Longitudinal Change in Renal Function After Radical Nephrectomy in Japanese Patients With Renal Cortical Tumors

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Abbreviations and Acronyms

BMI = body mass index
CKD = chronic kidney disease
eGFR = estimated glomerular filtration rate
ESRD = end stage renal disease
PN = partial nephrectomy
RCT = renal cortical tumor
RN = radical nephrectomy

Submitted for publication September 19, 2010.

Supplementary material for this article can be obtained at http://www.tmd.ac.jp/med/uro/files/journalofurology001.

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Purpose: We investigated the longitudinal change in renal function after radical nephrectomy in Japanese patients with renal cortical tumors and compared it with that after partial nephrectomy.

Materials and Methods: This retrospective study included 416 Japanese patients who underwent radical (341) or partial (75) nephrectomy between 1994 and 2009. We investigated the postoperative duration of freedom from new onset of an estimated glomerular filtration rate of less than 60 and 45 ml/minute/1.73 m^2, and the longitudinal change in renal function after surgery.

Results: The 3-year probability of freedom from new onset of an estimated glomerular filtration rate of less than 60 ml/minute/1.73 m^2 after radical and partial nephrectomy was 63% and 89%, respectively ($p < 0.001$). The corresponding incidence of an estimated glomerular filtration rate of less than 45 ml/minute/1.73 m^2 was 89% and 95%, respectively ($p = 0.247$). The estimated glomerular filtration rate decreased by 36% and 13% 1 year after radical and partial nephrectomy, respectively. During the next 5-year followup the estimated glomerular filtration rate after radical nephrectomy slightly but significantly increased by 5% but after partial nephrectomy it did not change significantly.

Conclusions: Radical nephrectomy is an independent risk factor for new onset of an estimated glomerular filtration rate of less than 60 ml/minute/1.73 m^2 in Japanese patients. However, relatively few patients have new onset of an estimated glomerular filtration rate of less than 45 ml/minute/1.73 m^2 even after radical nephrectomy. In Japanese patients renal function deteriorates immediately after radical nephrectomy but improves slightly but significantly thereafter.

Key Words: kidney, kidney neoplasms, nephrectomy, Japan, kidney function tests

CHRONIC kidney disease with eGFR less than 60 ml/minute/1.73 m^2 is an independent risk factor for death from all causes and for cardiovascular events in Western individuals.[1] In many patients CKD develops immediately after RN for RCT and the prevalence of CKD after RN increases steadily thereafter.[2] Recent studies showed that RN is associated with an increased risk of death from any cause compared with PN.[3,4]

However, to our knowledge it has not yet been determined whether RN increases CKD and the subsequent risk of any cause of death other than kidney cancer in Japanese patients compared with PN. Japanese individuals tend to have a different lifestyle, including diet and other behavior,

0022-5347/11/1856-2066/0
THE JOURNAL OF UROLOGY®

Vol. 185, 2066-2071, June 2011
Printed in U.S.A.
DOI:10.1016/j.juro.2011.02.005

than Western individuals.[5] Several studies have shown a lower prevalence of obesity and atherosclerosis in Japanese than in Western populations.[6,7] In terms of racial differences in renal function Imai et al reported a slower eGFR decrease in the Japanese general population.[8] Thus, a difference in renal function after RN may exist between Japanese and Western patients with RCT. Also, it was suggested that an eGFR of 45 instead of 60 ml/minute/1.73 m^2 may be a more critical cutoff for Japanese individuals.[9,10]

To date few groups have reported long-term renal function after RN in Japanese patients with RCT.[11] Moreover, the longitudinal change in renal function after RN has remained unclear even in Western patients. We investigated the longitudinal change in renal function after RN and compared it with that after PN in Japanese patients with RCT.

MATERIALS AND METHODS

Between 1994 and 2009, 580 consecutive Japanese patients underwent RN or PN for RCT at a Japanese national university hospital. Patients with ESRD, bilateral renal tumor or metastasis at surgery and those with less than 3-month followup were excluded from analysis. Thus, 341 patients with RN and 75 with PN were enrolled in this retrospective study.

In the study cohort PN was performed in patients with solitary, small and lateral RCT under warm ischemia in 12, under cold ischemia in 2 and without pedicle clamping in 61.[12] Since 1998, minimum incision endoscopic surgery,[13–15] which is gasless 1-port access minimally invasive surgery, has been performed in 215 and 64 patients undergoing RN and PN, respectively. The other 126 and 11 patients underwent open RN and PN, respectively.

Clinical characteristics, including age at surgery, gender, BMI, preoperative serum creatinine, preoperative eGFR, hypertension and diabetes mellitus, and pathological characteristics, including RCT histology, size and pT stage, were recorded. We calculated the modified Charlson-Romano index,[16,17] an objective measure of comparing comorbidity in patients. eGFR was calculated with the abbreviated equation developed at the Cleveland Clinic Laboratory for the Modification of Diet in Renal Disease Study, 186 $\times$ serum creatinine in $mg/dl^{-1.154}$ $\times$ age in $years^{-0.203}$ $\times$ 0.742 if female.[18] Although Imai et al recommended multiplying the value calculated using the equation by 0.881 for Japanese patients,[19] we used the eGFR value without multiplying it by the racial coefficient in accordance with a Japanese population based study.[9]

The end point of the current study was new onset eGFR less than 60 and less than 45 ml/minute/1.73 m^2. While eGFR 60 ml per minute/1.73 m^2 was chosen as the only cutoff value in some studies,[20,21] we also used eGFR 45 ml per minute/1.73 m^2 in accordance with previous studies showing that the value may be more critical in the Japanese population.[9,10] Postoperative duration of freedom from new onset eGFR less than 60 and less than 45 ml/minute/1.73 m^2 was estimated using the Kaplan-Meier method and compared between patients with RN and those with PN by the log rank test. Patients were followed until death or censoring. Reasons for censoring included loss to followup and recurrent disease. Univariate and multivariate Cox proportional hazards regression analysis was used to determine whether operation type (RN or PN) was associated with CKD after surgery. Diabetes mellitus was not included as an independent variable since it is accounted for in the Charlson-Romano index.

We then investigated longitudinal changes in eGFR and in the eGFR rate of decrease during the 5 years after surgery.

To compare patient clinical and pathological characteristics we used the Student t test for continuous variables, the Wilcoxon rank sum test for ordinal variables and the chi-square test for categorical variables. Longitudinal changes in eGFR and in the eGFR rate of decrease in the group were compared by 1-way ANOVA and the Kruskal-Wallis test. All statistical analysis was done using JMP® 7.0.1 with $p < 0.05$ considered significant.

RESULTS

Median age was 69 years, median BMI was 23.4 kg/m^2, median preoperative creatinine was 0.80 mg/dl and median preoperative eGFR was 96.4 ml/minute/1.73 m^2. Of the patients 71% were male, 30% had a Charlson-Romano index of greater than 2, 34% had hypertension and 15% had diabetes mellitus. There were no significant differences in clinical characteristics between the 2 groups. In contrast, pathological characteristics significantly differed between the 2 groups. In the RN group the incidence of benign disease was lower, tumor size was greater and tumor stage was higher.

Median followup was 45 months (IQR 21–87) in the 341 patients who underwent RN, of whom 44 had recurrent disease and 18 died of disease. Five of the 297 patients without recurrent disease died of causes other than kidney cancer, including cardiovascular disease related to CKD in one, other cancer in 2, Alzheimer's disease in 1 and suicide in 1. One of the 75 patients with PN had bone metastasis and 3 died of another cancer during the median followup of 37 months (range 11 to 82) ($p = 0.058$).

Ten and 2 patients with RN, and 5 and zero with PN had preoperative eGFR less than 60 and less than 45 ml/minute/1.73 m^2, respectively. During followup 126 of the 331 patients (38%) and 4 of the 70 (6%) who underwent RN and PN, respectively, and had preoperative eGFR greater than 60 ml/minute/1.73 m^2 showed new onset eGFR less than 60 ml/minute/1.73 m^2. In contrast, 33 of the 339 patients (10%) and 4 of the 75 (5%) who underwent RN and PN, respectively, and had preoperative eGFR greater than 45 ml/minute/1.73 m^2 showed new onset eGFR less than 45 ml/minute/1.73 m^2 after surgery.