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Purpose: We evaluated the change in renal function after renal cryoablation and partial nephrectomy based on tumor complexity according to the R.E.N.A.L. nephrometry score.

Materials and Methods: We retrospectively reviewed the data of patients who had a renal tumor in a solitary kidney, and underwent renal cryoablation and partial nephrectomy between December 2000 and January 2012. Renal tumor complexity was categorized into 3 groups by R.E.N.A.L. nephrometry score as low (4 to 6), intermediate (7 to 9) and high (10 to 12). All baseline demographic data, perioperative parameters and followup data including renal function were collected. Comparisons were made among similar tumor complexities.

Results: In the renal cryoablation and partial nephrectomy groups 29 patients (43 tumors) and 33 patients were identified, respectively. In all renal tumor complexities, renal cryoablation provided a better perioperative outcome in terms of median operative time, estimated blood loss, transfusion, hospital stay and complications. The median change in serum creatinine and estimated glomerular filtration rate was slightly greater in the partial nephrectomy group. However, the differences were not statistically significant for any of the tumor complexities. Three patients (10%) in the renal cryoablation group and 2 (6%) in the partial nephrectomy group required long-term dialysis.

Conclusions: In patients with solitary kidneys, renal cryoablation is associated with superior perioperative outcomes compared to partial nephrectomy. Specifically, partial nephrectomy is not associated with greater loss of renal function than renal cryoablation regardless of the extent of tumor complexity.

Key Words: kidney neoplasms, cryosurgery, nephrectomy

Abbreviations and Acronyms
EBL = estimated blood loss
eGFR = estimated glomerular filtration rate
LTP = local tumor progression
PN = partial nephrectomy
RCA = renal cryoablation
RCC = renal cell carcinoma
sCr = serum creatinine
WIT = warm ischemic time

Accepted for publication September 5, 2012.
Study received institutional review board approval.
* Nothing to disclose.
† Financial interest and/or other relationship with Intuitive, Ethicon, Covidien and Endocare.
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For another article on a related topic see page 1097.
Editor’s Note: This article is the first of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 1174 and 1175.

CHRONIC kidney disease correlates with an increasing risk of cardiovascular events, hospitalization and mortality.1 The risk of chronic kidney disease in patients with RCC is most associated with baseline renal function and the choice of treatment modality.2,3 Therefore, the modern management of renal cell carcinoma combines meticulous oncologic control with optimal preservation of renal function.

Partial nephrectomy has been considered the gold standard surgical treatment for small renal masses for imperative and elective indications.4 The introduction of minimally invasive
PN techniques has provided advantages in terms of postoperative recovery while offering functional and oncologic outcomes equivalent to those of the open surgical option.5

Renal cryoablation represents another attractive alternative for patients requiring active treatment.6,7 Mid-term cancer specific survival is greater than 90% in most published series.8 However, local recurrence and tumor progression are more likely with RCA than with PN.9,10

Tumors in a solitary kidney represent a challenging clinical scenario yet provide a unique opportunity to evaluate the effect of treatment type on loss of renal function. PN and RCA potentially affect renal function in different ways. With PN, renal hilar clamping with temporary renal ischemia and parenchymal resection represent 2 etiologies of possible functional loss. With RCA, normal tissue around the cryolesion can be damaged while complete treatment of the tumor is pursued.

Tumor complexity has traditionally been recognized as a crucial factor to consider in the treatment decision process for kidney tumors. Scoring systems as surrogate measures of tumor complexity have been proposed during the last few years to predict perioperative outcomes and complications after PN.11 However, differences in functional outcomes between PN and RCA based on tumor complexity have not been evaluated.

MATERIALS AND METHODS

Patient Selection

Our institutional review board approved prospectively maintained databases were queried to identify patients with a solitary functioning kidney who underwent RCA with a percutaneous or laparoscopic approach (59 patients) or minimally invasive PN with a laparoscopic or robotic approach (52) between December 2000 and January 2012 at our institution. Patients with multiple tumors treated in a single session, those with a tumor whose complexity could not be scored due to unavailable information and those without available information about postoperative renal function were excluded from the study.

In the RCA group 29 patients with 43 tumors and in the PN group 33 patients were included in the analysis. The complexity of each tumor was graded according to the R.E.N.A.L. nephrometry scoring system as low (4 to 6), intermediate (7 to 9) or high (10 to 12).12 Comparisons were made of treatment groups by considering tumors of similar complexity. The impact of tumor complexity was evaluated primarily on renal functional outcomes and secondarily on treatment outcomes.

Surgical Techniques and Surveillance Protocols

RCA was performed with double freeze-thaw cycles to extend the iceball 5 to 10 mm beyond the tumor edge. Intraoperative pre-cryoablation needle biopsies were performed in all patients. The choice of laparoscopic or percutaneous approach was based on tumor location and technical capability depending on the year of treatment. Our RCA techniques have been described previously.13,14 Patients were tentatively discharged home on the day of surgery with the percutaneous approach and on postoperative day 1 with the laparoscopic approach. Surveillance after RCA included renal function, radiological and histological study. Serial computerized tomography or magnetic resonance imaging was performed on postoperative day 1, at 3, 6 and 12 months, and then yearly. Computerized tomography guided percutaneous needle biopsy was done at 6 months postoperatively for some patients.

PN was performed with a laparoscopic or robotic approach as previously described.15,16 A clampless procedure was selectively used by the surgeon on the basis of tumor features. After PN with pathology confirmed malignant tumor, renal function and imaging studies were performed at 6 months postoperatively and then yearly.

Outcome Measures and Statistical Analysis

Study parameters included age, gender, ASA (American Society of Anesthesiologists) score, body mass index, medical comorbidities (hypertension, diabetes, heart disease, history of other cancer), tumor size, tumor complexity by the R.E.N.A.L. nephrometry score, tumor laterality, preoperative and postoperative renal function, operative time, EBL, WIT, cryoablative time, transfusion, conversion, intraoperative and postoperative complications, and hospital stay.

Renal function outcomes were determined by sCr and eGFR calculated using the Modification of Diet in Renal Disease equation.17 The most recent sCr within 6 months after the procedure (between 1 and 6 months) and the last followup sCr were used to represent postoperative renal function. The difference and percentage change of sCr and eGFR from the preoperative values were calculated to evaluate the impact of the procedure.

All patients were included in the analysis in an intent to treat fashion including those who underwent radical nephrectomy after RCA and PN. Postoperative complications were graded using the Clavien classification system.18 Local tumor progression in the RCA group was defined as persistence or enlargement of an enhancing lesion on postoperative followup imaging.19

All categorical data were compared with the Pearson chi-square and Fisher exact tests. Continuous variables were compared with the Wilcoxon rank sum and Kruskal-Wallis test. A 2-tailed p < 0.05 was considered statistically significant for all analyses. Analysis was performed using JMP® 9 (SAS).

RESULTS

Overall Comparison

Demographic data and tumor characteristics are summarized in supplementary table 1 (jurology.com). There was no significant difference in age, gender, body mass index, medical comorbidities and etiology of solitary kidney between the RCA and the PN groups. The most common solitary kidney etiology was contralateral RCC in both groups. Patients in the RCA group had a significantly higher ASA
score and smaller median tumor size compared to those in the PN group. Two-thirds of patients (63%) in the RCA group had previous RCC surgery in a treated kidney while none had prior surgery in the PN group (p < 0.001). In the RCA group 7 patients (16%) had von Hippel-Lindau disease. The distribution of tumor complexity was similar between the 2 groups (p = 0.97).

Perioperative outcomes are presented in supplementary table 2 (jurology.com). PN was significantly associated with a longer median operative time, higher median EBL and transfusion rate, longer median hospital stay, and more intraoperative and postoperative complications than RCA. Median WIT was 18 minutes in the PN group (4 patients were treated with the clampless procedure) and median ablative time was 18 minutes in the RCA group.

Five intraoperative complications (3 patients with hemorrhage requiring intraoperative transfusion and 2 with ureteral injuries) and 2 open conversions (due to hemorrhage and positive surgical margin from frozen section) occurred only in the PN group. Major postoperative complications (Clavien grade 3 or greater) occurred in 6 patients in the PN group and in 1 in the RCA group (p = 0.002). In the PN group 2 patients had urine extravasation and anuria requiring ureteral stent insertion, 1 patient had a small bowel fistula after ileal ureter replacement from ureteral injury requiring laparotomy and bowel reanastomosis, 1 had postoperative hemorrhage requiring nephrectomy, 1 had deep vein thrombosis with pulmonary emboli and 1 patient had renal insufficiency requiring long-term dialysis. Only 1 patient from the RCA group had postoperative bleeding requiring laparotomy. There was no perioperative mortality in either group.

Renal cell carcinoma was diagnosed in 58% of the RCA group and 73% of the PN group by histology. In the PN group 2 positive margins were reported (1 for oncocytoma and 1 for RCC). Median followup was 41 months in the RCA group and 17 months in the PN group. During followup 12 (28%) cases of LTP occurred in the RCA group whereas no progression was observed in the PN group (p < 0.001). There was no difference in LTP rate among tumor complexity levels. Median time of LTP diagnosis was 8.6 months (IQR 6.3–24.3) after the procedure. Renal vein thrombus developed in 1 patient with LTP and was treated with radical nephrectomy. RCA was performed again for 9 tumors while 2 cases of treatment failure were managed with surveillance. Metastasis occurred in 6 (21%) and 2 (6%) patients in the RCA and the PN groups, respectively. In the RCA group 1 patient died of lung metastasis. No cancer related deaths occurred in the PN group.

### Outcomes in Relation to Tumor Complexity

A comparison of outcomes in relation to tumor complexity is shown in table 1. The PN group had a significantly higher EBL regardless of tumor complexity (p < 0.001, p < 0.001 and p = 0.01 for low, intermediate and high complexity) as well as longer hospital stay (p < 0.001, p < 0.001 and p = 0.008 for low, intermediate and high complexity) compared with the RCA group. The operative time and transfusion rate in the PN group were significantly higher only for high complexity tumors (p = 0.04 and p = 0.03, respectively). The overall postoperative complication rate in the PN group was significantly higher for intermediate and high complexity tumors (p = 0.02 for both).

### Functional Outcomes

Patients in the PN group had a lower baseline mean sCr (1.2 vs 1.3 p = 0.03) than the RCA group. Postoperative renal function studies are summarized in table 2. The median (IQR) time for the most recent sCr within 6 months was 5.4 (3.8–6.3) and 3.2 (1.1–6.5) months in the RCA and PN groups, respectively (p = 0.06). The median time for the last followup was 33.4 (15.6–52) and 12.1 (4–38.7) months in the RCA and PN groups, respectively (p = 0.007).

There was no significant difference in the median change in sCr (1% vs 8%, p = 0.21) and eGFR (loss 1% vs 9%, p = 0.21) when comparing the results in the low complexity group between RCA and PN for the last followup value. Similar findings were noted in the intermediate complexity (sCr and eGFR both change 15% vs 16%, p = 0.92) and in the high complexity groups (sCr change 8% vs 11%, eGFR loss 8% vs 10%, p = 0.77 in both). The comparison using the most recent values within 6 months after the proce-

### Table 1. Comparison of surgical outcomes based on tumor complexity

<table>
<thead>
<tr>
<th></th>
<th>Low Complexity</th>
<th>Intermediate Complexity</th>
<th>High Complexity</th>
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<tbody>
<tr>
<td></td>
<td>RCA</td>
<td>PN</td>
<td>p Value</td>
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<tr>
<td></td>
<td>RCA</td>
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<tr>
<td></td>
<td>RCA</td>
<td>PN</td>
<td>p Value</td>
</tr>
<tr>
<td>No. pts</td>
<td>18</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Median operative mins (IQR)</td>
<td>150 (135–195)</td>
<td>165 (113–248)</td>
<td>0.71</td>
</tr>
<tr>
<td>Median mL EBL (IQR)</td>
<td>50 (35–63)</td>
<td>150 (100–350)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median days hospital stay (IQR)</td>
<td>1 (1–1)</td>
<td>3 (3–4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. transfusions (%)</td>
<td>1</td>
<td>2</td>
<td>0.09</td>
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<tr>
<td>No. intraop complications (%)</td>
<td>0</td>
<td>0</td>
<td>Not applicable</td>
</tr>
<tr>
<td>No. overall postop complications (%)</td>
<td>1 (6)</td>
<td>2 (15)</td>
<td>0.36</td>
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dure showed results similar to those of the last followup as no statistically significant difference was found for any level of tumor complexity between the groups.

The results were compared within each group of patients. In the RCA group the median decrease in eGFR (1% vs 15% vs 8%) for the last followup period was not statistically different among low, intermediate and high complexity tumors (p = 0.09). In the PN group intermediate complexity cases also had the greatest loss of renal function after the procedure. Nevertheless, the difference in median change in eGFR was not statistically significant among the 3 complexities (9% vs 16% vs 10%, p = 0.66). Three patients (10%) in the RCA group and 2 (6%) in the PN group required long-term dialysis (p = 0.54).

**DISCUSSION**

Nephron sparing surgery is the standard treatment for small renal masses when technically feasible.\(^7\) PN has been considered the first treatment option with excellent long-term outcomes. RCA also has an important role in the subgroup of high risk surgical cases, including those with a solitary kidney,\(^6,7\) whose management is challenging due to the greater risk of chronic kidney disease.

Baseline renal function, amount of preserved kidney and WIT are the most important factors associated with adverse functional outcomes after PN.\(^20\) RCA has a minimal impact on postoperative renal function regardless of baseline status.\(^21\)

In previous matched pair comparison studies of PN and RCA, the changes in postoperative renal function were not significantly different between these treatment options.\(^22,23\) However, a more reliable assessment of renal function can be obtained when considering patients with a solitary kidney as the confounding effect of the presence of a contralateral kidney can be eliminated.

Few studies in the setting of patients with a solitary kidney have been reported with conflicting results. Turna et al compared the outcomes of 3 minimally invasive nephron sparing techniques in a solitary kidney.\(^24\) They concluded that laparoscopic PN had better intermediate term oncologic outcomes but had significantly poorer renal function at 6 months compared with cryoablation and radio frequency ablation. Haber et al also found similar results between patients in the laparoscopic PN and RCA groups.\(^25\)

On the other hand, Goyal et al recently demonstrated no difference in postoperative renal function after PN and RCA.\(^26\) Mitchell et al also noted similar results for short-term renal function after open PN and percutaneous ablation techniques.\(^27\)

However, a limitation of previous studies is the difference between groups in terms of tumor characteristics. Small exophytic tumors tend to be treated with RCA while large and complex tumors are usually managed with PN.\(^7,28\) Tumor size was shown to influence treatment outcome.\(^29\) To date, no study has determined the impact of tumor complexity when comparing the outcomes of these 2 treatment modalities.

To our knowledge, this study represents the first comparing these 2 treatment modalities on the basis of tumor complexity. The findings of our overall comparative analysis are similar to those of previous reports comparing RCA and PN.\(^23,25-27\) RCA seems to provide better perioperative outcomes (operative time, EBL, transfusion, hospital stay and complications) but with higher LTP rates. Differences in perioperative outcomes also increased with increasing tumor complexity.

In this study LTP and the metastasis rate in the RCA group were higher than in previous studies.\(^26,27\) This finding might be explained by our patients undergoing RCA being high risk, with 91% having a history of contralateral RCC (73% in the PN group), 63% having a history of RCC in the treated kidney (none in the PN group) and 16% having von Hippel-Lindau disease (none in the PN group). Moreover LTP and metastasis may be more likely discovered due to the longer followup in the RCA group. Thus, oncologic findings from this study should be interpreted with caution.

When analyzing renal function we used change in sCr and eGFR for the end point. Values at 2 different points were used, with the most recent sCr within 6 months after the procedure being used to demonstrate the early to intermediate effect of treat-
ments, and the last followup sCr being used to represent the long-term effect on renal function. No significant differences were identified among similar tumor complexities in terms of change in renal function after PN and RCA.

Limitations of this study include the retrospective nonrandomized study design, which may account for a selection bias. Differences in patient demographics and the timing of renal function measurement between groups, as well as the limited sample, especially in the high complexity group, might have affected the study findings. Nevertheless, tumor in a solitary kidney does not represent a common scenario in clinical practice. Further studies with a larger population and a multivariable analysis would be useful to support these findings. The amount of preserved renal parenchyma has recently been suggested as a determinant factor in the assessment of renal function after PN. Given the retrospective design of the present study, we could not take this factor into consideration. Further investigations including these details would be useful.

CONCLUSIONS
RCA and PN are safe and effective treatments for renal tumors in a solitary kidney. RCA provides better perioperative outcomes. PN, even for increasingly complex tumors, is not associated with a worse renal functional outcome than RCA.

REFERENCES


