Original Study

The Effect of Patient and Surgical Characteristics on Renal Function After Partial Nephrectomy

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Abstract

In this study we identified patient characteristics linked to adverse renal function outcomes after partial nephrectomy. We performed a retrospective study of 387 patients between 2006 and 2014 who underwent a partial nephrectomy at Memorial Sloan Kettering Cancer Center. In univariable analysis, we determined that advanced age at surgery, large tumor size, male sex, longer ischemia time, smoking and hypertension were linked to lower postoperative GFR. In multivariable analysis, advanced age, lower preoperative GFR and longer ischemia time were independent predictors of postoperative decline in renal function.

Background: The purpose of the study was to identify patient and disease characteristics that have an adverse effect on renal function after partial nephrectomy. **Patients and Methods:** We conducted a retrospective review of 387 patients who underwent partial nephrectomy for renal tumors between 2006 and 2014. A line plot with a locally weighted scatterplot smoothing was generated to visually assess renal function over time. Univariable and multivariable longitudinal regression analyses incorporated a random intercept and slope to evaluate the association between patient and disease characteristics with renal function after surgery. **Results:** Median age was 60 years and most patients were male (255 patients [65.9%]) and white (343 patients [88.6%]). In univariable analysis, advanced age at surgery, larger tumor size, male sex, longer ischemia time, history of smoking, and hypertension were significantly associated with lower preoperative estimated glomerular filtration rate (eGFR). In multivariable analysis, independent predictors of reduced renal function after surgery included advanced age, lower preoperative eGFR, and longer ischemia time. Length of time from surgery was strongly associated with improvement in renal function among all patients. **Conclusion:** Independent predictors of postoperative decline in renal function include advanced age, lower preoperative eGFR, and longer ischemia time. A substantial number of subjects had recovery in renal function over time after surgery, which continued past the 12-month mark. These findings suggest that patients who undergo partial nephrectomy can experience long-term improvement in renal function. This improvement is most pronounced among younger patients with higher preoperative eGFR.

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Introduction

Renal cell carcinoma (RCC) has an annual estimated incidence of 64,000 cases in the United States.[1] Five-year relative survival rates have increased from 50% in 1975 to 1977 to 73% in 2003, largely because of the increasing use of abdominal imaging for unrelated indications, leading to a stage migration toward diagnosis of smaller, lower stage tumors.[2,3] Historically, radical nephrectomy (RN) has been the standard of care for renal masses. However, a growing body of evidence has indicated that after radical kidney surgery, patients are more likely to be diagnosed with chronic kidney disease (CKD) or end-stage renal disease—medical conditions that are associated with increased cardiovascular morbidity and risk of noncancer-related death.[4,5] Optimizing perioperative renal function has

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therefore become a key secondary goal in the surgical management of kidney tumors. Nephron-sparing surgery for renal cortical tumors has been shown to have superior renal functional outcomes while providing equivalent oncologic outcomes in appropriately selected patients.[6] Putative baseline clinical demographic factors that affect postoperative renal function in patients who undergo extirpative renal surgery include preoperative estimated glomerular filtration rate (eGFR), age at surgery, tumor size, and the presence of medical comorbidities such as diabetes and hypertension.[7,8] In a comparison between patients who underwent donor nephrectomy (DN) versus RN for a renal cortical tumor, at a mean follow-up of 15 months postsurgery, RN patients were more likely to have low eGFR, proteinuria, and de novo elevated creatinine levels than those who underwent DN.[9] These findings support the notion that nonsurgical factors as well as vulnerabilities affecting cancer patients play a role in subsequent renal function. Other lifestyle factors such as smoking might also have an effect on renal function, with some studies suggesting that current or former smokers are susceptible to CKD.[10]

The aim of this study was to investigate the natural history of renal function after surgery and to identify independent predictors of reduced postoperative renal function.

Patients and Methods

After institutional review board approval was obtained, data on 513 patients who underwent either partial nephrectomy (PN) or RN for kidney neoplasms at Memorial Sloan Kettering Cancer Center between 2006 and 2014 were collected from a kidney cancer surgical database for a single surgeon (J.A.C.) who obtains extensive perioperative medical data on each patient. All surgeries were performed with a minimally invasive approach and thus the tumor excision was completed under warm ischemia in the shortest amount of time possible to safely remove the tumor and repair the renal parenchymal defect. Patients were excluded for having 2 separate surgeries within 1 year (n = 11), transitional cell carcinoma (n = 3), receipt of chemotherapy (n = 52), or not having any postoperative eGFR measurements (n = 8). Because the number of patients receiving RN in this data set was small (n = 52), analysis was limited to patients who received PN. The final sample size for analysis was 387 patients with a total of 4026 eGFR measurements.

Serum creatinine (SCr) values were collected at the preoperative visit and at all postoperative visits. Patients were seen for follow-up visits in the clinic every 3 to 6 months postoperatively, on average. We used SCr to calculate eGFR values using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula[11] as follows: $\text{eGFR} = 141 \times \text{minimum}(\text{SCr}/\kappa,1)^{\alpha} \times \text{maximum}(\text{SCr}/\kappa,1)^{-1.209} \times 0.993^{age} \times 1.018$ (if female) $\times 1.159$ (if black), where SCr is in milligrams per deciliter, κ is 0.7 for women and 0.9 for men, α is -0.329 for women and -0.411 for men, minimum indicates the minimum of SCr/κ or 1, and maximum indicates the maximum of SCr/κ or 1. If patients had more than 1 measurement on the same date, the multiple measurements were averaged for analysis.

To explore trends in the data, we plotted the trajectory of each patient's eGFR from their immediate postoperative visit up to 5 years postoperatively, and used a locally weighted scatterplot smoothing to look at trends in the data overall. We analyzed the association between patient and disease characteristics with preoperative eGFR using the Wilcoxon rank sum test when continuous and Fisher exact test when categorical. The primary end point was postoperative eGFR over time. We fit linear mixed models to the data, incorporating a random intercept and random slope for each patient. Each model included a fixed effect for the factor of interest as well as a fixed effect for time. This model accounts for the correlation between multiple observations of eGFR within a patient, and allows each patient in the data to have an individual intercept and slope. A multivariable model incorporated factors selected on the basis of a combination of clinical and statistical considerations.

A P value $< .05$ was considered statistically significant. All analyses were conducted using R version 3.1.0 (R Core Development Team, Vienna, Austria) including the "nlme" package.

Results

Of the 387 patients included in our analysis, 64 (16.5%) had eGFR $\geq$ 90, 213 (55.0%) had eGFR 60 to 89, and 110 (28.4%) had eGFR $<$ 60 preoperatively. Patient and disease characteristics according to preoperative eGFR are presented in Table 1. Median age was 60.1 (range, 23.0-85.3) and most patients were male (255 patients [65.9%]) and white (343 patients [88.6%]). There were differences in age ($P < .001$), sex ($P = .001$), smoking status ($P = .005$), hypertension ($P < .001$), preoperative diastolic blood pressure (DBP; $P = .007$), tumor size ($P < .001$), and ischemia time ($P < .001$) according to preoperative eGFR.

Longitudinal postoperative eGFR trajectories for each patient are plotted in Figure 1. Median follow-up time was 24 months (range, 0-68). Included patients had a median of 9 eGFR measurements during follow-up (range, 2-76). On average, patients experienced an initial decline in eGFR after surgery, followed by a slight increase and stabilization. To further investigate the trend in postoperative eGFR over time, we fit a linear mixed model that included a fixed effect for time and a random intercept and slope for each patient and found that each 1-month increase in time was significantly associated with a 0.11 (95% confidence interval, 0.07-0.15) unit increase in eGFR ($P < .001$), indicating that there is a significantly increasing trend in postoperative eGFR over time.

In univariable analysis (Table 2), older age ($P < .001$), male versus female sex ($P = .040$), ever smoker status ($P = .001$), higher American Society of Anesthesiologists stage ($P < .001$), hypertension ($P < .001$), higher preoperative systolic blood pressure ($P = .003$), larger tumor size ($P = .002$), and longer ischemia time ($P < .001$) were associated with decreased postoperative eGFR over time. Only higher preoperative eGFR ($P < .001$) was associated with increased postoperative eGFR over time. Forty patients were missing data on ischemia time, so multivariable analysis is among 347 patients with complete data. In multivariable analysis incorporating age, smoking status, hypertension, tumor size, ischemia time, preoperative eGFR, and months from surgery as fixed effects (Table 3), only older age ($P < .001$) and longer ischemia time ($P = .015$) remained significantly independently associated with decreased postoperative eGFR over time. Higher preoperative eGFR ($P < .001$) and months from surgery ($P < .001$) remained significantly associated with increased postoperative eGFR over time.