Impact of Tumor Size on Renal Function and Prediction of Renal Insufficiency After Radical Nephrectomy in Patients With Renal Cell Carcinoma

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Abbreviations and Acronyms

DM = diabetes mellitus

GFR = glomerular filtration rate

PN = partial nephrectomy

RCC = renal cell carcinoma

RN = radical nephrectomy

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Purpose: From the perspective of oncological and functional outcomes partial nephrectomy is considered standard surgery for small renal tumors 4 cm or less. However, radical nephrectomy is commonly done for small tumors. It is important to predict postoperative renal function in patients to choose the most optimal surgical procedure.

Materials and Methods: We retrospectively reviewed the records of 271 patients treated with radical nephrectomy for renal cell carcinoma. Associations of tumor size and clinical variables with renal function were analyzed.

Results: Preoperatively the mean ± SD glomerular filtration rate was 74.38 ± 17.70 ml per minute/1.73 m^2 and 56 patients (20%) had renal insufficiency (glomerular filtration rate less than 60 ml per minute/1.73 m^2). The mean decrease in the glomerular filtration rate after radical nephrectomy was 24.2 ± 12.40 ml per minute/1.73 m^2 (31.5% ± 15%). Of 215 patients with a preoperative glomerular filtration rate of 60 ml per minute/1.73 m^2 or greater 165 (77%) had new onset renal insufficiency. Age, tumor size, preoperative glomerular filtration rate and hypertension were significantly associated with new onset renal insufficiency. Multivariate analysis revealed that age 60 years or greater, tumor size 7 cm or less and the preoperative glomerular filtration rate were independent risk factors for new onset renal insufficiency ($p < 0.05$). Finally, we developed a predictive model for new onset renal insufficiency after radical nephrectomy.

Conclusions: Tumor size 7 cm or less, age 60 years or greater and a decreased preoperative glomerular filtration rate were significant risk factors for new onset renal insufficiency in patients treated with radical nephrectomy. Partial nephrectomy might be considered an option according to the risk of postoperative renal insufficiency, especially in elderly patients with a tumor of 7 cm or less.

Key Words: kidney; carcinoma, renal cell; nephrectomy; renal insufficiency; risk factors

KIDNEY cancer accounts for 3% of all adult malignancies and RCC is the most common type of kidney cancer.[1] Widespread cross-sectional imaging has led to increased detection of renal tumors. Most of these tumors are relatively small and localized in the kidney.[2] This trend toward early stage disease eventually led to the prevalence of elective PN for T1 tumor (7 cm or less).[3] The advantage of PN is the ability to preserve renal function, which contributes to longer survival in patients treated with PN vs RN.[4–6]

Huang et al reported that the baseline estimated GFR in patients with

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renal cortical tumors 4 cm or less was lower than previously thought.[7] Generally it was noted that a decreased estimated GFR is associated with increased risk of death, cardiovascular events and hospitalization.[8] American Urological Association and European Association of Urology guidelines recommend PN as a standard operation for T1a tumor (4 cm or less).[9,10] Although the number of patients treated with PN has increased with time, RN remains the most common surgery for small renal tumors.[11] PN is associated with patient age, gender and residence, and tumor size and site.[11]

Tumor size is an important factor, as is tumor site, when making a decision regarding the surgical procedure (PN or RN). However, few groups have investigated the association of tumor size with renal function.[4,12] Thus, we questioned whether tumor size might have an impact on preoperative and postoperative renal function. It is also important to inform the patient of postoperative renal function when discussing the surgical procedure preoperatively. We evaluated the impact of tumor size on renal function before and after RN, and established a predictive model of postoperative renal insufficiency in patients who undergo RN.

MATERIALS AND METHODS

This retrospective study was done according to the ethical guidelines for clinical studies of the Ministry of Health, Labor and Welfare, Japan. It was approved by the ethics committee at our facility. We retrospectively reviewed the medical records of 478 patients with RCC treated at our institution between 1990 and 2008. A total of 437 patients underwent nephrectomy, including RN in 358 and PN in 79. Clinical data were obtained from individual patient medical charts. Of the patients 87 were excluded from study due to unavailable serum creatinine values before or 1 year after RN. Thus, in this study we analyzed the records of 271 patients who underwent RN.

Mean age of the 197 men and 74 women at diagnosis was 61 years (range 24 to 81). Tumors were staged according to the 2002 TNM staging system as stage I to IV in 185, 28, 36 and 22, respectively.[13] Of the tumors 242 were clear cell carcinoma and 28 were nonclear cell carcinoma.[14] Mean followup was 81 months (range 6 to 261). At last followup 193 patients showed no evidence of disease, 31 had metastasis, 36 had died of cancer and 11 had died of noncancer related events.

Clinical variables analyzed in this study included age, gender, hypertension, DM, hyperuricemia and proteinuria. Tumor size was measured by computerized tomography performed within 3 months before nephrectomy. Serum creatinine (sCr) in mg/dl was measured at hospitalization and 1 year after nephrectomy. GFR was estimated using the abbreviated Modification of the Diet and Renal Disease Study equation, GFR in ml/minute/1.73 m^2 = 186 × sCr in $mg/dl^{-1.154}$ × $age^{-0.203}$ × 0.742 if female × 1.210 if black.[15]

Data are shown as the mean ± SD. Age was analyzed as a dichotomous variable (less than 60 vs 60 years or greater) according to the National Kidney Foundation Practice Guidelines for Chronic Kidney Disease.[15] Variables between groups were compared by ANOVA and the Pearson chi-square test. The correlation between continuous variables was analyzed using Spearman's rank correlation coefficients. The outcome measures of renal function after nephrectomy were 1) renal function deterioration (30% or greater GFR decrease from before to after nephrectomy) and 2) new onset renal insufficiency (GFR less than 60 ml per minute/1.73 m^2). The 30% cutoff for renal function deterioration was chosen since the mean percent GFR decrease after RN was about 30% in previous reports.[16,17] The association of tumor size and clinical variables with renal function was analyzed using a logistic regression model. All p values are 2-tailed with $p < 0.05$ considered statistically significant. All statistical analysis was done with StatView® 5.0 and JMP®, version 8.

Using statistically significant variables from the multivariate stepwise logistic regression analysis the predicted probability of new onset renal insufficiency (GFR less than 60 ml per minute/1.73 m^2) was estimated using the formula, $p = 1/[1 + \exp(-k)]$. Logistic regression produced a score (k), which was determined using the equation, $k = a + b1X1 + b2X2 + \ldots + bnXn$, which is a linear combination of the predictors X1, X2 . . ., Xn in the model. Model coefficients a, b1, b2 . . ., bn were chosen to optimize the ability to predict the new onset renal insufficiency with $p < 0.05$ considered statistically significant.[18]

RESULTS

Mean preoperative GFR was 74.38 ± 17.70 ml per minute/1.73 m^2. GFR was less than 60 ml per minute/1.73 m^2 preoperatively in 56 patients (20%). Mean tumor size was 5.6 ± 3.02 cm. Preoperative GFR was significantly lower in patients older than 60 years and in those with hypertension, hyperuricemia, proteinuria or tumor size greater than 7 cm than in their respective counterparts. There was no significant difference in preoperative GFR between patients with tumors 4 cm or less and those with tumors 4 to 7 cm. Based on these results the tumor size cutoff was set to 7 cm in subsequent analyses. Preoperative renal insufficiency (GFR less than 60 ml per minute/1.73 m^2) was significantly associated with age, tumor size, hyperuricemia and proteinuria on univariate and multivariate analysis.

Postoperative mean GFR was 50.16 ± 13.18 ml per minute/1.73 m^2. The mean GFR decrease was 24.2 ± 12.40 ml per minute/1.73 m^2 (31.5% ± 15%). Of 271 patients 178 (65.7%) showed a greater than 30% decrease in GFR. The incidence of renal function deterioration (greater than 30% GFR decrease) was higher in patients with a tumor 7 cm or less than in those with a tumor greater than 7 cm (159 of 213 or 74.7% vs 19 of 58 or 32.8%, $p < 0.0001$). Univariate analysis revealed that tumor size, preoperative GFR and proteinuria were significantly associated