Development of a Screening Tool to Predict Chronic Kidney Disease Risk in Post-nephrectomy Living Kidney Donors

J.S. Park[a], H.K. Ahn[a], J. Na[a], H.H. Lee[b], Y.E. Yoon[c], M.G. Yoon[a], and W.K. Han[a,d,*]

[a]Department of Urology, Urological Science Institute, Yonsei University College of Medicine, Seoul, Republic of Korea; [b]Department of Urology, National Health Insurance Service Ilsan Hospital, Goyang, Gyeonggi-do, Republic of Korea; [c]Department of Urology, Hanyang University College of Medicine, Seoul, Republic of Korea; and [d]Brain Korea 21 PLUS Project for Medical Science, Department of Urology, Yonsei University, Seoul, Republic of Korea

ABSTRACT

Few studies have examined the long-term risks of kidney removal to donors despite the increase of frequency in kidney transplantation. This is the 1st study to develop prediction models of chronic kidney disease (CKD) for the 1-year period after donor nephrectomy in living donors. A prospective cohort of patients who underwent donor nephrectomy from March 1, 2006, to December 31, 2016, at the Severance Hospital, Seoul, South Korea, was used. CKD was defined as a glomerular filtration rate (GFR) <60 mL/min/1.73 m^2. GFR was estimated with the use of the abbreviated Modification in Diet and Renal Disease Study equation. Patients with a previous CKD history or estimated GFR <60 mL/min/1.73 m^2 were excluded, and those with 1-year post-nephrectomy follow-up were included. Among 440 patients who underwent donor nephrectomy, 144 (32.7%) developed a first-time onset of a GFR <60 mL/min/1.73 m^2 by 1 year after surgery. Our logistic regression models derived from these 3 variables predicted CKD with an area under the receiver operating characteristic curve of 0.796, an accuracy of 70.9%, and a sensitivity of 66.2% and specificity of 80.6%. This model could assist with decision making about potential donors and for surveillance of those at risk of post-nephrectomy CKD.

KIDNEY transplantation with the use of living kidney donors has increased along with the demand for renal transplantation; living-donor transplants provide better graft function and survival compared with deceased-donor kidney transplants [1]. However, we have underestimated the long-term risk to the donor and have only focused on the graft function of the donated kidney and the outcome for the recipient. There are few prospective studies of the outcomes for living kidney donors. The quality of these studies has been low; most use small sample sizes and a retrospective study design. To ensure the safety of kidney donation, most studies have examined whether the long-term risks of chronic kidney disease (CKD) or mortality in the donors are equal to or less than the general population [2,3]. But, the results of these studies are misleading because donors are selected from a healthy population. Therefore, the long-term outcomes should be equal to or better than the general population.

Mjoen et al and Muzaale et al compared outcomes for living kidney donors with healthy populations and raised concerns about the safety of living kidney donation [4,5]. Further studies have been performed to assess the risks. Taken together, the results have indicated that there are risks and benefits of living donation. Kidney donation results in no physical benefit for the donor, but it does have psychologic benefits (eg, a sense of gratification). It is important to clarify the risks to make informed and adequate decisions [6,7]. Donors who are likely to develop CKD should be strictly monitored after surgery. Risk factors for CKD development in kidney donors have been reported, but there are no screening tools for predicting CKD risk after donor nephrectomy. The objective of the present study was to develop prediction models of CKD in living donors.

*Address correspondence to Woong Kyu Han, MD, PhD, Department of Urology, Urological Science Institute, Yonsei University College of Medicine, 134 Shinchon-dong, Seodaemun-gu, Seoul, 120-752 Republic of Korea. E-mail: hanwk@yuhs.ac

230 Park Avenue, New York, NY 10169

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METHODS

We performed a prospective cohort study of patients who underwent living-donor nephrectomy from March 1, 2006, to December 31, 2016, at the Severance Hospital, Seoul, South Korea. The study design and protocols were approved by the Institutional Review Board of the Yonsei University Health System. Patients with a previous CKD history or estimated glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 were excluded from the study. To be included in the study, a patient must have received a 1-year post-nephrectomy follow-up examination.

Data on preoperative characteristics (eg, age, sex, height, weight, body mass index [BMI], body surface area [BSA], systolic blood pressure [SBP], diastolic blood pressure [DBP], hypertension, diabetes mellitus, pulmonary tuberculosis, and hepatitis) were recorded for each patient. We also recorded data on cigarette smoking (ie, never-smoker vs current smoker or history of smoking) and alcohol consumption (ie, current alcohol intake vs no current alcohol intake) behaviors. The results for preoperative laboratory data (eg, complete blood counts, routine chemistry, and electrolytes) were also recorded.

GFR is a valid marker for kidney performance [8]. We used the Modification of Diet in Renal Disease (MDRD) study equation to estimate GFR [9]. The equation was: GFR = 32788 × (serum creatinine)$^{-1.154}$ × (age)$^{-0.203}$ (× 0.742 if female). The study outcome variable was a new onset of estimated GFR <60 mL/min/1.73 m^2 at 1 year after surgery. We also analyzed those patients with estimated GFR <45 mL/min/1.73 m^2. GFR values below this threshold are associated with greater risks of complications and morbidity [10–12].

Statistical Analysis

The results were reported as mean ± SD for continuous variables and as percentage for categoric variables. For univariate analyses, the *t* test and chi-square test were used for continuous variables and categoric variables, respectively. For multivariate analysis, we used multivariate models of logistic regression that included all risk factors with statistically significant associations in the univariate analyses. We developed a multiple logistic regression model that included age and preoperative calcium and creatinine concentrations. Diagnostic indicators, such as accuracy, sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve (AUC) were also evaluated. We selected a cutoff value as the point on the ROC curve closest to the upper left corner. This method maximized the Youden index, giving equal weight to sensitivity and specificity [13]. SPSS software version 23.0 (Chicago, Illinois) was used for the statistical analyses. All statistical tests were 2 tailed, and a P value < .05 was considered to indicate a statistically significant result.

RESULTS

A total of 440 out of 1,109 patients who underwent living-donor nephrectomy from March 1, 2006, to December 31, 2016, were eligible for the study. The results for the characteristics of the study population are presented in Table 1. The study population comprised 183 (41.6%) men and 257 (58.4%) women. The mean age was 41.6 years and the mean BMI and BSA were 23.3 kg/m^2 and 1.7 m^2, respectively. Among the 440 patients, 20 (4.5%) had hypertension and 1 (0.2%) had diabetes mellitus. Eleven (2.5%) and 5 (1.1%) patients had pulmonary tuberculosis and hepatitis, respectively. One hundred thirty-one (29.8%) were smokers and 227 (51.6%) consumed alcohol.

Table 1. Characteristics of Healthy Kidney Donors (n = 440)

Age (y)	41.6 ± 11.8
Sex	
Male	183 (41.6%)
Female	257 (58.4%)
Height (cm)	164.6 ± 8.5
Weight (kg)	63.3 ± 10.2
BMI (kg/m^2)	23.3 ± 2.7
BSA (m^2)	1.7 ± 0.2
SBP (mm Hg)	121.5 ± 12.2
DBP (mm Hg)	75.9 ± 9.9
HTN	20 (4.5%)
DM	1 (0.2%)
TBc	11 (2.5%)
Hepatitis	5 (1.1%)
Smoking	131 (29.8%)
Alcohol,	227 (51.6%)
Hb (g/dL)	14.0 ± 1.5
Hct (%)	41.6 ± 4.6
TC (mg/dL)	185.1 ± 33.1
HDL-C (mg/dL)	54.1 ± 13.1
LDL-C (mg/dL)	109.9 ± 27.9
TG (mg/dL)	108.3 ± 65.4
Glucose (mg/dL)	93.2 ± 11.5
Ca (mg/dL)	9.2 ± 0.4
Uric acid (mg/dL)	4.8 ± 1.2
P (mg/dL)	3.6 ± 0.4
Cr (mg/dL)	0.8 ± 0.2

Abbreviations: BMI, body mass index; BSA, body surface area; Ca, calcium; Cr, creatinine; DBP, diastolic blood pressure; DM, diabetes mellitus; Hb, hemoglobin; Hct, hematocrit; HDL-C, high-density lipoprotein cholesterol; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; P, phosphorus; SBP, systolic blood pressure; TBc, pulmonary tuberculosis; TC, total cholesterol; TG, triglyceride.

A total of 144 out of 440 patients (32.7%) developed new onset of a GFR <60 mL/min/1.73 m^2 by 1 year after surgery (Table 2). The univariate analyses revealed that those who developed CKD by 1 year were significantly more likely to be older patients and to have higher SBP, DBP, serum uric acid, and creatinine levels, and lower serum calcium levels. The results of the multivariate analysis indicated that older patients and those with higher serum creatinine levels and lower serum calcium levels had a significantly greater risk of developing CKD.

Eleven patients (2.5%) developed a new onset of GFR <45 mL/min/1.73 m^2. The results of the univariate analysis revealed that these patients were older and had higher SBP, DBP, serum uric acid, and creatinine levels, and lower serum calcium levels. However, the multivariate analysis revealed that only age and serum creatinine were significantly higher in those with a GFR <45 mL/min/1.73 m^2 (Table 3).

Table 4 describes our logistic regression model, which was derived from the three variables age, serum calcium, and creatinine. These variables were significantly different in patients with new onset of GFR <60 mL/min/1.73 m^2 by 1 year of surgery. Our model was well calibrated (Hosmer-Lemeshow