
Computed tomography based renal parenchyma volume measurements prior to renal tumor surgery are predictive of postoperative renal function

Brian Kunzel, BS,¹ William Small, MD,² Michael Goodman, MD,³ John Pattaras MD,¹ Viraj Master, MD,¹ Kenneth Ogan, MD¹

¹Department of Urology, Emory University School of Medicine, Atlanta, Georgia, USA

²Department of Radiology, Emory University School of Medicine, Atlanta, Georgia, USA

³Rollins School of Public Health, Emory University School of Medicine, Atlanta, Georgia, USA

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Introduction: To determine whether preoperative computed tomography (CT) based renal parenchymal volume (RPV) measurements would be predictive of postoperative chronic kidney disease (CKD).

Materials and methods: From 2005 to 2010, 189 patients with preoperative CT imaging performed at Emory University Hospital underwent renal tumor surgery. Preoperative and postoperative renal function was determined by estimating glomerular filtration rate (GFR) using standard Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) equations. Preoperative CT measured RPV was calculated to determine association of predicted preserved renal parenchyma with postoperative renal function and the development of CKD (GFR < 60 mL/min/1.73 m²).

Results: For the entire cohort, radical nephrectomy (RN), lower preoperative GFR, and volume of kidney without tumor were associated with the development of CKD ($p < 0.05$). If the non-tumor bearing kidney constituted $\geq 50\%$ of the total bilateral preoperative RPV, then risks of developing CKD were decreased. In patients treated with partial nephrectomy (PN) or ablation, total bilateral preoperative RPV measurements predicted postoperative renal function (CKD ≥ 3 versus CKD < 3) to a significant degree ($p < 0.001$).

Conclusions: Preoperative CT based RPV measurements are independently associated with the development of CKD in patients undergoing renal tumor surgery. This provides urologists with another tool in the assessment of patients with renal tumors.

Key Words: kidney neoplasms, tomography, x-ray computed, organ size, kidney failure, chronic

Introduction

Management of renal tumors has undergone a tremendous evolution over the past several decades. Treatments must balance the goals of oncologic efficacy, preservation of renal function, surgery related perioperative morbidity, and overall survival. A preoperative evaluation that is able to predict change in renal function following surgery would allow better determination of treatment modality.

Morrisroe et al demonstrated a strong correlation between renal volume measurements taken from computed tomography (CT) imaging and nuclear renal scans in patients with normal and chronically obstructed kidneys. They concluded that CT imaging is a valuable diagnostic tool that may potentially independently assess kidney function in patients.¹ Johnson et al found that in potential transplant donors, renal parenchymal volume (RPV) determined on contrast-enhanced CT scans, correlated strongly with glomerular filtration rate (GFR) ($r = 0.62$). In fact, GFR showed a stronger correlation with RPV than with creatinine (Cr)-based estimated GFR (GFR) equations.²

Based on the above results, the purpose of this study was to evaluate whether preoperative CT imaging was

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Address correspondence to Dr. Kenneth Ogan, Department of Urology, Emory University School of Medicine, 1365 Clifton Road NE, Building B, Suite 1400, Atlanta, GA 30322 USA

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effective in predicting development of chronic kidney disease (CKD) following surgery for renal tumors. We evaluated correlations between preoperative RPV using CT imaging software and postoperative GFR calculations from serum Cr levels. Our hypothesis was that preoperative RPV would be predictive of postoperative renal function.

Materials and methods

In an Emory University Institutional Review Board approved study, preoperative CT imaging from 240 patients with renal masses performed at the Emory University Department of Radiology were reviewed. Patients were excluded if they had preexisting renal failure, bilateral tumors, or large tumors completely replacing normal kidney parenchyma. Of these 240, 189 had adequate CT studies that were evaluated using the 3D tools package available as part of the Volume Viewer software suite on the GE Healthcare (Waukesha, WI, USA) AW imaging workstation, software version ADW4.2. Using the scalpel function, normal RPV was separated from the tumor and collecting system on sequential images with the summation of parenchymal voxels throughout the remaining kidney after segmentation was complete, Figure 1.² Individual kidney parenchymal volumes were calculated and then the non-tumor bearing kidney was categorized as having either < 50% or \geq 50% of the total bilateral preoperative renal volume.

Preoperative and postoperative serum Cr levels were collected from electronic medical record review. Postoperative serum Cr levels were obtained approximately 4 months postoperatively to determine changes in renal function secondary to surgery. Two equations were used to calculate GFR, the Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) equations.^{3,4} Renal function was assessed using both in order to determine the reliability of one versus the other. Stages of CKD, as defined by The National Kidney Foundation Disease Outcomes Quality Initiative, were determined based on GFR calculations. Significant CKD \geq 3 was defined as an GFR < 60 mL/min/1.73m².³

Patient demographic and clinical characteristics were examined by calculating percentages and measures of central tendency and dispersion (means and standard deviations). The patients that underwent radical nephrectomy (RN) were compared to those treated with nephron-sparing surgery (NSS) with either partial nephrectomy (PN) or renal tumor ablation with respect to various baseline and postoperative measures of renal function including preoperative

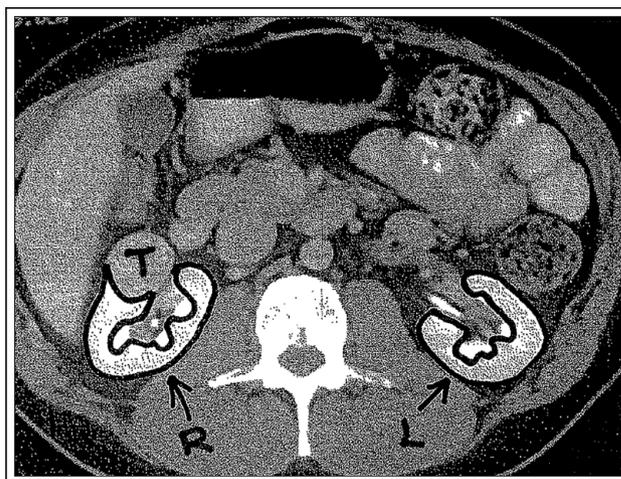


Figure 1. Preoperative CT volume measurement using the scalpel function. Right kidney RPV = 203.6 cc; Left kidney RPV = 213.1 cc; Total bilateral RPV = 416.7 cc (excluding tumor volume); Tumor volume = 13.5 cc. Non-tumor bearing (left) kidney categorized as having either < 50% or \geq 50% of the total preoperative normal kidney volume.

Cr, preoperative and postoperative GFR, and the proportions of subjects that had evidence of CKD calculated using the CG and MDRD equations, respectively. This comparison of the two surgery groups was carried out using Student's t-tests and Fisher's exact tests for continuous and categorical measures, respectively.

Factors associated with postoperative CKD were examined using multivariable logistic regression models. The independent variables in these models (one for CG and one for MDRD) included patient's age, sex, race, age adjusted Charlson Comorbidity Index (CCI), body mass index, type of surgery, preoperative CG- or MDRD-based kidney function depending on whether the outcome was defined as kidney failure (based on CG or MDRD equation). The independent variable of particular interest in these analyses was the RPV of the non-tumor bearing kidney (dichotomized as < 50% versus \geq 50%), which was calculated as non-tumor bearing RPV divided by the total bilateral RPV, Figure 1. Each model was limited to patients without baseline CKD (preoperative GFR \geq 60 mL/min/1.73 m²). The results of these multivariate analyses were expressed as adjusted odds ratios (OR) with the corresponding 95% confidence intervals (CI). The level of significance for all statistical tests was set using a cutoff of less than 0.05 for a two-sided alpha-error. All statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

TABLE 1. Demographic and clinical characteristics of 189 study participants

	Total	RN	NSS
Age day of surgery (yrs), mean (range)	61 (34-89)	64 (34-89)	59 (35-84)
Gender, n (%)			
Male	120 (64)	60 (32)	60 (32)
Female	69 (36)	38 (20)	31 (16)
Race/ethnicity, n (%)			
Caucasian	145 (77)	74 (39)	71 (38)
African American	34 (18)	22 (12)	12 (6)
Asian	1 (0.5)	1 (0.5)	0 (0)
Hispanic	2 (1)	0 (0)	2 (1)
Other	6 (3)	0 (0)	6 (3)
Unknown	1 (0.5)	1 (0.5)	0 (0)
BMI (kg/m ²), mean	30	30	31
HTN, n (%)	114 (60)	64 (34)	50 (26)
DM, n (%)	31 (16)	16 (8)	15 (8)
CCI, mean	3.1	3.6	2.5
Age adjusted CCI, mean	4.8	5.5	4
Tumor volume (cc), mean/median	105 / 38	178 / 84	27 / 15
Multifocal disease, n (%)	11 (6)	6 (3)	5 (3)
Surgical type, n (%)	189 (100)	98 (52)	91 (48)
Surgical approach, n (%)			
Open	73 (38)	25 (13)	48 (25)
Laparoscopic	111 (59)	73 (39)	38 (20)
Robotic	5 (3)	0 (0)	5 (3)
Histologic type, n (%)			
Clear cell RCC	130 (69)	72 (38)	58 (31)
Papillary RCC	22 (12)	8 (4)	14 (8)
Chromophobe RCC	6 (3)	4 (2)	2 (1)
Mixed clear/papillary RCC	2 (1)	2 (1)	0 (0)
Unclassified carcinoma	3 (2)	2 (1)	1 (1)
Other malignant	4 (2)	2 (1)	2 (1)
Oncocytoma	16 (8)	5 (2)	11 (6)
Angiomyolipoma	4 (2)	1 (0.5)	3 (1.5)
Other benign	2 (1)	2 (1)	0 (0)
T stage, n (%)			
Tx	18 (9.5)	0 (0)	18 (9.5)
T0	22 (12)	8 (4)	14 (8)
T1a	61 (32)	20 (10)	41 (22)
T1b	43 (23)	26 (14)	17 (9)
T2	11 (6)	11 (6)	0 (0)
T3a	18 (9.5)	17 (9)	1 (0.5)
T3b	16 (8)	16 (8)	0 (0)
T3c	0 (0)	0 (0)	0 (0)

RN = radical nephrectomy; NSS = nephron sparing surgery; BMI = body mass index

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TABLE 2. Renal function outcomes by surgery type

	RN patients n = 98	NSS patients n = 91	p value*
Preop Cr (mg/dL), mean (SD)	1.08 (0.41)	1.09 (0.42)	0.792
Preop eGFR (mL/min/1.73 m ²)			
CG, mean (SD)	75.0 (38.7)	82.6 (49.3)	0.138
MDRD, Mean (SD)	71.1 (20.4)	72.8 (24.6)	0.609
Preop CKD ≥ 3			
CG, %	32.7	26.4	0.426
MDRD, %	29.6	30.8	0.875
Postop eGFR (mL/min/1.73 m ²)			
CG, mean (SD)	51.3 (26.9)	72.9 (37.5)	< 0.001
MDRD, mean (SD)	45.9 (14.0)	63.7 (21.1)	< 0.001
Postop CKD ≥ 3			
CG, %	68.4	37.4	< 0.001
MDRD, %	82.7	44	< 0.001
Postop decrease in eGFR			
CG, Mean %	33.3	8.9	< 0.001
MDRD, Mean %	34.2	9.9	< 0.001

*calculated based on t-test for continuous variables and Fischer's exact test for categorical variables

RN = radical nephrectomy; NSS = nephron sparing surgery

eGFR = estimated glomerula filtration rate; CG = Cockcroft-Gault

MDRD = modification of diet in renal disease; CKD = chronic kidney disease

Results

Characteristics of the 189 patients that had adequate CT imaging studies for review prior to renal surgery are found in Table 1. Multifocal disease did not affect volume estimations in either group.

Renal function outcomes in patients that underwent RN versus NSS are listed in Table 2. While renal function outcomes varied based on which equation was used to calculate GFR (CG versus MDRD), these were not statistically significant. There was no difference in preoperative renal function in these groups as defined by mean serum Cr, mean GFR, and percent of patients with CKD ≥ 3. However, postoperative renal function was worse in the RN group for all of the renal function parameters examined ($p < 0.001$).

Determinants of postoperative CKD ≥ 3 as calculated by the CG equation are presented in Table 3. After controlling for covariates, independent predictors of CKD ≥ 3-CG included RN versus NSS (OR 9.49; 95% CI: 3.08, 29.30; $p < 0.001$) and preoperative CKD = 2 versus CKD = 1 (OR 9.19; 95% CI: 2.52, 33.57; $p = 0.001$). Non-tumor bearing kidney volume ≥ 50% of total preoperative RPV (compared to < 50%) was associated with a strong and statistically significant protective effect (OR 0.23, 95% CI 0.08, 0.63; $p = 0.004$).

When the analysis was repeated separately for patients undergoing RN versus NSS the results were consistent with the overall model, but the confidence intervals were wide due to reduced sample sizes and diminished statistical power (results not shown).

Also as shown in Table 3, the corresponding results for postoperative CKD ≥ 3 as calculated by the MDRD equation were consistent with those obtained for CKD-CG with respect to RN versus NSS (OR 18.15; 95% CI: 5.96, 55.30; $p < 0.001$), preoperative CKD = 2 versus CKD = 1 (OR 16.02; 95% CI: 4.48, 57.25; $p < 0.001$), and percent of nonl-tumor bearing kidney volume ≥ 50% versus < 50% (OR 0.14; CI 0.04, 0.41; $p < 0.001$). Similarly, compared to the CG analyses, stratification on type of surgery did not produce appreciably different magnitude of association.

A t-test was also used to compare the total bilateral preoperative RPV measurements in patients with and without postoperative CKD treated with NSS. The mean total bilateral preoperative RPV in 57 patients with postoperative CKD < 3-CG (mean = 408.6 cc) was statistically significantly higher ($p < 0.001$) than the 34 patients with postoperative CKD ≥ 3-CG (mean = 309.9 cc). Similarly, the mean total bilateral preoperative RPV in 51 patients with postoperative CKD < 3-MDRD (mean = 407.9 cc) was statistically significantly higher

TABLE 3. Determinants of postoperative CKD ≥ 3 (GFR < 60 mL/min/1.73 m²)*

	OR	CG 95% CI	p value	OR	MDRD 95% CI	p value
Age adjusted CCI						
< 3	1.0 (ref)			1.0 (ref)		
3-5	1.58	0.44-5.67	0.49	2.41	0.60-9.74	0.22
> 5	1.42	0.25-7.92	0.69	5.32	0.78-36.25	0.09
Type of surgery						
NSS	1.0 (ref)			1.0 (ref)		
Radical	9.49	3.08-29.30	< 0.001	18.15	5.96-55.30	< 0.001
Preop CKD-CG						
1	1.0 (ref)					
2	9.19	2.52-33.57	0.001			
Preop CKD-MDRD						
1				1.0 (ref)		
2				16.02	4.48-57.25	< 0.001
% non-tumor bearing kidney volume						
< 50%	1.0 (ref)			1.0 (ref)		
$\geq 50\%$	0.23	0.08-0.63	0.004	0.14	0.04-0.41	< 0.001

*all models adjusted for age, sex, race and BMI

CG = Cockcroft-Gault; MDRD = modification of diet in renal disease; CI = confidence interval; CCI = Charlson Comorbidity Index; NSS = nephron sparing surgery; GFR = glomerular filtration rate; CKD = chronic kidney disease

($p < 0.001$) than the 40 patients with postoperative CKD ≥ 3 -MDRD (mean = 325.7 cc). And so total bilateral preoperative RPV measurements predicted postoperative renal function (CKD ≥ 3 versus CKD < 3) to a significant degree in patients undergoing NSS. The same analyses for tumor volume demonstrated no discernible difference in patients with kidney failure and in those whose CKD remained < 3 . The p values for CG- and MDRD-based comparisons were 0.648 and 0.804, respectively.

Discussion

The volume of kidneys and other organs can be accurately measured with CT imaging with error rates of less than 3%.⁵ Additionally, with newer software programs nonfunctional renal tissue such as the renal sinus and tumor can be excluded from these measurements, thus providing a more accurate determination of functional parenchyma. This software technology is available with most CT imaging systems and can easily be, as was done in our study, learned and accurately executed by non-radiology personnel. Investigators from our institution have previously reported intraobserver and interobserver variabilities of 3% and 8%, respectively, for the measurement of RPV.⁶ Thus, functional RPV can be accurately and

reproducibly measured with standard CT imaging, which currently is the test of choice for the evaluation of renal tumors.

The correlation between CT imaging renal volume measurements and renal function has been studied in a number of different settings. Morrisroe et al evaluated the utility of CT based RPV measurements as a surrogate marker for differential renal function. In their study, CT volume measurements strongly correlated with differential renal function measured on nuclear renal scans in normal and chronically obstructed kidneys. Interestingly, these volume measurements were calculated in non-contrast as well as contrast images.¹ In addition, Ng et al demonstrated a correlation in differential renal volume calculated on noncontrast CT imaging and differential Cr clearance measured on 24 hour urine samples in obstructed kidneys.⁷ Johnson et al found that in potential transplant donors, RPV determined on contrast-enhanced CT scans, correlated strongly with GFR ($r = 0.62$).² Finally, Kaplon et al demonstrated that simply measuring renal parenchymal thickness on non-contrast and contrast CT imaging correlated well with differential renal function as measured on nuclear renography. These authors concluded that this approach provided a rapid estimation of renal function using a single measurement, which could be

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done without sophisticated reconstruction.⁸ Thus, as the above studies illustrate, CT based measurements of renal parenchyma correlate well with renal function as determined by renal scintigraphy and GFR.

The utility of CT based RPV measurements in predicting postoperative renal function following RN and nephron-sparing surgery (NSS) has been scantily studied. However, there is an increasing body of evidence suggesting that preserved RPV and other nonmodifiable factors are the primary determinants of long term postoperative renal function.⁹ Sorbellini et al published the seminal paper in which a nomogram based on pre and postoperative variables was developed to predict postoperative renal insufficiency (Cr > 2.0 mg/dL) in a cohort of patients undergoing RN and PN. Similar to our study, they found that nonmodifiable factors such as age, gender, preoperative Cr and percent change in kidney volume were associated with postoperative renal insufficiency, and thus along with American Society of Anesthesia Performance Score, used for nomogram modeling. Following internal statistical validation the nomogram demonstrated impressive accuracy in predicting the 7 year probability of renal insufficiency in patients undergoing surgery with a concordance index of 0.835.¹⁰

Sharma et al measured RPV loss by comparing preoperative to postoperative CT imaging in patients with renal tumors undergoing PN in a solitary kidney.¹¹ As such, they demonstrated a moderate degree of correlation ($r = 0.48$, $p = 0.03$) between CT measured mean percent RPV loss (19.7%, range 0 to 45.4%) and the mean percent GFR loss (19.2%) at 2 to 6 months following PN. Specifically, this correlation was only found in patients with preoperative decreased renal function and did not correlate with GFR loss in the immediate postoperative period.

Similar to our study, Tanaka et al retrospectively investigated whether postoperative renal function in patients with renal tumors could be predicted preoperatively based on a combination of preoperative serum Cr and estimated preserved RPV.¹² Their cohort of patients either underwent RN (76) or PN (26). For each patient postoperative preserved RPV was estimated from preoperative CT or MRI imaging and compared to actual RPV measured on postoperative imaging. For patients undergoing a PN, the planned tumor resection line with an 8 mm normal tissue margin was used to estimate postoperative RPV. Postoperative GFR was predicted by multiplying the preoperative GRF to the ratio of estimated preserved postoperative RPV to preoperative RPV. Predicted postoperative GFR was similarly compared to actual

GFR 2-4 weeks postoperatively. Results demonstrated a strong correlation ($r = 0.74$, $p < 0.01$) between predicted and actual postoperative RPV for the RN group. In addition, there was a strong correlation ($r = 0.82$, $p < 0.01$) between predicted and actual postoperative GFR. Similarly, for the PN group, strong correlations were found between predicted and actual postoperative RPV ($r = 0.87$, $p < 0.01$) and GFR ($r = 0.98$, $p < 0.01$). Likewise, Simmons et al in a cohort of patients undergoing PN calculated percent of functional volume preservation using CT imaging and noted a 96% correlation between predicted and observed long term GFR, again suggesting that preoperative GFR and the percent of functional volume preservation are the primary determinants of long term functional outcomes.¹³

Our results are confirmatory as patients with worse preoperative renal function (CKD = 2 versus CKD = 1) and less RPV in the non-tumor bearing kidney (< 50% versus $\geq 50\%$) had an increased risk of renal failure (CKD ≥ 3). Specifically in the NSS group, total bilateral preoperative RPV in patients with postoperative CKD < 3-MDRD (mean = 407.9 cc) was statistically significantly higher ($p < 0.001$) than the 40 patients with postoperative CKD ≥ 3 -MDRD (mean = 325.7 cc). As such, total bilateral preoperative RPV measurements predicted postoperative renal function (CKD ≥ 3 versus CKD < 3) to a significant degree in patients undergoing NSS. While this measurement may overestimate postoperative renal function since a margin of normal tissue is sacrificed during NSS, the amount of normal tissue excised or ablated is typically small. Alternatively, for future studies a predicted line of resection could be used to estimate preserved postoperative RPV, which may be important for more complex tumors or those involving the renal hilum. Interestingly, the same analyses for tumor volume demonstrated no discernible difference in patients with kidney failure and in those whose CKD remained < 3.

The limitations of this study include its retrospective nature and the relatively small sample size of approximately 200 patients. Secondly, the contribution of warm/cold ischemic time was unable to be determined, as it was not recorded in all patients undergoing PN. However, ischemia time seems to have more of an impact on short term renal function rather than intermediate and long term renal function.⁹ Thirdly, postoperative CT volume measurements were not collected and thus we were unable to calculate the actual amount of tissue spared for patients undergoing NSS. Similarly, the amount of remaining RPV in the surgically treated kidney following NSS was not estimated at the time of surgery. As such we measured

the total preoperative bilateral RPV to determine the predicted postoperative RPV. This will obviously over predict the remaining renal volume for NSS patients, the amount of which will be determined by the extent of normal parenchyma excised or ablated during surgery. Potentially, predictions of total preserved renal parenchyma in NSS patients could be made based on volumetric CT measurements and preoperative planned surgical planes of dissection. These measurements could then be correlated with postoperative imaging to determine accuracy.

Conclusions

Preoperative CT-based RPV measurements are predictive of postoperative development of CKD ≥ 3 in patients undergoing renal tumor surgery. If the non-tumor bearing kidney constituted $< 50\%$ of the total bilateral preoperative RPV there was an independent risk of developing CKD ≥ 3 for RN and NSS. Total bilateral preoperative RPV measurements predicted postoperative renal function (CKD ≥ 3 versus CKD < 3) to a significant degree in patients undergoing NSS. Along with other known factors (preexisting renal insufficiency, CCI and RN), this easily accessed information can be used to help determine the best treatment modality and counsel patients preoperatively.

CT volume measurements of the kidneys prior to renal tumor surgery are easily calculated. In conjunction with other assessments, these measurements enhance urologists' ability to determine treatment options and counsel patients. \square

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