Oncological Outcomes of Partial Nephrectomy for Multifocal Renal Cell Carcinoma Greater Than 4 cm

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Purpose: Despite aggressive screening patients with hereditary renal cancers can present with large multifocal tumors. We present oncological outcomes in patients with hereditary renal cell carcinoma treated with partial nephrectomy for multifocal solid tumors with the largest lesion greater than 4 cm.

Materials and Methods: Between 1995 and 2008 we identified 58 patients with hereditary renal cell carcinoma treated at our institution with partial nephrectomy for solid tumors greater than 4 cm. Data collected included demographic parameters, tumor size, pathological findings and laterality. Overall and metastasis-free survival was calculated based on information from the most recent followup evaluation and imaging.

Results: The cohort included 41 patients (71%) with von Hippel-Lindau disease, 10 (17%) with Birt-Hogg-Dubé syndrome and 7 (11%) with hereditary papillary renal carcinoma. Mean age was 43.7 years (range 18 to 63) and mean largest tumor size was 5.3 cm (range 4 to 13). A mean of 6.4 kidney tumors (range 1 to 44) was resected. There was a predominance of nuclear grade 2 tumors (51 cases or 85%) and clear cell histology (44 or 73%), followed by papillary type I histology (7 or 11.7%). Overall and metastasis-free survival rates were 93% and 96.5%, respectively, at a median followup of 45 months (range 2 to 163).

Conclusions: Metastasis-free and overall survival of our patients is similar to that in the literature of those who undergo partial nephrectomy for T1B tumors in the sporadic population. Multifocality does not affect oncological outcomes at intermediate followup. Partial nephrectomy can be offered to patients with hereditary disease who present with multifocal tumors greater than 4 cm.

Key Words: kidney; carcinoma, renal cell; neoplastic syndromes, hereditary; nephrectomy; mortality

Abbreviations and Acronyms

BHD = Birt-Hogg-Dubé

CT = computerized tomography

HPRC = hereditary papillary renal carcinoma

NSS = nephron sparing surgery

RCC = renal cell carcinoma

VHL = von Hippel-Lindau

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MANAGEMENT of RCC is challenging in patients with multifocal renal tumors and hereditary syndromes who are predisposed to RCC formation. These patients are predisposed to synchronous bilateral, multifocal tumors in the kidneys at an early age and most manifest recurrence or de novo tumor formation even after aggressive partial nephrectomy.[1–3] To avoid the surgical morbidity of repeat renal intervention and decrease the likelihood of metastatic disease an approach was developed in this patient population to recommend surgical removal of renal tumors with partial nephrectomy when the largest tumor becomes 3 cm.[4,5] However, despite aggressive screening some of these patients present with larger tumors due to delayed diagnosis or comorbidity.

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While recent data demonstrate that partial nephrectomy for T1b tumors is oncologically equivalent to radical nephrectomy and may even confer a survival benefit in the sporadic population, to our knowledge there are no studies evaluating the oncological outcome of clinical T1b renal masses in the presence of multifocal disease.[6–9]

Our ongoing clinical experience and aggressive nephron sparing approach in patients with multifocal and hereditary kidney cancer have provided a unique opportunity to evaluate the oncological outcomes of partial nephrectomy in patients with clinical T1b or greater RCC in the presence of multifocal disease.

MATERIALS AND METHODS

Between 1995 and 2008, 60 planned partial nephrectomies were done at our institution in a total of 58 patients who presented with multifocal renal masses with the largest solid renal tumors greater than 4 cm. All patients were evaluated on a National Cancer Institute institutional review board approved protocol. All patients had known germline mutations of *VHL*, *BHD* or *Met* genes, leading to the clinical diagnosis of VHL disease, BHD syndrome or HPRC, respectively. Data analyzed included demographics, hospital admission history, physical examination, operative reports, discharge summaries, progress notes, records of all subsequent operative interventions and the most recent imaging. Pathology reports were reviewed for the number of tumors resected, pathological stage, and highest grade and histology of the largest tumor removed.

All patients underwent preoperative evaluation with computerized tomography of the chest and CT or magnetic resonance imaging of the abdomen and pelvis. No case was preoperatively or intraoperatively suspicious for locally advanced or metastatic disease. Regardless of tumor size and multifocality all planned NSS was successful in all patients.

All patients were followed at regular intervals after surgery starting 3 months after the procedure and at least once yearly after visit 1. Each visit included clinical and laboratory examination with complete blood count, routine chemistry studies, liver function tests, and imaging with CT of the chest and contrast enhanced CT or magnetic resonance imaging of the abdomen and pelvis.

Oncological outcomes were evaluated by overall, cancer specific and metastasis-free survival, and the need for subsequent surgical intervention on the operated renal unit. Overall survival was determined by chart review and telephone contact with death from any cause verified using the Social Security Death Index. Cancer specific and metastasis-free survival was attributed to patients with documented evidence of cancer progression as the cause of death. Survival data were obtained on the entire cohort and no patient was lost to followup. The probability of overall and cancer specific survival was determined using the Kaplan-Meier method.

RESULTS

A total of 60 operations (60 kidneys) were performed in 58 patients, including 22 men (38%) and 36 women (62%). Two patients who presented with T1b tumors bilaterally underwent staged bilateral partial nephrectomy. Eight patients underwent prior partial nephrectomy of the ipsilateral kidney while 20 underwent prior partial nephrectomy of the contralateral kidney. No prior or subsequent intervention was done for tumors larger than 4 cm. Mean age was 43.7 years (range 18.5 to 63.3). Of the patients 41 (71%) had VHL disease, 10 (17%) had BHD syndrome and 7 (12%) had HPRC. Tumors were on the right side in 35 cases (58%) and on the left side in 25 (42%).

Table 1 lists tumor pathological characteristics. Up to 44 tumors per patient were removed (mean 6.4, range 1 to 44). Largest mean tumor size was 5.3 cm (range 4.1 to 18). Of the surgeries 87% were done for pathological stage T1b and 73% of tumors were clear cell RCC. Fuhrman nuclear grade 2 was present in 85% of cases.

Median followup in the entire cohort was 45 months (range 2 to 163). The figure shows overall, cancer specific and metastasis-free survival of all 58 patients. The 5-year overall survival rate was 93.3%. Two patients (3.5%) died of nontumor related causes and 1 (1.7%) died of advanced metastatic disease. Five-year cancer specific and metastasis-free survival rates were 96.7% and 96.5%, respectively. Two of the 58 patients (3.4%) had distant metastasis. Table 2 lists details on patients with metastatic disease. Five patients (8.6%) required repeat intervention with open partial nephrectomy at a median time to re-intervention of 55 months (range 48 to 101). No patient underwent subsequent nephrectomy for any reason.

Table 1. *Tumor pathological characteristics*

	No. (%)
Largest tumor Fuhrman nuclear grade:	
1	3 (5)
2	51 (85)
3	6 (10)
RCC histological subtype:	
Clear cell	44 (73.3)
Papillary type 1	7 (11.7)
Chromophobe	5 (8.3)
Hybrid	3 (5)
Oncocytic	1 (1.7)
TNM stage:	
T1b	52 (87)
T2	8 (13)