Uric Acid Levels Correlate with Baseline Renal Function and High Levels are a Potent Risk Factor for Postoperative Chronic Kidney Disease in Patients with Renal Cell Carcinoma

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Purpose: We investigated the relationship between preoperative uric acid and the glomerular filtration rate preoperatively and postoperatively in patients with renal cell carcinoma.

Materials and Methods: Included in study were 1,534 patients who underwent radical or partial nephrectomy for renal cell carcinoma between 1994 and 2008. Uric acid was measured preoperatively. The estimated glomerular filtration rate was calculated using the MDRD (Modification of Diet in Renal Disease) equation preoperatively and postoperatively within 7 days, and at 3 months, and 1 and 3 years. We looked for correlations of uric acid with the glomerular filtration rate, patient demographics and comorbidities. We also evaluated the predictive value of uric acid for the preoperative glomerular filtration rate and new onset chronic kidney disease, defined as a glomerular filtration rate of less than 60 ml/minute/1.73 m^2, after nephrectomy using multivariate regression analysis.

Results: Mean ± SD uric acid was 5.2 ± 1.5 mg/dl (range 1.3 to 11.3). Mean preoperative uric acid correlated with the preoperative glomerular filtration rate ($r = -0.313$, $p < 0.001$) and was associated with prevalent chronic kidney disease. On multivariate regression analysis a decreased preoperative glomerular filtration rate correlated significantly with earlier year of surgery, older age, male gender, hypertension, high uric acid and larger tumors (each $p < 0.001$). Hypertension, male gender and high body mass index correlated with high uric acid (each $p < 0.001$). Older age ($p < 0.001$), diabetes mellitus ($p = 0.002$), low preoperative glomerular filtration rate ($p < 0.001$) and high preoperative uric acid ($p = 0.002$) were significant predictors of new onset chronic kidney disease 3 years after nephrectomy.

Conclusions: Increased preoperative uric acid was an independent predictor of a low preoperative glomerular filtration rate and new onset chronic kidney disease in patients with renal cell carcinoma who underwent nephrectomy.

Key Words: kidney; nephrectomy; carcinoma, renal cell; chronic renal insufficiency; uric acid

Abbreviations and Acronyms

CKD = chronic kidney disease

GFR = glomerular filtration rate

RCC = renal cell carcinoma

Submitted for publication November 5, 2012.

Study received Samsung Medical Center institutional review board approval.

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MULTIPLE groups have examined the outcomes and predictive factors related to CKD after radical or partial nephrectomy for RCC. CKD is a significant predictor of hospitalization, morbidity and mortality from any cause.[1,2] Patients with RCC may be at a higher risk for CKD because of other risk factors, including older age, diabetes, hypertension, smoking and low preoperative GFR.[3–5] Recent reports of patients with RCC showed that

0022-5347/13/1894-1249/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2012.11.043
Vol. 189, 1249-1254, April 2013
Printed in U.S.A.

RCC is a potential cause and outcome of decreased GFR. Independent predictors of low preoperative GFR in patients with RCC include year of surgery, tumor size, the Charlson-Romano index and hypertension.[6,7]

Recently, the role of hyperuricemia in hypertension, diabetes and CKD has attracted interest. Hyperuricemia is a common problem in the general population that may be present in up to 10% of adults.[8] A high incidence of hyperuricemia was found in elderly patients with a kidney transplant in the late period after transplantation, which correlated with renal allograft impairment.[9,10] In the urological field uric acid is usually evaluated in patients with urinary stones.

However, little is known about the relationship between serum uric acid and GFR in patients with RCC. Therefore, we investigated the association between serum uric acid, and preoperative and postoperative renal function in a large cohort of patients with RCC who underwent nephrectomy.

MATERIALS AND METHODS

Patients

This retrospective study was approved by the Samsung Medical Center institutional review board. Included in study were 1,534 patients who underwent radical or partial nephrectomy for RCC between October 1994 and December 2008. Clinical data on age, gender, height, weight, body mass index, hypertension, diabetes and tobacco use history were recorded at hospital admission for operation. Blood pressure was classified as normal—systolic less than 120 mm Hg and diastolic less than 80 mm Hg, prehypertension—systolic 120 to 139 or diastolic 80 to 89 mm Hg, stage I—systolic 140 to 159 or diastolic 90 to 99 mm Hg, or stage II—systolic 160 mm Hg or greater, or diastolic greater than 100 mm Hg, according to the guidelines of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.[11] A history of hypertension was defined as self-reported hypertension with or without ongoing pharmacological treatment.

Serum uric acid was measured preoperatively. Serum creatinine was measured preoperatively, postoperatively within 7 days, and at 3 months, and 1 and 3 years. GFR was calculated using the abbreviated MDRD-GFR equation, GFR in ml/min/1.73 m^2 = 186.3 × creatinine$^{-1.154}$ × age$^{-0.203}$ (× 0.742 if female). CKD was defined as a decrease in estimated GFR to less than 60 ml/minute/1.73 m^2. Tumor T stage was classified according to the American Joint Committee on Cancer/UICC TNM system.[12] The Fuhrman grading system was used to measure nuclear grade.[13] Tumor size was defined as the maximal longest tumor dimension on preoperative computerized tomography. Patients were excluded from study if tumors showed benign pathological results. Patients who received immunotherapy or chemotherapy for metastatic disease preoperatively or postoperatively were also excluded.

Statistical Analyses

Continuous variables are shown as the mean ± SD or the mean and range. Pearson correlation coefficients (r) were calculated to evaluate correlations between the preoperative GFR and characteristics such as patient age, body mass index, uric acid and tumor size. Possible associations between mean GFR and the year of surgery, gender, diabetes mellitus, hypertension and blood pressure classification were evaluated. All variables associated with preoperative GFR were used in a multivariate regression model that included all patients. Associations between age, gender, body mass index, diabetes and hypertension, and preoperative uric acid were also evaluated.

On univariate and multivariate analyses logistic regression models were used to identify potentially significant factors associated with new onset CKD 3 years after nephrectomy in 1,332 patients with preoperative MDRD-GFR greater than 60 ml/minute/1.73 m^2. We corrected p values and the 95% CIs for ORs using the Bonferroni method due to multiple testing.[14] All p values were 2-sided and $p < 0.05$ was considered statistically significant. All data analyses were done with SPSS®, version 19.0.

RESULTS

Table 1 lists the clinical characteristics of the 1,534 study patients at radical or partial nephrectomy. Mean patient age was 54.1 ± 11.7 years (range 20 to

Table 1. *Patient characteristics*

No. pts	1,534	
No. yr (%):		
1994–1999	268	(17.5)
2000–2004	570	(37.2)
2005–2008	696	(45.4)
Mean ± SD age (range)	54.1 ± 11.7	(20–86)
No. gender (%):		
M	1,083	(70.6)
F	451	(29.4)
Mean ± SD body mass index (kg/m^2)	24.5 ± 3.1	
Mean ± SD uric acid (mg/dl)	5.2 ± 1.5	
No. diabetes mellitus (%):	191	(12.5)
No. hypertension (%):	497	(32.4)
No. hypertension stage (%):		
Normal	392	(25.6)
Prehypertension	656	(42.8)
I	372	(24.3)
II	114	(7.4)
No. tobacco use history (%):		
No	1,087	(71.0)
Yes	454	(29.0)
No. American Society of Anesthesiologists score (%):		
1	682	(44.5)
2	774	(50.5)
3	78	(5.1)
Mean ± SD preop creatinine (mg/dl)	1.04 ± 0.64	
Mean ± SD MDRD-GFR (ml/min/1.73 m^2)	80.6 ± 20.1	
No. nephrectomy (%):		
Radical	1,248	(81.4)
Partial	286	(18.6)
Mean ± SD tumor size (cm)	5.1 ± 3.3	