Investigation of Systolic Blood Pressure, Diastolic Blood Pressure, and Pulse Pressure in Living Kidney Donors After Donor Nephrectomy

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ABSTRACT

Kidney transplants from living donors have increased, but few studies have examined the long-term risks of live donor nephrectomy. This is the first study to report the blood pressure (BP) changes associated with cardiovascular disease and linked to chronic kidney disease (CKD) 1 year after live donor nephrectomy. This study examined a prospective cohort of patients who underwent donor nephrectomy between March 1, 2006, and December 31, 2016, at the Severance Hospital, Seoul, South Korea. CKD was defined as a glomerular filtration rate (GFR) of < 60 mL/min/1.73m^2. Patients with a history of hypertension or CKD or an estimated GFR < 60 mL/min/1.73m^2 were excluded; those examined after 1 year post-nephrectomy were included in the study population. Among 420 patients who underwent donor nephrectomy, 137 (32.6%) developed a first-time onset of a GFR < 60 mL/min/1.73m^2 by the first year after surgery. After propensity score–matching the age, systolic BP ($P < .001$) and pulse pressure ($P = .006$) were significantly associated with the groups with newly developed CKD. Systolic BP and pulse pressure decreased significantly at 1 year after donor nephrectomy. These differences decreased after donor nephrectomy, possibly lowering the risk of cardiovascular disease.

KIDNEY transplants from living donors have increased because they provide better graft function and survival compared with transplants from deceased donors [1], but the long-term risk for living kidney donors has been underestimated. Focus has centered mainly on the health of the recipient, with few prospective studies on the outcomes of living kidney donors. Furthermore, these studies have small sample sizes and a retrospective study design, and their research interests are limited mainly to identifying chronic kidney disease (CKD) after live donor nephrectomy [2–5].

Cardiovascular disease (CVD) is a major cause of morbidity and mortality in patients with CKD [6]. Blood pressure (BP) is a powerful CVD risk factor that directly acts on the arterial walls and is responsible for various CVDs, such as cerebrovascular accidents and ischemic heart disease [7]. Previous studies reported the importance of both systolic BP (SBP) and diastolic BP (DBP) and demonstrated the prognosis of CVD in relation to SBP and DBP [8]. Recent studies have associated pulse pressure (PP) with CVDs, especially myocardial infarction and congestive heart failure [7,8]. Elevated PP apparently reflects increased arterial stiffness [7,8].

We are the first to demonstrate the relationship between the SBP, DBP, and PP of living kidney donors and the risk of developing CKD 1 year after donor nephrectomy.

MATERIALS AND METHODS

A prospective cohort of patients who underwent live donor nephrectomy between March 1, 2006, and December 31, 2016, at the Severance Hospital, Seoul, South Korea, was studied. The

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Table 1. Characteristics of Healthy Kidney Donors at 1 year Postsurgery

	Total (n = 420)	Normal Functioning Kidney (n = 283)	Chronic Kidney Disease (GFR < 60 mL/min/1.73m^2) after 1 Year (n = 137)	P^*	$P^\dagger$
Age, y	41.0 ± 11.7	38.3 ± 11.5	46.6 ± 10.1	< .001	< .001
Sex, n (%)					
Male	177 (42.1)	120 (42.4)	57 (41.6)	.877	
Female	243 (57.9)	163 (57.6)	80 (58.4)		
BMI, kg/m^2	23.2 ± 2.7	23.1 ± 2.8	23.5 ± 2.5	.083	
SBP, mm Hg	121.4 ± 12.3	119.8 ± 11.1	124.8 ± 14.0	< .001	.325
DBP, mm Hg	75.8 ± 10.0	75.1 ± 9.4	77.2 ± 10.9	.054	
PP, mm Hg	45.7 ± 10.3	44.7 ± 9.6	47.6 ± 11.4	.006	.178
DM, n (%)	0 (0)	0 (0.0)	0 (0.0)	1.000	
TBc, n (%)	11 (2.6)	8 (2.8)	3 (2.2)	1.000	
Hepatitis, n (%)	5 (1.2)	3 (1.1)	2 (1.5)	.663	
Smoking, n (%)	126 (30.0)	82 (29.0)	44 (32.1)	.510	
Alcohol, n (%)	217 (51.7)	154 (54.4)	63 (46.0)	.105	

Continuous variables are displayed as mean ± standard deviation.
Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; GFR, glomerular filtration rate; PP, pulse pressure; SBP, systolic blood pressure; TBc, pulmonary tuberculosis.
*P-value calculated using the t-test (continuous data) or chi-square test or Fisher's exact test (categorical data).
†P-value calculated using logistic regression for multivariate analysis.

Institutional Review Board of the Yonsei University Health System approved the study design and protocols. Patients with a past history of hypertension, CKD, or an estimated glomerular filtration rate (GFR) of < 60 mL/min/1.73m^2 were excluded. Only patients who were examined at 1 year post-nephrectomy were included.

Data on preoperative characteristics (eg, age, sex, body mass index, SBP, DBP, hypertension, diabetes mellitus, pulmonary tuberculosis, and hepatitis) were recorded for each patient. We also recorded data on cigarette smoking (ie, never smoked vs current smoker or history of smoking) and alcohol consumption (ie, current alcohol intake vs no current alcohol intake) behaviors.

GFR is a valid marker for kidney performance [9]. We used the modification of diet in renal disease study equation to estimate the GFR [10]:

$$\text{GFR} = 32788 \times (\text{serum creatinine})^{-1.154} \times (\text{age})^{-0.203} (\times 0.742, \text{if female})$$

The study outcome variable was determined as the novel onset of GFR < 60 mL/min/1.73m^2 at 1 year postsurgery. GFR values below this threshold are associated with greater risks of complications and morbidity [11–13].

Propensity Score Matching

Propensity score matching (PSM) was used to control confounding factors in the study cohorts [14]. A 1:1 PSM was performed in each group with a novel onset of GFR < 60 mL/min/1.73m^2 at 1 year postsurgery and those without. Propensity scores were calculated for each patient using logistic regression based on the age covariate. Seventeen patients were excluded from the groups with a novel onset of GFR < 60 mL/min/1.73m^2 at 1 year postsurgery and 163 patients from the groups with normal functioning kidneys. One hundred twenty patients with novel onsets of

Table 2. Characteristics of Healthy Kidney Donors After Propensity Score Matching

	Propensity Score-Matched Pairs			
	Normal Functioning Kidney (n = 120)	Chronic Kidney Disease (GFR < 60 mL/min/1.73m^2) After 1 Year (n = 120)	P^*	$P^\dagger$
Age, y	44.7 ± 10.0	45.1 ± 9.6	.768	
Sex, n (%)				
Male	49 (40.8)	50 (41.7)	.896	
Female	71 (59.2)	70 (58.3)		
BMI, kg/m^2	23.6 ± 2.7	23.5 ± 2.5	.904	
SBP, mm Hg	120.1 ± 11.1	123.6 ± 13.5	.027	.029
DBP, mm Hg	75.4 ± 9.3	76.0 ± 10.5	.677	
PP, mm Hg	44.7 ± 8.8	47.7 ± 11.4	.023	.026
DM, n (%)	0 (0.0)	0 (0.0)	1.000	
TBc, n (%)	3 (2.5)	3 (2.5)	1.000	
Hepatitis, n (%)	2 (1.7)	1 (0.8)	1.000	
Smoking, n (%)	36 (30.0)	42 (35.0)	.408	
Alcohol, n (%)	65 (54.2)	57 (47.5)	.302	

Continuous variables are displayed as mean ± standard deviation.
Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; GFR, glomerular filtration rate; PP, pulse pressure; SBP, systolic blood pressure; TBc, pulmonary tuberculosis.
*P-value calculated using the t-test (continuous data) or chi-square test or Fisher's exact test (categorical data).
†P-value calculated using logistic regression for multivariate analysis.

Table 3. Trends of Systolic Blood Pressure Changes After Live Donor Nephrectomy

	Systolic Blood Pressure (mm Hg)										
	Preoperative	Post-op		Post-op		Post-op		Post-op		Post-op	
	Baseline	1 Week	*P*	1 Month	*P*	3 Months	*P*	6 Months	*P*	1 Year	*P*
Total (n = 420)	121.4 ± 12.3	114.7 ± 11.2	< .001	114.4 ± 10.6	< .001	114.9 ± 10.4	< .001	115.8 ± 10.4	< .001	115.5 ± 11.1	< .001
Normal functioning kidney (n = 283)	119.8 ± 11.1	113.9 ± 11.4	< .001	113 ± 10.4	< .001	113.8 ± 10.1	< .001	115.4 ± 10.6	< .001	114.5 ± 11.3	< .001
Chronic kidney disease after 1 year (n = 137)	124.8 ± 14.0	116 ± 10.7	< .001	117.2 ± 10.6	.004	116.8 ± 10.9	< .001	116.4 ± 10.1	< .001	117.4 ± 10.5	< .001
P	< .001	.224		.007		.072		.536		.092	

Table 4. Trends of Diastolic Blood Pressure Changes After Live Donor Nephrectomy

	Diastolic Blood Pressure (mm Hg)										
	Preoperative	Post-op		Post-op		Post-op		Post-op		Post-op	
	Baseline	1 Week	*P*	1 Month	*P*	3 Months	*P*	6 Months	*P*	1 Year	*P*
Total (n = 420)	75.8 ± 10.0	74.3 ± 9.5	.283	73.1 ± 8.7	< .001	73.0 ± 8.9	< .001	74.2 ± 8.5	.001	74.1 ± 8.6	.004
Normal functioning kidney (n = 283)	75.1 ± 9.4	74.1 ± 9.5	.812	72.0 ± 8.4	.001	72.4 ± 8.4	.003	73.2 ± 8.9	.010	73.4 ± 8.9	.037
Chronic kidney disease after 1 year (n = 137)	77.2 ± 10.9	74.8 ± 9.4	.058	75.5 ± 8.8	.136	74.1 ± 9.8	.017	75.8 ± 7.6	.060	75.6 ± 8.0	.053
P	.054	.614		.007		.217		.047		.087	

Table 5. Trends of Pulse Pressure Changes After Live Donor Nephrectomy

	Pulse Pressure (= Systolic Blood Pressure - Diastolic Blood Pressure) (mm Hg)									
	Preoperative	Post-op		Post-op		Post-op		Post-op		
	Baseline	1 Week	*P*	1 Month	*P*	3 Months	*P*	6 Months	*P*	1 Year	*P*
Total (n = 420)	45.7 ± 10.3	40.4 ± 7.0	< .001	41.2 ± 8.1	< .001	41.9 ± 8.1	< .001	41.6 ± 7.0	< .001	41.4 ± 7.5	< .001
Normal functioning kidney (n = 283)	44.7 ± 9.6	39.9 ± 6.8	< .001	41.0 ± 8.1	.001	41.5 ± 7.4	.001	42.2 ± 6.8	.036	41.2 ± 7.3	.003
Chronic kidney disease after 1 year (n = 137)	47.6 ± 11.4	41.2 ± 7.4	.002	41.7 ± 8.1	.004	42.7 ± 9.7	.017	40.6 ± 7.3	< .001	41.8 ± 7.9	.006
P	.006	.209		.528		.351		.141		.603	

GFR < 60 mL/min/1.73m^2 at 1 year postsurgery were matched with 120 patients with normal functioning kidneys. The logistic regression model for PSM was assessed based on the goodness-of-fit statistics proposed by Lemeshow and Hosmer (P = .983) [15].

Statistical Analysis

Results were reported as means ± standard deviations for continuous variables and as percentages for categorical variables. For univariate analyses, the t test and χ^2 test were used for continuous variables and the Fisher exact test for categorical variables. For the multivariate analysis, we used the multivariate models of logistic regression that included all statistically significant risk factors in the univariate analyses. Statistical analyses were performed on the SPSS software version 24.0 (SPSS Inc, Chicago, IL, United States). All statistical tests were 2-tailed, and a P value < .05 was considered statistically significant.

RESULTS

This study included 420 patients out of 1109 who underwent living donor nephrectomy between March 1, 2006, and December 31, 2016. The study population consisted of 177 (42.1%) men and 243 (57.9%) women (Table 1). The mean age was 41.0 ± 11.7 years, and the mean body mass index was 23.2 ± 2.7 kg/m^2. None of the patients had diabetes mellitus. Eleven (2.6%) patients had pulmonary tuberculosis, and 5 (1.2%) patients had hepatitis. A total of 126 (30.0%) of the patients smoked, and 217 (51.7%) consumed alcohol.

Among the 420 patients, 137 (32.6%) developed novel onsets of GFR < 60 mL/min/1.73m^2 at 1 year postsurgery (Table 1). Univariate analyses revealed that those who developed CKD within 1 year were significantly more likely to be older patients and to have higher SBP and PP. However, in multivariate analysis, only age was significantly (P < .001) associated with a risk of developing CKD. After PSM, SBP (P = .029) and PP (P = .026) were the only parameters associated with developing CKD within 1 year, both in univariate and multivariate analysis (Table 2).

Table 3 shows the trends of SBP changes after donor nephrectomy. SBP decreased significantly (P < .001) from 121.4 ± 12.3 mm Hg to 115.5 ± 11.1 mm Hg at 1 year postsurgery. The significant decrease was noted as early as 1 week after surgery (P < .001). Similar significant decreases were noted in the subgroup analysis of those with a normal functioning kidney (P < .001) and those who developed CKD after 1 year (P < .001). Preoperative SBP was significantly higher in those who developed CKD after 1 year; however, this gap was decreased and there were no significant differences after 1 year.

Table 4 shows the trend of DBP. DBP decreased significantly (P = .004) from 75.8 ± 10.0 mm Hg to 74.1 ± 8.6 mm Hg at 1 year postsurgery. In the subgroup analysis, for the group who developed CKD after 1 year, DBP decreased but not significantly (P = .053). For the group with normal kidney function, DBP decreased significantly after 1 year (P = .037). There were no significant differences in the

preoperative DBP and no significant differences in DBP remained the same after 1 year.

Table 5 shows the trends of PP. PP significantly decreased 1 year after surgery ($P < .001$) and was observed in both the group with normal kidney function and the group that developed CKD after 1 year. Similarly to SBP, preoperative PP was significantly different between the 2 groups ($P = .006$); however, there were no significant differences after 1 year.

DISCUSSION

This is the first study to report how changes in SBP, DBP, and PP affect CKD development after live donor nephrectomy. A few studies reported that the BP changes in living kidney donors [16,17]; however, these studies did not measure the PP, which reflects arterial stiffness and is reportedly associated with CVD [7,8]. Although SBP was found to be more strongly associated with CVD than DBP in individuals 45 years or older [8], PP generally was associated with myocardial infarction and congestive heart failure [7,8]. Therefore, assessing PP after live donor nephrectomy is more pertinent to assessing the risk of CKD.

Textor et al [17] measured the BP of living kidney donors and found that the BP fell in both normotensive and hypertensive donors, with a greater decrease noted in hypertensive donors. Our study yielded similar results, with the SBP and PP decreasing significantly in both the normal kidney function group and those who developed CKD after 1 year. Interestingly, another study observed that the BP increased after kidney donation; but when compared with the normal population, the BP in donors decreased significantly [16]. This discrepancy was most likely due to the wide age gap prior to donation (45 ± 11 years) and at evaluation (57 ± 11 years). As BP is strongly influenced by age, an age-matched comparison would be necessary. One final study used siblings of donors as controls and found no significant differences in BP [18], suggesting that measuring BP changes may indeed not be a reliable indicator of CVD risk in kidney donors.

Identifying high BP and effectively modifying behavior with education from professional clinicians can help decrease BP. Living donors often see themselves not as patients but as healthy people. In our institution, we continuously follow up with living donors and provide education programs to help them maintain a healthy lifestyle using nonpharmacologic methods. We believe that the decreased BP observed in our study was achieved through high adherences to the nonpharmacologic recommendations provided by our programs. Although some other underlying mechanisms might also lower the BP in uninephrectomy donors, further long-term studies are needed to identify these mechanisms.

CKD, which developed in some of the patients in our study, has been found to be an independent risk factor for CVD [19]. No studies have demonstrated a relationship between CVD and kidney donors who developed CKD after surgery. Since we did not observe any CVD during our study period, we used PP to infer the risk of CVD. The group that developed CKD after donor nephrectomy had significantly higher SBP or PP before surgery. These differences decreased after surgery, with all differences disappearing 1 year postsurgery. No significant differences were observed in DBP before or after surgery for the group that developed CKD after kidney donation. The strong association between SBP and CVD observed in previous studies might explain why SBP, and not DBP, was significantly associated with the groups that developed CKD 1 year postsurgery. Both SBP and DBP are needed to assess CVD risk in men aged 35 to 44 years old; but for men aged 45 to 57 years old, higher CVD risk was associated with an elevated SBP and low DBP, which resulted in high PP [8]. This might explain why SBP, not DBP, was associated with developing CKD—the mean age of the donors in our study who developed CKD was 46 years old.

There are several limitations to this study. Firstly, although PP is associated with a risk of developing CVD, we could not conclude that live donor nephrectomy decreased CVD risk. Secondly, our study was a retrospective study of a single institution; broadening the patient population to other institutions would strengthen our findings. Third, although there is no information regarding ambulatory BP because of the nature of the retrospective study, ambulatory BP monitoring would increase sensitivity of detection. Therefore, we plan to monitor ambulatory BP only in patients with elevated BP after donor nephrectomy in our future study. Finally, the modification of diet in renal disease study equation is widely used to assess any associations between GFR, mortality, and morbidity [11,12,20]; however, any formulaic inadequacies or uncalibrated serum creatinine concentrations could affect the accuracy of the GFR estimates.

Most studies have focused on the factors associated with the risk of developing CKD in living kidney donors. What is more important is to consider the risk of developing CVD because CVD is a major cause of morbidity and mortality in patients with CKD. High SBP and PP—an indicator of arterial stiffness and risk of CVD—are significantly associated with the risk of developing CKD in living kidney donors. Our study looked at how PP, SBP, and DBP changed after donor nephrectomy. We found that elevated preoperative PP and SBP decreased after donor nephrectomy. We believe that this improvement stems from our institutional program that routinely checks the donor's health status and teaches behavior modification using nonpharmacologic methods. The underlying mechanisms that caused SBP and PP to decrease after donor nephrectomy needs to be investigated further.

CONCLUSIONS

The key finding in this study was the significant decrease in SBP and PP—known risk factors for developing CVD—after live donor nephrectomy. Enrolling in our regular medical surveillance program could help living donors maintain a healthy lifestyle and a healthy BP, thereby reducing the risk of developing CKD and /or CVD after kidney donations.

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