described by Weld and colleagues.<sup>7</sup> In the current study, 17-gauge (1.4 mm) probes (Galil Medical, Plymouth Meeting, PA) were used in each case to perform a double freeze-thaw cycle. In each case, an

iceball was created during the first and second freeze cycles that completely engulfed the renal tumor and a margin of normal renal parenchyma.

In all cases, intraoperative laparoscopic ultrasonography was used to obtain accurate measurements of the target lesion(s) and to obtain adequate tissue depth to assure complete ablation. On the basis of the cross-sectional measurements of the tumor, probe number was determined to ensure that the entire tumor was treated along with a rim of normal tissue.

The probes were placed under ultrasonographic guidance directly into the targeted renal mass, using the laparoscopic ultrasound probe to precisely deploy each needle. Rather than using thermocouple measurements to establish the adequacy of freezing, we relied on ultrasound to determine whether our endpoint has been reached, knowing that a 1-cm margin of ice (hypoechoic area) around the lesion correlates to a tumor edge temperature of  $-40^{\circ}\text{C}$ . Each freeze cycle was terminated once an iceball large enough to cover the lesion was seen on ultrasonography.

Between the first and second freeze cycles, an active thaw was used. After the second freeze cycle, a short active thaw was used to remove the cryoablation probes, and the iceball was then left to thaw passively. All cryoablated masses underwent biopsy intraoperatively either before or after cryoablation.

For hilar renal masses, efforts were made to dissect the renal vasculature off the renal mass. If a 1-cm margin could not be achieved in this manner, the main renal artery or an appropriate segmental branch(es) was clamped with laparoscopic bulldog clamps (Klein Medical, San Antonio, TX). The renal arterial supply was interrupted in these cases to minimize the heat sink effect, and the iceball was extended up to the renal arterial segment that was clamped.

### Follow-up

Standard follow-up after cryoablation included a telephone conversation 1 week postoperatively to inquire about recovery and discuss the histopathology of the biopsy. Six weeks postoperatively, the patients were seen in the office, and follow-up imaging with either contrast-enhanced CT or MRI was arranged for the 3-month postoperative visit. The follow-up protocol is then established based on each patient's histopathology and the results of the 3-month imaging evaluation. MRI was used in patients with renal insufficiency or because of patient preference. Treatment failure was defined as enhancement or growth of the cryoablated site. Chest radiography and a complete metabolic panel, including liver function tests, complete blood cell count, renal function, and serum electrolyte levels, were also obtained at each follow-up visit.

### Results

Forty-four consecutive patients with a total of 51 renal masses, who underwent laparoscopic renal cryoablation between August 2005 to May 2007 were entered in the database. The study group had 29 men and 15 women with an average age of 73 years (range 19 to 91 yrs). In the current series, there were 32 (62.7%) exophytic, 7 (13.7%) endophytic, and 7 (13.7%) mesophytic lesions. There were an additional 5 (9.8%) lesions within 5 mm of the renal hilum, classified separately as hilar.

Thirty-six (71%) patients were accessed by the transperitoneal approach. A mean of three cryoprobes was used per lesion (range 1–7 cryoprobes). The first freeze cycle averaged 7.8 minutes, and the second freeze cycle averaged 7.1 minutes.

For group 1, the average preoperative and postoperative creatinine level was 1.15 mg/dL and 1.17 mg/dL, respectively ( $P = 0.462$ ). The long-term (defined as the most recent follow-up serum creatinine) postoperative creatinine level was 1.18 mg/dL. Group 2 had a preoperative creatinine level of 1.4 mg/dL and an immediate postoperative creatinine level of 1.55 mg/dL ( $P = 0.18$ ); the long-term creatinine level was 1.6 mg/dL.

The mean hospital stay was 1.7 days (range 1–4 days) for group 1 and 3.5 days (range 1–16 days) for group 2 ( $P = 0.02$ ).

Histopathologic data for groups 1 and 2 are presented in Table 1. At intraoperative biopsy, group 1 had a malignancy rate of 46.7%, and group 2 had a malignancy rate of 66.7% ( $P = 0.079$ ). In addition, there were 8 (26.7%) benign lesions in group 1 and 5 (23.8%) benign lesions in group 2. Four (13.3%) biopsy procedures in group 1 were not diagnostic, and four (13.3%) patients did not have a biopsy procedure because they already had a tissue diagnosis. All lesions in group 2 were biopsied. Two (9.5%) biopsy procedures in group 2 were nondiagnostic.

With a mean follow-up of 11 months (range 1–18 months), there were no recurrences in group 1. Group 2, with a mean follow-up of 9 months, had one (4.8%) recurrence. The sin-

gle recurrence was in a patient with a history of a solitary kidney because of an earlier radical nephrectomy for a 10-cm grade 3 conventional RCC.

The patient had undergone an ablative procedure for a mass in the solitary remaining kidney at an outside institution and had a rim of enhancement at the medial margin of the ablation site 6 months later. He underwent laparoscopic cryoablation using five, 1.47 cm cryoprobes of the entire area that had previously been ablated. His tumor recurred within 4 months, and he underwent an open partial nephrectomy. The pathology report revealed a grade 3 conventional clear-cell carcinoma with a negative margin. At a follow-up of 6 months, he is now without evidence of disease and has a stable creatinine level of 2.6 mg/dL.

All other lesions were both nonenhancing on CT or MRI and were decreasing in size. Fourteen lesions were followed for more than 12 months: Eight from group 1 and six from group 2. There were no recurrences.

There were no complications in group 1. Group two had 13 (62%) complications, including two mortalities. The first death was from aspiration pneumonia in a patient who died on postoperative day 16, and the second death was from a myocardial infarction that occurred on postoperative day 37. In addition, patients in this cohort had three other complications: A cerebrovascular accident, a myocardial infarction, and a pulmonary embolism.

There was one open conversion for a patient who had a previous open partial nephrectomy for RCC. Extensive fi-

TABLE 1. COMPARISON OF LARGE AND SMALL RENAL MASSES

	Group 1	Group 2	P value
Number of patients	23	21	
Number of tumors	30	21	
Average age	70.2	77.6	0.04
ASA classification	1.8 (range 1–3)	2.1 (range 1–3)	0.06
Tumor size	1.8 (0.7–3.0)	4.0 (3.1–7.5)	<0.0001
Blood loss	78 mL	398 mL	0.13
Creatinine (mg/dL)			
Preoperative	1.15	1.40	0.1
Immediate postop	1.17	1.55	0.018
Long-term postop	1.18	1.60	0.027
Pathology	14 malignant RCC (46.7%) (9 clear cell, 2 conventional RCC, 2 papillary, 1 chromophobe)	14 malignant RCC (66.7%) (10 clear cell, 3 papillary, 1 conventional)	0.079
	8 benign (26.7%) (6 oncocytoma, 1 AML, 1 myelolipoma)	5 benign (23.8%) (4 oncocytoma, 1 myelolipoma)	
	4 nondiagnostic (13.3%)	2 nondiagnostic (9.5%)	
	4 not performed (13.3)		
Length of hospitalization (days)	1.65	3.52	0.02
Complications (%)	0	13 (62%) Mortalities—2 (9.5%) Transfusions—8 (38%) Other—3 (1 MI, 1 CVA, 1 PE)	0.0007
Follow-up (months)	9.0 (3–20)	11.0 (0–20)	0.2
Recurrences (%)	0	1 (4.76)	0.15

ASA = American Society of Anesthesiologists; preop = preoperative; postop = postoperative; RCC = renal-cell carcinoma; AML = angiomylipoma; MI = myocardial infarction; CVA = cardiovascular accident; PE = pulmonary embolism.

brosis and reactive tissue from his previous surgery made the hilar dissection too difficult to identify the correct tissue plains.

Hemorrhage with blood transfusion was the most common complication and comprised 61.5% of the group 2 complications. Eight of 21 patients in group 2 (38%) needed blood transfusions. Group 1 patients had an average blood loss of 78 mL, and group 2 patients had an average blood loss of 498 mL. The mean preoperative hematocrit of the patients in whom bleeding occurred was 36.5%, and they were transfused at an average hematocrit of 26.01%. This is compared with a total mean preoperative hematocrit of 41% in those who did not need a transfusion. Of the eight lesions in patients who received a transfusion, the average size was 4.7 cm. The average size of the tumors in patients who did not need transfusions was 2.3 cm.

We evaluated all our complications and stratified them with respect to tumor size and found that of our 13 complications, the average size of the lesions were 4.7 cm. All of our complications were with lesions larger than 3.0 cm. When we compared complication rates with respect to depth of invasion, the individual complication rate for the exophytic, endophytic, and mesophytic lesions were 25%, 28.6%, and 0%, respectively. The mean EBL for the exophytic, endophytic, and mesophytic tumors was 103 mL, 62.5 mL, and 53 mL, respectively. The exophytic lesions had more blood loss than the endophytic and the mesophytic lesions combined—103 mL *v* 57 mL, respectively ( $P = 0.13$ ).

## Discussion

Renal cryoablation is a minimally invasive option for carefully selected patients with renal tumors. Gill and coworkers<sup>8</sup> reported on 51 patients undergoing renal laparoscopic cryotherapy with an average tumor size of 2.3 cm. The 3-year cancer-specific survival was 98%. While the patient population in this series was older and had medical comorbidities, there was a remarkably low complication rate (7%). Similarly, in our previously published cryoablation series of 31 patients with a minimum follow-up of 3 years, we reported a low complication rate (9.8%) with a mean tumor size of 2.1 cm (range 0.5–4.0 cm).<sup>7</sup>

The low morbidity of our previous experience and the 3-year efficacy data that we reported (97% of patients without evidence of enhancement) prompted us to expand our indications for cryoablation to larger tumors.

The increased complication rate that we experienced was surprising and engendered evaluation of our database. Of the 51 lesions studied in the current series, we noted that all complications occurred in tumors that were 3.0 cm or larger by preoperative radiographic criteria. Indeed, we had an elevated complication rate of 62% with larger tumors. The most common complication was hemorrhage necessitating transfusion. The mean size of tumors necessitating transfusion was 4.7 cm, compared with a tumor size of 2.2 cm in patients who did not need transfusion.

Whereas the majority of laparoscopic renal cryoablation studies have had patients with primarily exophytic lesions, the current series included patients with endophytic, mesophytic, and hilar lesions. Eight of the 134 (6.25%) complications came from the exophytic cohort. In contrast to laparoscopic or open partial nephrectomy, in which the challenges

and risks increase as tumors become more endophytic, we believe that exophytic renal tumors undergoing cryoablation do have an increased risk of bleeding, which is evident in the current series in which bleeding increased with exophytic lesions. The increased bleeding with exophytic tumors may be caused by the mechanical lever effect; the length of the lever arm with an exophytic tumor increases the torque at the base of the tumor, and there is less tissue anchoring the tumor to the kidney. While exophytic tumors are easier to target and will likely have less recurrences when larger series have matured, great technical care should be taken to ablate exophytic tumors carefully to minimize the risk of bleeding.

In the current series, there was a single open conversion (2%), which was because of adherent fat around the tumor. This lesion measured 4.4 cm. This patient had previously undergone a contralateral nephrectomy for RCC and a previous open partial nephrectomy on the ipsilateral side; conversion was deemed necessary to assure precise ablation.

Our two postoperative mortalities and three cardiovascular events were largely because of the age and the comorbidities of our patients. Indeed, the average age in our series was 75 years, and all but two patients had significant comorbidities. The two patients who died had mean tumor sizes of 5.5 cm and 3.5 cm. Both tumors had been under active surveillance and had demonstrated significant growth on follow-up evaluation. It is also important to note that the higher nonhemorrhagic complication rate in group 2 may be explained by the generally sicker (higher American Society of Anesthesiologists grade) nature of this cohort.

The results of our series confirm our and others' findings that with short-term follow-up, laparoscopic cryoablation is effective in the management of small renal masses. Indeed, with our small renal mass cohort, there were no recurrences, and there was a single recurrence in the larger renal mass group in a complex patient.

Postcryoablation creatinine levels (1.4 mg/dL) were consistent with preoperative levels (1.3 mg/dL), which suggests that renal function was unaffected during the ablation, as has been previously documented.<sup>8,10</sup> The 46.7% and 66.7% rate of malignancy detection for small and large renal masses, respectively, was consistent with previous data on small, less than 3 cm lesions.<sup>9</sup>

Laparoscopic cryoablation remains a very promising management modality for small renal cortical neoplasms. Over the past few years, there have been substantial improvements in cryoablation technologies and in the imaging technologies used to target cryoablation that will likely yield improved long-term results. Similarly, refinements in patient selection criteria, such as laparoscopic renal cryoablation of tumors less than 3.0 cm as suggested by the current study, will further help to optimize the treatment of patients with small renal masses.

## Conclusions

Laparoscopic cryoablation is an effective and safe treatment modality for small renal cortical neoplasms. Previously, the morbidity of laparoscopic renal cryoablation has been documented to be minimal. This has been primarily for small renal masses—less than 3 cm in diameter. Although equally effective, laparoscopic cryoablation for larger renal

cortical neoplasms (larger than 3.0cm in diameter) is associated with higher complication rates. Therefore, laparoscopic cryoablation should be performed only for smaller than 3.0 cm lesions.

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### Abbreviations Used

CT = computed tomography

EBL = estimated blood loss

MRI = magnetic resonance imaging

RCC = renal-cell carcinoma



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