Compensatory Structural and Functional Adaptation after Radical Nephrectomy for Renal Cell Carcinoma According to Preoperative Stage of Chronic Kidney Disease

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Abbreviations and Acronyms

BMI = body mass index
CKD = chronic kidney disease
CT = computerized tomography
FRV = functional renal volume
GFR = glomerular filtration rate
RCC = renal cell carcinoma
RN = radical nephrectomy
SNGFR = single nephron GFR

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Purpose: We investigated structural hypertrophy and functional hyperfiltration as compensatory adaptations after radical nephrectomy in patients with renal cell carcinoma according to the preoperative chronic kidney disease stage.

Materials and Methods: We retrospectively identified 543 patients who underwent radical nephrectomy for renal cell carcinoma between 1997 and 2012. Patients were classified according to preoperative glomerular filtration rate as no chronic kidney disease—glomerular filtration rate 90 ml/minute/1.73 m^2 or greater (230, 42.4%), chronic kidney disease stage II—glomerular filtration rate 60 to less than 90 ml/minute/1.73 m^2 (227, 41.8%) and chronic kidney disease stage III—glomerular filtration rate 30 to less than 60 ml/minute/1.73 m^2 (86, 15.8%). Computerized tomography performed within 2 months before surgery and 1 year after surgery was used to assess functional renal volume for measuring the degree of hypertrophy of the remnant kidney, and the preoperative and postoperative glomerular filtration rate per unit volume of functional renal volume was used to calculate the degree of hyperfiltration.

Results: Among all patients (mean age 56.0 years) mean preoperative glomerular filtration rate, functional renal volume and glomerular filtration rate/functional renal volume were 83.2 ml/minute/1.73 m^2, 340.6 cm^3 and 0.25 ml/minute/1.73 m^2/cm^3, respectively. The percent reduction in glomerular filtration rate was statistically significant according to chronic kidney disease stage (no chronic kidney disease 31.2% vs stage II 26.5% vs stage III 12.8%, $p < 0.001$). However, the degree of hypertrophic functional renal volume in the remnant kidney was not statistically significant (no chronic kidney disease 18.5% vs stage II 17.3% vs stage III 16.5%, $p=0.250$). The change in glomerular filtration rate/functional renal volume was statistically significant (no chronic kidney disease 18.5% vs stage II 20.1% vs stage III 45.9%, $p < 0.001$). Factors that increased glomerular filtration rate/functional renal volume above the mean value were body mass index ($p=0.012$), diabetes mellitus ($p=0.023$), hypertension ($p=0.015$) and chronic kidney disease stage ($p < 0.001$).

Conclusions: Patients with a lower preoperative glomerular filtration rate had a smaller reduction in postoperative renal function than those with a higher preoperative glomerular filtration rate due to greater degrees of functional hyperfiltration.

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

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RADICAL nephrectomy and partial nephrectomy are standard treatment options in patients with renal cell carcinoma.[1,2] However, one of the major problems in the treatment of RCC is that RN significantly increases the risk of postoperative chronic kidney disease with an estimated GFR less than 60 ml/minute/1.73 m^2.[1] The development of CKD has been associated with an increased risk of cardiovascular events and all cause mortality in large, population based studies, even when controlling for confounding factors.[3,4]

Previous studies have established that predictors of reduced GFR after renal surgery are older age, diabetes mellitus, type of surgery (radical vs partial nephrectomy) and low preoperative GFR.[1,5,6] In particular, preoperative GFR is a crucial factor in predicting the degree of postoperative decline in GFR. The decrease in postoperative GFR was smaller in patients with a preoperative GFR less than 60 ml/minute/1.73 m^2 than in those with a preoperative GFR greater than 60 ml/minute/1.73 m^2.[7,8] In addition, functional renal volume has recently been proposed as a factor affecting postoperative GFR.[9–11]

After RN the process of compensation by the remnant kidney results in structural hypertrophy and functional hyperfiltration in the glomeruli. Regarding compensatory structural adaptations, some studies have shown that the degree of structural hypertrophy in the remnant kidney is significantly correlated with postoperative recovery of renal function.[12,13] However, with respect to functional adaptation, the degree of hyperfiltration after RN in the clinical setting is unknown. In several experimental animal models of reduced renal parenchyma, the fractional reabsorption of sodium is acutely reduced after nephrectomy but is rapidly restored to preoperative levels.[12,13] However, there have been no studies to date that have investigated functional compensatory adaptations in humans.

In light of these findings we measured the preoperative and postoperative functional renal volume in patients undergoing RN and the degree of hypertrophy according to preoperative CKD stage. Additionally, the change in the functional filtration rate was examined through a comparison of glomerular filtration rates per functional renal volume (GFR/FRV) across the groups. It would be informative and meaningful to clarify the structural and functional adaptations that take place after renal surgery.

MATERIALS AND METHODS

Patients

This retrospective study was approved by the institutional review board of Samsung Medical Center. Among the 780 patients who underwent RN 543 were enrolled in this study between October 1997 and December 2012, and had GFR and CT available from before the operation and 1 year after the operation. Clinical data were obtained from individual patient medical records at admission for surgery. Patients with bilateral RCC, a solitary kidney, preoperative GFR less than 30 ml/minute/1.73 m^2, undergoing hemodialysis, and CT performed elsewhere showing an absence of venous phase and/or delay phase CT were excluded from the study. We calculated GFR using the chronic kidney disease Epidemiology Collaboration (CKD-EPI) equation.[14]

The patients were divided into 3 groups according to the NKF-KDOQI (National Kidney Foundation-Kidney Disease Outcomes Quality Initiative) Guidelines for Chronic Kidney Disease.[15] Patients with no CKD had a preoperative GFR of 90 ml/minute/1.73 m^2 or greater. Those with stage II CKD had a preoperative GFR between 89 and 60 ml/minute/1.73 m^2. Finally, those with stage III CKD had a GFR between 30 and 59 ml/minute/1.73 m^2.

Volume Measurement

Patients with preoperative CT within 60 days of renal surgery were included in the study. CT was performed using a 16 or 64 multi-detector CT scanner (Siemens, Erlangen, Germany) using the standard clinical abdominopelvic imaging protocol. CT images of the renal parenchyma with a 5 mm slice thickness were used. Functioning renal parenchyma was defined as normally enhancing areas on CT. Cross-sectional CT images of the preoperative venous phase were exported to Xelis software (Infinitt, Seoul, South Korea). Initially a threshold of 50 HU was chosen. After the observer manually rendered the tumor area, the software automatically calculated the 3-dimensional tumor volume. Volume was calculated as the mean of the 2 results by 2 observers.

The overall preoperative FRV was calculated by summing the FRV of the operated kidney minus the volume of the tumor and the FRV of the remnant kidney based on preoperative CT. The postoperative FRV of the remnant kidney was obtained from CT images taken 1 year after surgery. In addition, the preoperative GFR per unit volume (GFR/FRV) was obtained by dividing the preoperative GFR by the overall FRV (operated kidney volume plus remnant kidney volume). Likewise, the postoperative GFR per unit volume (GFR/FRV) was determined by dividing the postoperative GFR by the postoperative FRV (volume of the remnant kidney).

Statistical Analysis

Continuous variables are expressed as mean (SD) or median (IQR). Categorical variables are expressed as absolute values and percentages. We compared the correlation of the 2 volumes for each observer using the interobserver correlation. Continuous and categorical variables were compared using ANOVA and the chi-square test in the 3 groups. ANOVA was used to compare the changes in GFR, loss of kidney volume, hypertrophic volume and GFR/FRV before treatment and 1 year after surgery. Logistic regression analyses were used to identify factors associated with the increase in GFR/FRV greater than the mean value. All tests were 2-sided and statistical significance was defined as $p < 0.05$. All data analyses were performed using SPSS® version 20.0.