

Surgical Management of Bilateral Synchronous Kidney Tumors: Functional and Oncological Outcomes

Matthew N. Simmons^{*,†} Ricardo Brandina[†] Adrian F. Hernandez[†] and Inderbir S. Gill[‡]

From the Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, Ohio (MNS, AFH), and USC Institute of Urology, Keck School of Medicine, University of Southern California, Los Angeles, California (RB, ISG)

Purpose: We evaluated renal functional and oncological outcomes after sequential partial nephrectomy and radical nephrectomy in patients with bilateral synchronous kidney tumors.

Materials and Methods: A total of 220 patients treated from June 1994 to July 2008 were included in the study. Estimated glomerular filtration rate, and overall, cancer specific and recurrence-free survival were assessed.

Results: Patients underwent sequential partial nephrectomy (134), partial nephrectomy followed by radical nephrectomy (60) or radical nephrectomy followed by partial nephrectomy (26). Final estimated glomerular filtration rate after bilateral surgery was 59, 36 and 35 ml/minute/1.73 m² in these 3 groups, respectively ($p < 0.001$). The order in which partial nephrectomy and radical nephrectomy were conducted did not affect functional outcomes. Overall survival of patients with bilateral cancer was 86% at 5 years and 71% at 10 years, cancer specific survival was 96% at 5 and 10 years, and recurrence-free survival was 73% at 5 years and 44% at 10 years. Overall survival was decreased in patients with tumors larger than 7 cm ($p = 0.003$). Patients with postoperative stage III or greater chronic kidney disease had decreased overall survival due to noncancer causes ($p = 0.007$).

Conclusions: Patients treated with sequential surgery for bilateral synchronous kidney tumors have 5 and 10-year oncological outcomes comparable to those of patients with unilateral kidney cancer. Decreased overall survival was significantly associated with tumor size larger than 7 cm and postoperative stage III or greater chronic kidney disease. Nephron sparing surgery should be conducted for all amenable bilateral kidney masses given the negative impact of renal functional decline on overall survival.

Key Words: carcinoma, renal cell; nephrectomy; treatment outcome; glomerular filtration rate

PATIENTS who present with localized sporadic synchronous bilateral kidney tumors pose a unique treatment challenge. Debate has centered on how to best treat these patients to achieve oncological control with maximal renal functional preservation. Surgical options include partial and/or radical nephrectomy, the planning for which

must include numerous variables including tumor size, stage, location and preoperative kidney function.¹

Currently there are limited intermediate and long-term oncological data in the literature pertaining to patients treated with sequential bilateral kidney surgery. Additionally there are minimal data to characterize the func-

Abbreviations and Acronyms

CKD = chronic kidney disease

CSS = cancer specific survival

CT = computerized tomography

eGFR = estimated glomerular filtration rate

GFR = glomerular filtration rate

OS = overall survival

PN = partial nephrectomy

RCC = renal cell carcinoma

RFS = recurrence-free survival

RN = radical nephrectomy

SCr = serum creatinine

WIT = warm ischemia time

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* Correspondence: Center for Urologic Oncology, Cleveland Clinic Glickman Urological and Kidney Institute, 9500 Euclid Ave. Q10-1, Cleveland, Ohio 44195 (telephone: 216-636-0066; FAX: 216-636-4492; e-mail: simmonm2@ccf.org).

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tional impact of bilateral kidney surgery and how functional outcomes are affected by tumor characteristics, procedure selection or patient risk factors. This report describes renal functional and oncological outcomes in a large contemporary cohort of patients with bilateral synchronous tumors who underwent sequential bilateral kidney surgery during a 14-year period from June 1994 to July 2008.

METHODS

This retrospective analysis was conducted using an institutional review board approved kidney tumor database at the Cleveland Clinic. Of 486 patients who underwent sequential bilateral kidney surgery between April 1994 and July 2008, 220 were selected for analysis. Study inclusion criteria were presence of bilateral synchronous kidney tumors at initial presentation, presence of contrast enhancement on CT in bilateral masses, sequential open, or laparoscopic radical or partial nephrectomy within a 6-month period, and preoperative eGFR 30 or greater ml/minute/1.73 m². Exclusion criteria were metachronous tumor presentation, presence of nodal or metastatic disease on CT, or diagnosis of von Hippel-Lindau disease or urothelial carcinoma.

Preoperative clinical evaluation consisted of physical examination, abdominopelvic CT and chest x-ray. Radiological tumor staging was conducted according to the 2002 TNM staging system.² The selection of open or laparoscopic radical or partial nephrectomy was based on patient factors (performance status, baseline kidney function, preference for laparoscopic surgical approach), tumor factors (stage, size, location), and surgeon expertise and preference. All surgical specimens were evaluated by staff pathologists with specialized training in genitourinary pathology.

Renal functional evaluation was conducted using serum creatinine values obtained immediately before initial surgery, immediately before second surgery, and 3 to 6 months after the second surgery. The Modification of Diet in Renal Disease 2 equation was used to calculate eGFR.³ CKD staging was conducted according to the National Kidney Foundation Disease Outcomes Quality Initiative Clinical Practice Guidelines.⁴ CKD stage was defined as stage I—90 or greater ml/minute/1.73 m², stage II—60 to 89 ml/minute/1.73 m², stage III—30 to 59 ml/minute/1.73 m², stage IV—15 to 29 ml/minute/1.73 m² and stage V—less than 15 ml/minute/1.73 m².

Oncological followup consisted of CT or magnetic resonance imaging and chest x-ray annually during the first 5 years after surgery, and every 2 years thereafter. All deaths were confirmed with primary family members via telephone interview or using the Social Security Death Index on-line database (<http://ssdi.rootsweb.com/>). End points for oncological analysis included overall, cancer specific and recurrence-free survival. CSS was defined as death primarily due to metastatic RCC. Recurrence was defined as radiologically verified local recurrence, or progression to nodal or metastatic disease during the study period.

All parametric data were expressed as means and standard deviations, and differences in means among patient groups at specific points were evaluated using the Kruskal-Wallis test and 1-way ANOVA. Trend analysis was conducted using the Jonckheere-Terpstra test. Kaplan-Meier analysis was conducted to calculate percent survival and freedom from outcomes at specific times. Differences in survival were compared using the log rank test with $p \leq 0.05$ considered significant for all analyses.

RESULTS

Table 1 summarizes demographic and operative data. Patients were grouped according to surgical management based on sequential PN (PN-PN, 134), PN followed by RN (PN-RN, 60) or RN followed by PN (RN-PN, 26). Age, body mass index and gender were similar among groups. Patients who underwent RN had higher Charlson Comorbidity Index scores ($p < 0.001$). In the PN-PN group the first surgery was conducted for the largest tumor in 63% of cases, and average tumor diameter was 4 cm for the first PN vs 3.5 cm for the second PN ($p = 0.89$). In the PN-RN and RN-PN groups the first surgery was conducted for the largest tumor in 82% and 92% of patients, respectively. Tumor size, tumor stage and WIT were equivalent for tumors treated with PN in all groups. RN average tumor diameter was larger in the RN-PN group vs the PN-RN group (10 vs 6.9 cm, $p = 0.5$). In the PN-PN group 79% of tumors were malignant vs 88% and 90% in the PN-RN and RN-PN groups, respectively ($p = 0.06$). Fuhrman grade was equivalent for all tumors treated with PN and was higher in tumors treated with RN.

Modification of Diet in Renal Disease 2 eGFR data are summarized in table 2. Patients were categorized based on largest tumor in the kidney treated with PN. RN kidney tumor size was not used for categorization because loss of the functional renal unit was independent of tumor size. Patients who underwent PN-PN exhibited a 29% decrease in eGFR, and PN-RN and RN-PN groups exhibited 51% and 53% decreases in eGFR, respectively. Figure 1 shows eGFR trends after surgery based on tumor size and preoperative CKD stage. Linear trendline analysis demonstrated that patients who underwent PN-PN had lower eGFR decreases in all groups. Trendlines for patients who underwent PN-RN and RN-PN were parallel in all groups suggesting equivalency of the eGFR decrease regardless of the order of PN or RN. Of the patients with preoperative CKD stage I to II (159) 14% had progression to postoperative stage IV or greater CKD. Patients with preoperative stage III CKD demonstrated eGFR decreases of 12%, 43% and 53% in the PN-PN, PN-RN and RN-PN groups, respectively, and 36% of these patients had progression to stage

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