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ORIGINAL ARTICLE

Renal function and oncologic outcomes in nephron sparing surgery for renal masses in solitary kidneys

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Abstract
Introduction With low life expectancy rates in hemodialysis patients, the preservation of renal parenchyma must be weighed against the oncological outcomes in considering partial nephrectomy (PN) in solitary kidneys. The main objective of this study was to assess the oncologic and functional outcomes after PN in patients with solitary kidneys.
Methods A retrospective analysis of the Columbia University Medical Center Urologic Oncology database found 38 patients who underwent PN in the setting of a solitary kidney from 1988–2008. Chronic kidney disease (CKD) was defined as GFR of <60 cc/min/1.73 m^2. Kaplan–Meier analysis was used to estimate overall survival, cancer-specific survival, and local recurrence-free survival.
Results The study group was followed for a median of 29 months, with a mean age of 63.2 years (range 35–83). Only one patient required postoperative long-term hemodialysis. Two out of 38 patients had a Clavien III postoperative complication. Twenty-one (55.3%) of the patients had preoperative CKD, while 29 (76%) patients had CKD postoperatively. Those who had CKD at the most recent follow-up had significantly larger tumors removed ($P < 0.05$). Of the 32 patients with renal cell carcinoma (RCC), 6 (18.8%) had a local recurrence at a median 32.6 months. The 5-year overall, disease-specific, and recurrence-free survival rates were 59.6, 77.5, and 45.7%, respectively.
Conclusion PN in the setting of a solitary kidney poses difficult challenges for surgical and clinical management. Nephron sparing surgery for the treatment of RCC is feasible with low surgical complication rates, satisfactory disease-specific survival rates, and acceptable preservation of renal function.

Keywords Solitary kidney · Nephron sparing surgery · Partial nephrectomy · Glomerular filtration rate

Introduction

Nephron sparing surgery (NSS) is important in those who need to optimize postoperative renal function, such as those with underlying renal disease or those with tumors in a solitary kidney. In a study of over a million subjects, Go et al. [1] found that decreased GFR was independently predictive of mortality. In patients with solitary kidneys, preservation of renal parenchyma becomes even more important as 5-year survival rates on hemodialysis are 35%, and life expectancy is decreased fourfold compared to healthy subjects [2].

Laparoscopic techniques, cryotherapy and radio frequency ablation can be safely done in select patients with renal masses in solitary kidneys [3, 4]. However, open partial nephrectomies is considered the reference standard, and may be the appropriate treatment in complex surgical patients or those with a prior history of treatment on the solitary kidney, which can make the procedure technically demanding [5, 6]. Characterizing the factors that influence the functional and oncological outcome of NSS in patients who have a solitary kidney has therefore become increasingly important.

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Methods

The Institutional Review Board approved Columbia University Urologic Oncology Database was retrospectively reviewed. Between 1988 and 2009, 1,327 consecutive patients underwent renal surgery for the treatment of renal cell carcinoma (RCC), 546 of which were partial nephrectomies (PN). Of those, 38 patients underwent a PN in a functional or anatomically solitary kidney. All procedures were done open and not laparoscopically. Patients who had cryoablation of the current renal mass were excluded. Comorbidity was measured using the Charlson comorbidity index [7], and 30-day postoperative complications were categorized using the Clavien system [8].

Sterile ice-slush was placed around the kidney for superficial hypothermia for all patients for 10–15 min immediately after occluding the renal artery [9, 10]; 7-French Jackson-Pratt drains or Penrose drains were placed at the discretion of the attending surgeon and discontinued when the output was clinically satisfactory.

Estimated GFR was calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) equation: [11] GFR in ml/min/1.73 per $m^2 = 186.3 \times$ serum creatinine$^{-1.154} \times$ age$^{-0.203} \times 1.212$ (if the patient is black) $\times$ 0.742 (if the patient is female). The immediately postoperative GFR was calculated from measurements of sCr within 24 h postoperatively, while the long-term postoperative GFR was calculated at the most recent follow-up visit. Chronic kidney disease (CKD) was defined as a GFR < 60 ml/min/1.73 m^2 [12]. End stage renal disease (ESRD) was defined as GFR <15 ml/min/1.73 m^2 or any dialysis occurring more than 30 days after PN.

Kaplan–Meier analysis was used to estimate overall survival, cancer-specific survival, and recurrence-free survival. All *P*-values are two-sided, and *P*-value <0.05 was considered significant. All statistical analyses were performed using Stata SE, version 8.0.

Results

Table 1 demonstrates the clinical, surgical, and pathological data. Overall, the median follow-up time was 29.0 months (range 1–168), and 8 (18.9%) were followed for more than 5 years. The median total cold ischemia time was 32 min (range 18–55). Two patients had Clavien grade III complications; no patient required immediate postoperative hemodialysis. One patient (2.6%) required permanent long-term hemodialysis beginning 6 weeks postoperatively, but no other patient required hemodialysis to the last known follow-up.

Nine patients (23.7%) had prior open partial nephrectomies on the solitary kidney. Seven patients had one prior PN, and two patients had three prior PN on the solitary kidney. Those who had a prior partial nephrectomy on the solitary kidney did not differ significantly in total cold

Table 1 Clinical, surgical, and pathological data regarding patients undergoing PN in a solitary kidney

Variables	
Clinical	
Patient age, median (range)	64 (35–83)
Males, *N* (%)	29 (76.3%)
BMI, median (range)	26.2 (23–38.6)
Charlson Comorbidity Index, *N* (%)	
0–1	9 (23.7%)
2	11 (29%)
3	11 (29%)
≥4	7 (18.3%)
Reason for solitary kidney, *N* (%)	
Contralateral radical nephrectomy	
Due to renal mass	29 (70.7%)
Due to benign causes	5 (12.2%)
Functional solitary kidney	2 (4.9%)
Congenital solitary kidney	2 (4.9%)
Surgical	
Intraoperative transfusion, *N* (%)	5 (13.9%)
Length of hospital stay, median (range)	6 (3–17)
Total Cold Ischemia Time, min median (range)	32 (18–55)
Clavien 30 day postoperative complication class, *N* (%)	
I	3/38 (7.9%)
II	7/38 (18.4%)
III	2/38 (5.3%)
Pathological	
Histology	
RCC	
Clear cell	27 (71.1%)
Papillary	4 (10.5%)
Unclassified	1 (2.6%)
Oncocytoma	3 (7.9%)
Sarcoma	1 (2.6%)
Transitional cell carcinoma	2 (5.2%)
Tumor size	
<4 cm	22 (57.9%)
>4 cm	16 (42.1%)
Grade (total RCC: 32)	
1	3/32 (9.4%)
2	18/32 (56.2%)
3	11/32 (34.4%)
T stage (total RCC: 32)	
pT1a	15/32 (46.9%)
pT1b	5/32 (15.6%)
pT2	2/32 (6.3%)
pT3a	8/32 (25%)
pT3b	2/32 (6.3%)
Surgical margin	
Negative	26/32 (81.2%)
Positive	6/32 (18.8%)

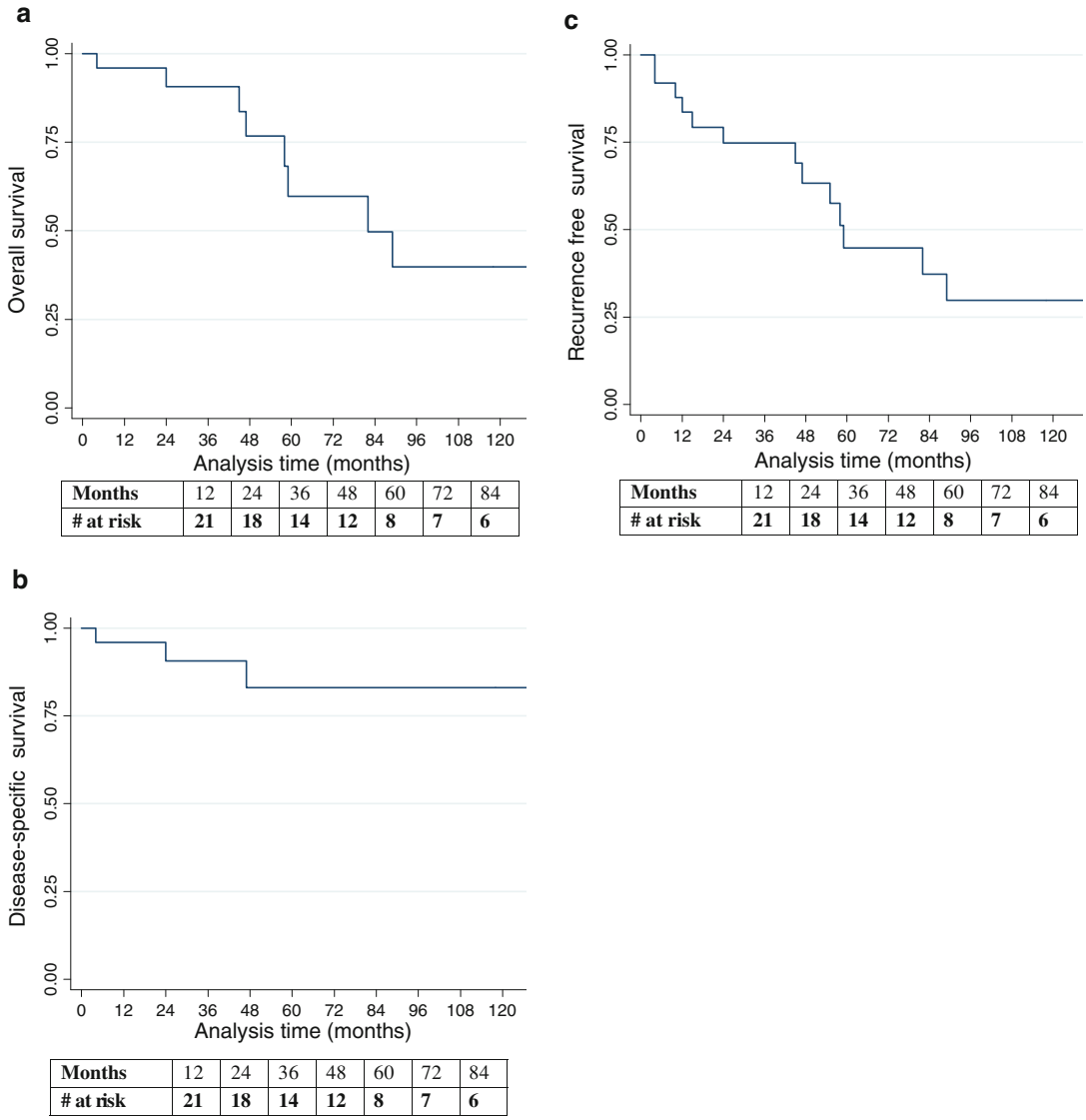

Fig. 1 Kaplan–Meier estimates of overall survival (**a**), disease-specific survival (**b**), and recurrence-free survival (**c**)

Table 2 Characteristics according to preoperative and long-term postoperative GFR

Variable	Preoperative GFR < 60	Preoperative GFR > 60	*P*-value	Postoperative GFR < 60	Postoperative GFR > 60	*P*-value
Number	21	17		29	9	
Mean age	65.3 ± 10.5	60.5 ± 12.0	0.19	63.1 ± 11.6	63.2 ± 11.1	0.51
Charlson comorbidity index			0.04			0.46
0–1	3 (14.3%)	6 (35.3%)		8 (27.6%)	1 (11.1%)	
2	5 (23.8%)	6 (35.3%)		6 (20.7%)	5 (55.6%)	
≥3	13 (61.9%)	5 (29.4%)		15 (51.7%)	3 (33.3%)	
Clavien complication class			0.23			0.74
I	3 (33.3%)	0		3 (27.3%)	0	
II	4 (44.4%)	3 (100%)		6 (54.5%)	1 (100%)	
III	2 (22.2%)	0		2 (18.2%)	0	
Mean diameter of tumor (cm)	4.2	3.7	0.28	4.4	2.7	0.02
Mean total cold ischemia time (min)	31.7	35.1	0.70	33.5	25	0.52

Table 3 Characteristics according to history of prior partial nephrectomy on the solitary kidney

Variable	No prior surgery	Prior surgery	*P*-value
Number	29	9	
Age, mean	63.1 ± 10.8	63.2 ± 13.5	0.51
Preoperative GFR, mean	56.5	46.8	0.08
Immediately postoperative GFR, mean	46.5	43.4	0.34
Long-term postoperative GFR, mean	45.7	41.1	0.30
GFR > 30 at last follow-up			
Yes	22 (24.1%)	7 (77.8%)	0.64
No	7 (75.9%)	2 (22.2%)	

ischemia time ($P = 0.26$), the rate of postoperative complications ($P = 0.30$), or length of hospital stay (7 vs. 5 days, respectively $P = 0.28$) compared to those with a surgically naïve kidney. There was one Clavien grade III postoperative complication and three Clavien grade II complications. No patient required hemodialysis at any point postoperatively.

The median tumor size was 3.25 cm (range 0.9–11 cm). Thirty-two patients had RCC, and 4 (12.5%) of the 32 patients with RCC had multiple renal masses that were taken out at the same time of surgery; the number of masses removed ranged from 1 to 4, and ranged in size from 0.7 to 3.7 cm. Three of these four were clear cell RCC, and the remaining one was papillary RCC.

Of the 32 patients with RCC, 2 (6.3%) patients had prior metastatic disease that was treated with sunitinib and radiation therapy and are excluded for the oncologic outcomes and survival analyses. Five of the 30 patients (16.7%) had a positive surgical margin, 2 patients had T3 disease, and one had multiple renal masses. Two out of five patients with positive surgical margins developed local recurrence compared to four out of 25 patients (15.6%) with negative margins; however, the difference was not significant ($P = 0.25$). Of the four patients with multiple renal masses, three of them had a local recurrence. In total, six of the 30 (20.0%) were observed to have a local recurrence at a median 32.0 months (range 7.1–62.4 months).

At the time of review, 8/30 (26.7%) patients had died, 3 from progression of RCC. The estimated overall survival rates at 1 year and 5 years were 96.0 and 59.7%, respectively (Fig. 1a). The disease-specific survival rates at 1 year and 5 years were 97.0 and 83.1% (Fig. 1b), respectively, while the recurrence-free survival rates were 83.6 and 44.8% at 1 year and 5 years, respectively (Fig. 1c). The overall survival rates did not differ significantly between those who had and did not have prior surgery on the solitary kidney ($P = 0.53$), and did not differ between those with a GFR < 60 and GFR ≥ 60 preoperatively ($P = 0.85$) or postoperatively ($P = 0.46$).

Table 2 describes the characteristics of patients according to the preoperative GFR and long-term postoperative GFR measured at the most recent follow-up. Median preoperative GFR was 58.0, with 4 patients (10.5%) having a preoperative GFR < 30. Those who had a preoperative GFR < 60 had more comorbidities ($P = 0.04$), while those who had a long-term GFR < 60 at the most recent follow-up had significantly larger tumors ($P = 0.02$).

The median GFR immediately postoperatively was 42 (range 16–101), a 13.1% median decrease from the preoperative GFR. The median GFR at the most recent follow-up was 43.0 (range 5.4–89.5) at a median time of 12.5 months postoperatively, which represents a mean percent decrease from the preoperative GFR of 14.8%. Of the 17 patients who had preoperative GFR ≥ 60 and the 34 patients with a preoperative GFR ≥ 30, 9 (52.9%) and 29 (85.3%) maintained a GFR above those cutoffs after NSS, respectively.

Table 3 describes the characteristics of those who had prior surgery on the solitary kidney against those with surgically naïve solitary kidneys. There were no significant differences between those with surgically naïve solitary kidneys compared to those who had repeat PN in GFR immediately after surgery (46.5 vs. 43.4, respectively, $P = 0.34$) or at the most recent follow-up period (45.7 vs. 41.1, respectively, $P = 0.30$). Likewise, the percentage of people who had a GFR > 30 at the most recent follow-up period did not differ significantly between the surgically naïve and repeat PN groups (75.9 vs. 77.8%, respectively, $P = 0.64$).

Discussion

Renal masses in a solitary kidney pose unique challenges in management, as the surgical and oncological risks of renal preservation with NSS must be weighed against the morbidity and mortality associated with hemodialysis and renal transplantation if the patient is left anephric.

Long-term renal function and peri-operative safety are especially important considerations in patients with solitary kidneys who have had prior procedures performed on the solitary kidney. In a study of 25 patients who underwent repeat open partial nephrectomies, Liu and colleagues [5] reported a complication rate of almost 50%, with 88% of patients avoiding dialysis and a minimal change in GFR at 1 year postoperatively. In this cohort, only one patient had a Clavien grade III complication, no patient developed acute renal failure, and no patients required hemodialysis at any point, which is comparable to prior published reports of complication rates with repeat NSS for renal masses in solitary kidneys [5, 13] and NSS for surgically naïve solitary kidneys [14–17]. None of the nine patients in this cohort who had prior partial nephrectomies on the solitary kidneys required hemodialysis at any time postoperatively, and there was a minimal decrease in the GFR (10%) postoperatively. These results support the findings by Liu et al. [5] that repeat partial nephrectomies in solitary kidneys can be performed safely with adequate long-term renal function.

Long-term renal function is essential in patients with a solitary kidney. Go et al. [1] found that patients with a GFR 15–30 and a GFR < 15 were 3.2 and 5.9 times as likely to die of any cause than those with GFR > 60. In the study cohort, the majority of patients with a mass in a solitary kidney presented with CKD at baseline. However, 90% of the patients were able to avoid ESRD at a median follow-up time of 29.0 months, and only one patient required any postoperative hemodialysis. The United States Renal Data System found that avoidance of hemodialysis is extremely important; the 5-year survival rate is only 35% for patients on hemodialysis [2]. The low hemodialysis rate in this study is consistent with the rates after NSS on a solitary kidney in other series [14, 16–18], showing that sufficient renal preservation is possible and may help improve the prognosis of patients.

Oncologic safety is a primary consideration in NSS on a solitary kidney. In this series, the overall survival rate at 5 years was 60% and the 5-year disease-specific survival rate was 83%, with those having higher stage disease having significantly lower survival rates. The 5-year survival rate in this series is almost twice that of those on hemodialysis (35%) and those with ESRD (39%) [2]. Other published series [14–17] report overall 5-year survival rates ranging from 75 to 87% and 5-year disease-specific survival rates ranging from 81 to 90%, showing that NSS in a solitary kidney has a favorable survival advantage compared to leaving the patient on hemodialysis. The disease-specific survival in this cohort is comparable to other series, even with a higher proportion of T3 disease (29%) and grade 3 disease (34%) [14, 15]. The relatively higher rate of positive surgical margins compared to other reported studies [14, 15] may also be due to the presence of higher-risk disease. Routine frozen sections were performed to ensure negative margins. Although those with positive margins had higher rates of local recurrence, the total number of patients (five, excluding the two with prior metastases) is too small to make any conclusions or correlations. The decreased overall survival may also be due to a higher rate of comorbidities in this cohort, as almost a fifth of the cohort had CACI scores ≥ 4; a score of 4 is associated with a 4.4 elevated risk of death compared to those with a CACI score of zero [19].

There are several limitations to this study that warrant consideration. This study has the limitations of a retrospective design, with a relatively small number of patients. This may not allow for the detection of subtle relationships between preoperative status and postoperative GFR levels, and clinical factors with local recurrence and overall survival that may be present in larger cohorts. In addition, the recruitment period of 21 years with changing surgical techniques and multiple surgeons may introduce an additional bias to the study.

Conclusions

NSS in the setting of a solitary kidney poses difficult challenges in clinical as well as surgical management. Nephron sparing surgery for the treatment of renal mass in solitary kidneys is feasible with low surgical complication rates, and acceptable renal function outcome. There is a low likelihood of requiring temporary or permanent hemodialysis, and the long-term disease-specific and recurrence-free survival rates are acceptable. These outcomes compare favorably with the outcomes associated with the morbidity and mortality rates of rendering the patient anephric by radical nephrectomy and subsequent hemodialysis. We feel that NSS in the setting of solitary kidneys affords the patient the best probability of mitigating the risks of long-term renal dysfunction without significantly compromising oncologic outcomes.

Conflict of interest statements The authors declare that they have no conflict of interest.

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