

## Clinical, Pathologic, and Functional Outcomes After Nephron-Sparing Surgery in Patients with a Solitary Kidney: A Multicenter Experience

Adam C. Mues, M.D.,<sup>1</sup> Ruslan Korets, M.D.,<sup>2</sup> Joseph A. Graverson, M.D.,<sup>5</sup> Ketan K. Badani, M.D.,<sup>2</sup>  
Vincent G. Bird, M.D.,<sup>3</sup> Sara L. Best, M.D.,<sup>4</sup> Jeffrey A. Cadeddu, M.D.,<sup>4</sup> Ralph V. Clayman, M.D.,<sup>5</sup>  
Elsbeth McDougall, M.D.,<sup>5</sup> Kurdo Barwari, M.D.,<sup>6</sup> Pilar Laguna, M.D.,<sup>6</sup> Jean de la Rosette, M.D.,<sup>6</sup>  
Louis Kavoussi, M.D.,<sup>7</sup> Zhamshid Okhunov, M.D.,<sup>7</sup> Ravi Munver, M.D.,<sup>8</sup> Sutchin R. Patel, M.D.,<sup>9</sup>  
Stephen Nakada, M.D.,<sup>9</sup> Matvey Tsivian, M.D.,<sup>10</sup> Thomas J. Polascik, M.D.,<sup>10</sup>  
Arieh Shalhav, M.D.,<sup>11</sup> W. Bruce Shingleton, M.D.,<sup>12</sup> Emilie K. Johnson, M.D.,<sup>13</sup>  
J. Stuart Wolf, Jr., M.D.,<sup>13</sup> and Jaime Landman, M.D.<sup>5</sup>

### Abstract

**Background and Purpose:** Surgical management of a renal neoplasm in a solitary kidney is a balance between oncologic control and preservation of renal function. We analyzed patients with a renal mass in a solitary kidney undergoing nephron-sparing procedures to determine perioperative, oncologic, and renal functional outcomes.

**Patients and Methods:** A multicenter study was performed from 12 institutions. All patients with a functional or anatomic solitary kidney who underwent nephron-sparing surgery for one or more renal masses were included. Tumor size, complications, and recurrence rates were recorded. Renal function was assessed with serum creatinine level and estimated glomerular filtration rate.

**Results:** Ninety-eight patients underwent 105 ablations, and 100 patients underwent partial nephrectomy (PN). Preoperative estimated glomerular filtration rate (eGFR) was similar between the groups. Tumors managed with PN were significantly larger than those managed with ablation ( $P < 0.001$ ). Ablations were associated with a lower overall complication rate (9.5% vs 24%,  $P = 0.01$ ) and higher local recurrence rate (6.7% vs 3%,  $P = 0.04$ ). Eighty-four patients had a preoperative eGFR  $\geq 60$  mL/min/1.73 m<sup>2</sup>. Among these patients, 19 (23%) fell below this threshold after 3 months and 15 (18%) at 12 months. Postoperatively, there was no significant difference in eGFR between the groups.

**Conclusions:** Extirpation and ablation are both reasonable options for treatment. Ablation is more minimally invasive, albeit with higher recurrence rates compared with PN. Postoperative renal function is similar in both groups and is not affected by surgical approach.

### Introduction

THE SURGICAL TREATMENT of patients with an enhancing renal mass in a solitary kidney presents a unique challenge of maintaining adequate renal function while simultaneously

removing the tumor to provide oncologic control. Patients with significant losses in renal function may need hemodialysis and experience an increase in overall morbidity and mortality.<sup>1,2</sup>

Open partial nephrectomy (OPN) is the reference standard for the management of a renal mass in a solitary kidney.<sup>3</sup>

<sup>1</sup>New York University School of Medicine, New York, New York.

<sup>2</sup>Department of Urology, Columbia University Medical Center, New York, New York.

<sup>3</sup>Department of Urology, University of Florida Medical Center, Gainesville, Florida.

<sup>4</sup>Department of Urology, University of Texas Southwestern Medical Center, Dallas, Texas.

<sup>5</sup>Department of Urology, University of California, Irvine, Orange, California.

<sup>6</sup>Department of Urology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands.

<sup>7</sup>Smith Institute for Urology, North Shore-LIJ Health System, New Hyde Park, New York.

<sup>8</sup>Department of Urology, Hackensack University Medical Center, Hackensack, New Jersey.

<sup>9</sup>Department of Urology, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin.

<sup>10</sup>Division of Urology, Duke University Medical Center, Durham, North Carolina.

<sup>11</sup>Section of Urology, University of Chicago Medical Center, Chicago, Illinois.

<sup>12</sup>Department of Urology, Ochsner Clinic Foundation, Baton Rouge, Louisiana.

<sup>13</sup>Department of Urology, University of Michigan Medical Center, Ann Arbor, Michigan.

Minimally invasive approaches, however, such as laparoscopic partial nephrectomy (LPN), renal cryoablation, and radiofrequency ablation (RFA), have been safely and effectively performed in patients with a solitary kidney.<sup>4</sup> In the current study, we evaluated multicenter data on patients with a functional or anatomic solitary kidney (congenital or acquired) and a renal cortical neoplasm (RCN) who underwent a nephron-sparing procedure (open or minimally invasive) to assess perioperative data, oncologic outcomes, complications, and the effects on renal function.

## Patients and Methods

### Study population

A retrospective multicenter study was performed collecting data from 12 institutions. Institutional Review Board approval was obtained from each institution before compiling the patient data. All patients with a functional or anatomic solitary kidney (congenital or acquired) who underwent nephron-sparing surgery for one or more renal masses were included. There was no standardized definition (estimated glomerular filtration rate [eGFR]) of a nonfunctioning kidney. Similarly, there was no standard test to diagnose a nonfunctioning kidney. Patients with preexisting metastatic disease were excluded from the study.

### Study design

Procedures performed included OPN, LPN, laparoscopic cryoablation (LCA), percutaneous cryoablation (PCA), and RFA (laparoscopic and percutaneous). Clinical data, including age, preoperative serum creatinine, tumor size, and surgical approach, were recorded. Operative time, estimated blood loss (EBL), length of hospital stay (LOS), and method of vascular control of the hilum (when performed) were documented. Histopathology was determined from either a pretreatment biopsy (ablative treatments) or analysis of the final surgical specimen. Ischemia times (warm *vs* cold), complication rates (Clavien classification), tumor recurrences, and renal function outcomes were documented.

Tumor persistence was defined as contrast enhancement of the tumor bed on CT or MRI on the first postoperative imaging study. Local recurrence was defined as tumor bed enhancement on CT or MRI in patients who had previously undergone postoperative imaging with negative results. Renal function was measured by serum creatinine level and eGFR on postoperative day 1 and at 1, 3, 6, and 12 months. eGFR was calculated using the four variable Modification of Diet in Renal Disease equation. Outcomes from patients after ablative therapy (cryoablation and RFA) were compared with those in patients undergoing extirpative surgery (OPN and LPN). Similarly, patients undergoing OPN were compared with those who underwent LPN.

### Statistical analysis

Univariate analyses were performed with chi-square and *t* test for categorical and continuous variables, respectively. For variables where the distribution did not conform to the normality assumption, the Mann-Whitney and Kruskal-Wallis tests were used. All statistical tests were two-sided, and a *P* value < 0.05 was considered statistically significant. Statistical analysis was performed using Stata v 9.0 software (College Station, TX).

## Results

Between February 1998 and September 2010, a total of 205 procedures were performed for RCN in solitary kidneys. There were 195 patients who had an anatomic solitary kidney and 3 patients with a functional solitary kidney. Ninety-eight patients underwent 105 ablation procedures, and 100 patients underwent partial nephrectomy (PN) (50 OPN and 50 LPN). Table 1 summarizes clinical, surgical, and perioperative data comparing all forms of ablation with PN. Patients undergoing PN had significantly larger tumors than patients having ablation (mean of 3.9 cm *vs* 2.5 cm, *P* < 0.001) respectively.

EBL, LOS, and complication rates were significantly lower for ablation procedures compared with PN. In the ablation group, there was one case of inadvertent skin freezing during an LCA. Postablation complications classified by the Clavien system demonstrated five patients (grade I), one patient (grade II), one patient (grade IIIa), and two patients with (grade IIIb). Intraoperative complications in the PN group consisted of four cases of severe intraoperative bleeding necessitating transfusion, one renal artery injury, and one pleural injury. Postoperative complications for PN included 10 patients with grade I, 2 patients with grade II, and 6 patients with grade IIIb complications.

Three (2.9%) patients had tumor persistence after ablation. One patient underwent laparoscopic RFA with a salvage LCA performed 1.5 months later. One patient had persistence after PCA and was treated with repeated PCA, and one patient underwent LCA and was treated with salvage laparoscopic RFA. Postoperative imaging after salvage procedures demonstrated no evidence of persistence or recurrence in any of the patients.

There were nine (8.6%) recurrences after ablation (seven local, two patients with metastatic disease). Five (56%) recurrences were managed with a minimally invasive nephron-sparing approach with no subsequent cancer recurrence. One patient underwent an OPN and has had no evidence of recurrence. The other patient initially underwent a percutaneous RFA and was subsequently treated with a laparoscopic radical nephrectomy (LRN). Adrenal metastasis then developed in this patient. Two patients with metastatic recurrence were managed by medical oncology. There were no cancer-specific deaths in the group, and one patient death was from an unrelated malignancy.

There were four recurrences after PN. Three (3%) were local recurrences after OPN. One patient presented with a 7-cm tumor and had a positive margin after OPN. This patient underwent LRN and was placed on hemodialysis. Two patients were treated with a repeated nephron-sparing surgery (OPN and laparoscopic RFA) and have had no evidence of recurrence to date. A solitary metastatic liver lesion developed in one patient after an LPN for a 6.8-cm tumor. This lesion was treated with surgical resection. There were four (4%) deaths in the PN group that were all unrelated to renal-cell carcinoma or chronic kidney disease.

Within the PN group, patients undergoing OPN were compared with those undergoing LPN for differences in renal function and oncologic outcomes (Table 2). The mean operative times, ischemia times, and EBL were significantly lower for LPN compared with OPN; however, there was no statistical difference in complication rates. LPN patients classified by the Clavien system demonstrated six patients (grade I),

TABLE 1. PARTIAL NEPHRECTOMY *VERSUS* ABLATION: CLINICAL, SURGICAL, AND PATHOLOGIC OUTCOMES

Variable	Ablation	Partial nephrectomy	P value
# patients	98	100	
# procedures	105	100	–
Mean age (years) (range)	64 (38–86)	64 (35–92)	0.85
Mean tumor size (cm) (range)	2.5(1–4.4)	3.9 (1–10)	<0.001
Mean preoperative creatinine (mg/dL)	1.4	1.4	0.65
Side: # (%)			
Left	48 (46)	42 (42)	0.39
Right	50 (48)	56 (56)	
Unknown	7 (6)	–	
Mean operative time (min)(range)	155 (69–300)	169 (68–270)	0.10
Median EBL (mL)(range)	50 (5–400)	400 (25–3900)	<0.001
Pathology: # (%)			
Clear-cell	51 (49)	70 (70)	
Papillary	5 (4.7)	18 (18)	
Chromophobe	–	6 (6)	
Oncocytoma	13 (12)	3 (3)	–
AML	6 (5.7)	3 (3)	
Nondiagnostic	8 (7.6)	–	
No biopsy	22 (21)	–	
Mean length of stay (days)(range)	1.7 (1–8)	4.1 (1–21)	<0.001
# Intraoperative complications (%)	1 (1)	6 (6)	0.16
# Postoperative complications (%)	9 (8.6)	18 (18)	0.05
Mean follow-up (months)	31	24	0.04
# Tumor persistence	3 (2.9)	0	0.25
# Local recurrences (%)	7 (6.7)	3 (3)	0.04
# Metastasis	2 (1.9)	1 (1)	0.33
# Deaths (%)	0 (0)	1 (1)	0.50

EBL=estimated blood loss; AML=acute myeloid leukemia.

TABLE 2. OPEN PARTIAL NEPHRECTOMY *VERSUS* LAPAROSCOPIC PARTIAL NEPHRECTOMY: CLINICAL, SURGICAL, AND PATHOLOGIC OUTCOMES

Variable	OPN	LPN	P value
Number	50	50	–
Mean tumor size (cm) (range)	4.3 (1.6–10)	3.6 (1–9.2)	0.13
Mean preoperative creatinine (mg/dL)	1.4	1.4	0.52
Side: # (%)			
Left	21 (42)	21 (42)	0.86
Right	27 (54)	29 (58)	
Cold ischemia:			
No	18 (36)	50 (100)	–
Yes	32 (64)	–	
Mean ischemia time (min)(range)	35 (0–91)	22 (0–40)	<0.001
Mean operative time (min)(range)	190 (68–270)	152 (91–268)	0.001
Median EBL (mL)(range)	250 (75–3000)	175 (25–3900)	0.01
Pathology: # (%)			
Clear-cell	40 (80)	30 (60)	
Papillary	7 (14)	11 (22)	
Chromophobe	3 (6)	4 (8)	0.07
Oncocytoma	–	3 (6)	
AML	–	2 (4)	
# positive margins (%)	8 (16)	1 (2)	0.01
# Intraoperative complications (%)	4 (8)	2 (4)	0.68
# Postoperative complications (%)	8 (16)	10 (20)	0.80
Mean follow-up (months)	23	25	0.59
# Local recurrences (%)	3 (6)	0	0.24
# Metastasis	0	1 (2)	1.0

OPN=open partial nephrectomy; LPN=laparoscopic partial nephrectomy; EBL=estimated blood loss; AML=acute myeloid leukemia.

TABLE 3. CLAVIEN-DINDO COMPLICATION CATEGORY AND EXPLANATION COMPLICATIONS  $\geq$  IIIA AND IIIB

Clavien-Dindo classification	Ablation (# complications)	Partial nephrectomy (# complications)
IIIA	Hypervolemia/congestive heart failure requiring radiologic intervention (1)	None
IIIB	Urine leak requiring ureteral stent (2)	Open conversion (1) Clot retention with irrigation (1) Urine leak requiring ureteral stent (4)

two patients (grade II), and two patients (grade IIIB). OPN patients had four patients with grade I, two patients with grade II, and two patients with grade IIIB (Table 3).

There was no statistically significant difference in the eGFR preoperatively or postoperatively when comparing PN and ablation (Table 4). Similarly, there was no significant difference when comparing OPN *vs* LPN (Table 5). We evaluated all patients with a preoperative eGFR greater than 60 mL/min/1.73 m<sup>2</sup> in whom a drop below 60 mL/min/1.73 m<sup>2</sup> developed after treatment of their renal mass. Twenty-three percent (19/84) patients fell below 60 mL/min/1.73 m<sup>2</sup> after 3 months and 18% after 12 months. Next, differences in eGFR were determined based on tumor size. In patients who underwent ablation, 32% who had a tumor size of <4 cm decreased to an eGFR below 60 mL/min/1.73 m<sup>2</sup>. In patients with a tumor size  $\geq$  4 cm, 50% fell below this level ( $P=0.60$ ). In PN patients, 27% with a tumor <4 cm and 36% with a tumor  $\geq$  4 cm dropped below 60 mL/min/1.73 m<sup>2</sup> ( $P=0.60$ ).

Two (1%) patients with initial end-stage renal disease (preoperative eGFR of <15 mL/min/1.73 m<sup>2</sup>) underwent nephron-sparing surgery. There was only one patient with a preoperative eGFR >15 mL/min/1.73 m<sup>2</sup> who dropped below this level to be considered end stage (preoperative eGFR of 16 dropped to 7.85 mL/min/1.73 m<sup>2</sup> after OPN).

Renal function after extirpative and ablative therapies was compared after stratifying by acquired *vs* congenital solitary kidneys. In both the ablation and PN groups, there was no statistically significant difference in eGFR between congenital and acquired solitary kidneys ( $P=0.31$  and  $P=0.26$ ).

## Discussion

Patients with a renal mass in a solitary kidney represent an imperative need for a nephron-sparing procedure. Consequences of nephron loss include reduced renal function and

a decrease in a patient's overall health. Go and colleagues<sup>2</sup> demonstrated that a decrease in GFR independently predicted for an increase in hospitalization, cardiovascular related events, and mortality.

Nephron-sparing surgery performed in a solitary kidney represents an excellent model for accurately assessing changes in renal function. Historically, patients with solitary kidneys have been able to maintain renal function after nephron-sparing procedures. Fergany and colleagues<sup>3</sup> reported on 400 solitary kidney patients with a renal mass treated with OPN. After a mean follow-up of 44 months, function was preserved without the need for dialysis in 95.5% of patients. OPN is the primary NSS option performed for patients with a solitary kidney; however, minimally invasive techniques, such as LPN, cryoablation, and RFA, have been implemented as well. Turna and coworkers<sup>4</sup> presented outcomes after minimally invasive therapy in a cohort of 101 patients with a solitary kidney. Patients underwent LPN, LCA, or percutaneous RFA. eGFR at 6 months revealed that function decreased in 89%, 72.2%, and 55.2% with LPN, LCA, and percutaneous RFA, respectively. Preoperative eGFR and procedure type were significant independent predictors of decreased renal function. Two (5.6%) patients remained on permanent dialysis after LPN, while no patients in the LCA or RFA groups needed dialysis.<sup>4</sup>

Renal ischemia is a known factor leading to the cellular degeneration of nephrons and a decrease in overall renal function after PN. La Rochelle and coworkers<sup>5</sup> followed 84 patients who underwent OPN in a solitary kidney. Patients either were exposed to no ischemia, warm ischemia, or cold ischemia. Although the immediate eGFR decrease in patients without clamping was lower than with either type of ischemia ( $P<0.001$ ), eGFR 1 month later was not significantly different between the three groups ( $P=0.17$ ). A multi-institutional

TABLE 4. POSTOPERATIVE SERUM CREATININE, % CHANGE IN POSTOPERATIVE SERUM CREATININE, AND ESTIMATED GLOMERULAR FILTRATION RATE (ABLATION *VERSUS* PARTIAL NEPHRECTOMY)

Time	Ablation	Partial nephrectomy	P value
	Estimated GFR (mL/min/1.73 m <sup>2</sup> )	Estimated GFR (mL/min/1.73 m <sup>2</sup> )	
Preoperative	59	59	0.91
3 months	52	53	0.76
12 months	51	52	0.78

Calculated using Mean Modification of Diet in Renal Disease equation.

GFR=glomerular filtration rate.

TABLE 5. POSTOPERATIVE SERUM CREATININE, % CHANGE IN POSTOPERATIVE SERUM CREATININE, AND ESTIMATED GLOMERULAR FILTRATION RATE (OPEN *VERSUS* LAPAROSCOPIC PARTIAL NEPHRECTOMY)

Time	Open partial nephrectomy	Laparoscopic partial nephrectomy	P value
	Estimated GFR (mL/min/1.73 m <sup>2</sup> )	Estimated GFR (mL/min/1.73 m <sup>2</sup> )	
Pre-operative	57	60	0.56
3 months	50	54	0.50
12 months	50	52	0.65

Calculated using Mean Modification of Diet in Renal Disease equation.

GFR=glomerular filtration rate.



study observed factors predicting renal function after OPN in a solitary kidney under both cold and warm ischemia. Warm ischemia was performed in 360 cases and cold ischemia in 300 cases with a mean follow-up of 2.6 years. Three months after OPN, the median eGFR decreased by a similar rate in both groups (cold 21% and warm 2%,  $P=0.7$ ). On multivariable analysis, the strongest independent predictors of renal function were preoperative eGFR and the estimated percentage of parenchyma spared ( $P=0.00001$ ). Percentage of parenchyma spared, however, was only subjectively assessed during surgery. The type and duration of ischemia were not statistically significant predictors of postoperative eGFR.<sup>6</sup>

Ablative procedures are associated with lower complication rates and higher recurrence rates relative to extirpative procedures.<sup>7</sup> Kunkle and colleagues<sup>8</sup> reported recurrence rates in 1375 tumors treated with either cryoablation (5.2%) or RFA (12.9%).<sup>8</sup> In the current study, ablation procedures also had a significantly higher local recurrence rate compared with PN (6.7% *vs* 3%,  $P=0.04$ ). In this study, patients undergoing PN had larger and possibly more complex tumors. This provides additional evidence that PN seems to have an advantage over ablation in terms of recurrence rates. It should be stated, however, that the current study was not sufficiently powered to make definitive conclusions about recurrence-free survival or disease-specific survival.

Patients undergoing LPN had significantly shorter ischemia times, operative times, and less blood loss compared with OPN patients. In addition, patients also had a lower positive margin rate and recurrence rate compared with OPN. While LPN is a reasonable treatment approach in patients with a solitary kidney, these findings are likely a function of patient selection. Patients undergoing OPN may have had tumors that were more complex (endophytic or hilar). Data to stratify tumors by complexity were not available for analysis.

Previous data have associated LPN with a higher complication rate compared with OPN.<sup>9,10</sup> In the current study, there were no differences in complication rates between OPN and LPN ( $P=1.0$ ). Case selection may contribute to these results; however, this study is limited in that it did not analyze or stratify tumors by complexity.

We found no significant change in eGFR from preoperative values to those obtained 3 and 12 months after either PN or ablation. We did notice, however, a significantly lower postoperative day 1 serum creatinine level in ablation *vs* PN ( $P=0.0002$ ) and in LPN *vs* OPN ( $P=0.005$ ). There are several factors that may contribute to this transient change, such as the method of hilar clamping, patient hydration, diuretic administration, and anesthesia effects. There was no long-term difference in either serum creatinine level or eGFR, however. There were 9.6% of patients who had a congenital solitary kidney (4.1% ablation, 15% LPN). We hypothesized that congenital solitary kidneys would be larger and more robust compared with solitary kidneys that are acquired, and therefore these patients would have a higher renal reserve before surgery and have less damage to their kidney postoperatively. Because of the limited number of patients, however, we are unable to establish any definitive conclusions regarding this group of patients.

Limitations include a nonrandomized retrospective design and variability with how procedures were performed depending on institution. There was no standardization with surgical technique, ablation protocols (equipment, number of treatment probes, and duration of ablation), type of hilar

clamping, or definition of operative time. We did not quantify tumor complexity with a standardized system (such as R.E.N.A.L. [radius; exophytic/endophytic; nearness; anterior/posterior; location] nephrometry score) nor did we have a system for determining the volume or percent of renal parenchyma that was spared after PN or ablation. This would have provided value in determining how patients were selected for treatment. Patients undergoing ablation had significantly smaller tumors compared with those who underwent PN, and follow-up for both the PN and ablation cohorts was relatively short.

Local recurrence was defined as tumor bed enhancement after cross-sectional imaging with intravenous contrast in patients who had previously had an unenhanced tumor bed. This designation may have artificially inflated the number of recurrences because none of these patients underwent a post-treatment biopsy. In addition, the exact date of the tumor recurrences is not known; therefore, we are unable to identify at what point recurrences occurred. Lastly, we were unable to make any substantial conclusions regarding differences in function between congenital and acquired solitary kidneys because of the small number in each group ( $n=19$ ).

## Conclusions

For patients with a solitary kidney, PN and ablation are both reasonable treatment options. Postoperative renal function appears to be similar for either surgical or ablative treatment based on eGFR and is not affected by surgical approach to PN (OPN *vs* LPN). Ablative therapy may offer improved short-term benefits; however, our data demonstrated that recurrence rates were higher with ablation compared with PN. LPN demonstrated shorter ischemia times compared with OPN and exhibited no significant change in complication or recurrence rates.

## Disclosure Statement

No competing financial interests exist.

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Address correspondence to:

*Jaime Landman, M.D.*  
*Department of Urology*  
*University of California, Irvine*  
*333 City Blvd. West, Suite 2100*  
*Orange, CA 92868*

*E-mail: landmanj@uci.edu*

#### **Abbreviations Used**

CT = computed tomography  
EBL = estimated blood loss  
eGFR = estimated glomerular filtration rate  
LCA = laparoscopic cryoablation  
LOS = length of stay  
LPN = laparoscopic partial nephrectomy  
LRN = laparoscopic radical nephrectomy  
MRI = magnetic resonance imaging  
OPN = open partial nephrectomy  
PCA = percutaneous cryoablation  
PN = partial nephrectomy  
RCN = renal cortical neoplasm  
RFA = radiofrequency ablation