Renal Allograft Function Is a Risk Factor of Left Ventricular Remodeling After Kidney Transplantation

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ABSTRACT

Background. Cardiovascular disease is the leading cause of morbidity and mortality in kidney transplantation (KT) patients. The prevalence of left ventricular hypertrophy increases with the progression of renal insufficiency.

Methods. We investigated the association between the progression of renal insufficiency and left ventricular hypertrophy after KT. We reviewed KT patients at Seoul National University Hospital from January 1973 to December 2009. The creatinine elevation ratio (CER, the percentage change in the creatinine level from 1 month to 5 years after transplant) was calculated as follows: (creatinine level at 5 years minus creatinine level at 1 month)/creatinine level at 1 month $\times$ 100.

Results. The study population was classified into a high-CER group (CER $\geq$25%) and low-CER group (CER <25%). Mean left ventricular mass index (LVMI) values were 135.7 and 134.7 g/m^2 before KT and 101.7 and 123.7 g/m^2 at 5 years after KT in the low-CER and high-CER groups, respectively. The LVMI before or 1 year after KT was not different between the 2 groups, but the LVMI at 5 years post-transplant was higher in the high-CER group than in the low-CER group. The LVMI increased after its initial decrease in the high-CER group, whereas its reduction was maintained in the low-CER group during the 5 years after KT ($P = .009$, repeated-measures analysis of variance).

Conclusions. These data suggest that deterioration of renal allograft function is associated with left ventricular remodeling after KT.

CARDIOVASCULAR disease is the leading cause of morbidity and mortality in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD) [1,2]. Left ventricular hypertrophy (LVH), which occurs in response to volume and pressure overload, is frequently found and is a well-established risk factor for cardiovascular disease in patients with CKD [3–5]. The prevalence of LVH increases with the progression of renal insufficiency in patients with CKD [6].

LVH has been reported to regress in the early period after successful kidney transplantation (KT) [7–10]. Decreased blood pressure, a balanced volume status, and corrected uremic state have been suggested to have a positive effect on myocardial stress and to result in the regression of left ventricular (LV) remodeling after KT [7–10]. However, some studies have reported that high arterial stiffness caused by old age, hypertension and diabetes mellitus, the use of immunosuppressive agents, persistent arteriovenous fistula, and clinical infection may cause continuous LV remodeling after KT [11–15]. The deterioration of graft function may also cause the progression of LVH after KT. However, limited data are available about whether the progression of graft dysfunction induces the recurrence of LVH in KT patients [14,16]. Therefore,

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we investigated the prognostic effect of graft function on LVH after KT.

METHODS

Study Population

From January 1, 1973, to December 31, 2009, 1085 KTs were performed at Seoul National University Hospital. These patients comprised a retrospective KT cohort. One hundred twenty-eight KT recipients who received an echocardiographic examination before and 1 year and 5 years after KT were enrolled in this study.

Creatinine Elevation Ratio

The percentage change in the creatinine level from 1 month to 5 years after transplant, for example, the creatinine elevation ratio (CER), was calculated as follows:

$$\text{CER} = (\text{serum creatinine level at 5 years minus serum creatinine level at 1 month})/\text{serum creatinine level at 1 month} \times 100$$

The study population was classified into 2 groups, according to the CER achieved: the high-CER group included patients with a CER $\geq$25%, and the low-CER group included those with a CER $<$25%. The primary end point of this study was the association between CER and LVH.

Clinical Data

The following clinical parameters were collected at the time of KT: the date of transplantation and information of recipients (age, date of birth, sex, cause of ESRD, comorbidities such as diabetes and hypertension, history of cardiovascular disease, and renal replacement therapy). Physical examination findings, including anthropometric measurements (height and weight) and measurements of the resting office blood pressure, were recorded just before and after KT and serially assessed. The regimens of immunosuppressive medication, presence of post-transplant diabetes, cardiovascular complications, and graft function were also serially collected.

Echocardiographic Examination

Echocardiographic examinations were performed before KT and 1 year and 5 years after KT. In the 2-dimensional presentation, linear measurements of the LV diastolic dimension (LVIDd), LV posterior wall thickness (PWT), and septal wall thickness (IVSD) were obtained. The left ventricular ejection fraction (EF) was estimated. Left ventricular mass (LVM) was calculated in accordance with the 2005 consensus guidelines of the American Society

Table 1. Pre-Transplant Clinical Characteristics of Patients

Before Transplantation	Total (n = 128)	Low-CER (n = 87)	High-CER (n = 41)	*P* Value*
Age at transplant (years)	43.4 ± 11.4	43.5 ± 11.4	43.1 ± 11.6	.846
Male, n (%)	84 (65.6)	60 (69.0)	24 (58.5)	.319
BMI (kg/m^2)	23.8	25.0	21.4	.333
SBP (mm Hg)	136 ± 32	136 ± 28	135 ± 40	.834
DBP (mm Hg)	85 ± 17	83 ± 17	89 ± 18	.060
Smoking history, n (%)	27 (21.1)	21 (24.1)	6 (14.6)	.254
Dialysis duration (months)	33	29	40	.166
Dialysis modality, n (%)				.172
Preemptive	11 (8.6)	10 (11.5)	1 (2.4)	
Hemodialysis	87 (68.0)	60 (69.0)	27 (65.9)	
Peritoneal dialysis	16 (12.5)	10 (11.5)	6 (14.6)	
Hemodialysis + peritoneal dialysis	14 (10.9)	7 (8.0)	7 (17.14)	
Cause of end-stage renal disease, n (%)				.858
Glomerulonephritis	56 (43.8)	35 (40.2)	21 (51.2)	
Diabetes	21 (16.4)	15 (17.2)	6 (14.6)	
Hypertensive nephrosclerosis	13 (10.2)	10 (11.5)	3 (7.3)	
Others	14 (10.9)	9 (10.3)	5 (12.2)	
Unknown	24 (18.8)	9 (10.3)	15 (36.6)	
Pre-operative medical condition, n (%)				
Diabetes	25 (19.5)	16 (18.4)	9 (22.0)	.639
Hypertension	113 (88.3)	79 (90.8)	34 (82.9)	.241
Ischemic heart disease	11 (8.6)	10 (11.5)	1 (2.4)	.104
Cerebrovascular infarction	6 (4.7)	3 (3.4)	3 (7.3)	.375
Cholesterol (mg/dL)	167 ± 34	164 ± 35	175 ± 32	.103
Triglyceride (mg/dL)	117 ± 72	119 ± 80	112 ± 48	.633
LDL cholesterol (mg/dL)	93 ± 29	92 ± 30	98 ± 29	.322
HDL cholesterol (mg/dL)	50 ± 23	48 ± 19	55 ± 29	.146
Deceased-donor kidney transplantation, n (%)	33 (25.8)	20 (23.0)	13 (31.7)	.832

Continuous variables are reported as mean ± standard deviation; categorical variables are listed as total number.

Abbreviations: BMI, body mass index; CER, creatinine elevation ratio; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVH, left ventricular hypertrophy; SBP, systolic blood pressure.

*Continuous variables were compared by use of the Student *t* test; categorical variables were compared by use of the χ^2 test or the Mann-Whitney U test. CER was calculated as follows: CER = (creatinine level at 5 years minus creatinine level at 1 month)/creatinine level at 1 month × 100.