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Successful kidney transplantation ameliorates arterial stiffness in end-stage renal disease patients

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Two tables and one figure are included.

Abstract

PURPOSE: Successful kidney transplantation (KTx) can ameliorate bodily damage caused by end-stage renal disease (ESRD). Arterial stiffness (AS) is one of the critical factors, that shorten the survival of patients due to cardiovascular events. KTx may reduce AS as well; however, this has not been investigated well. We therefore conducted a retrospective study using non-invasive pulse wave velocity (PWV), which is a useful index of aortic damage.

PATIENTS and METHODS: Fifty-eight consecutive kidney recipients (34 men, 24 women) were enrolled in this study. Mean age at transplantation was 40.5±12.3 years and the dialysis period was 73.1±95.8 months. The brachial-ankle PWV was measured preoperatively and six months postoperatively. First, we investigated the relationship between the PWV and the other parameters related to AS. Second, we studied the pre- to post-transplant change in PWV to evaluate the amelioration of AS after successful kidney transplantation.

RESULTS: PWV showed significant positive correlations with age, systolic blood pressure (BP), diastolic BP and abdominal aortic calcification index. After successful KTx, PWV significantly decreased. ($P<0.01$) In addition, systolic and diastolic BP significantly decreased. ($P<0.01$ and $P<0.05$, respectively) CONCULUSION: Successful KTx ameliorates AS in ESRD patients. This might explain the improved cardiovascular prognosis of ESRD patients who undergo kidney transplantation.

Introduction

Chronic kidney disease (CKD) is one of the main risk factor for cardiovascular events. Arterial stiffness (AS) is accelerated in patients with end stage renal disease (ESRD) and leads to cardiovascular events.[1] Patients on dialysis suffer higher rates of cardiovascular morbidity and mortality than the general population. Successful kidney transplantation (KTx) can reduce the cardiovascular risk and improve cardiovascular survival for dialysis patients.[2,3] Artery damage is one of the major factors determining the high prevalence of cardiovascular disease (CVD) in patients with ESRD.[4] KTx may ameliorate arterial stiffness as well; however, this observation is not completely confirmed.

In clinical studies, pulse wave velocity (PWV) is a highly reproducible index of arterial rigidity. Repeatability studies have made it quiet feasible to investigate arterial stiffness in cardiovascular epidemiological studies.[5-7] PWV is an independent predictive parameter for overall and cardiovascular mortality and a strong predictor of prognosis in patients with ESRD.[8] In this study, we investigated the effect of kidney transplantation on arterial stiffness using noninvasive PWV, which is a useful index of aortic damage.

Methods

Patients

Fifty-eight consecutive kidney recipients (34 men, 24 women) were enrolled in this study. Mean

age at transplantation was 40.5±12.3 years and the dialysis period was 73.1±95.8 months. They were maintained with a quadruple immunosuppression comprised of tacrolimus, mycophenolate mofetil, methylprednisolone, and basiliximab. The inclusion requirement was stable renal function for six months after kidney transplantation.

Vascular parameters

First, patients rested in a supine position for five minutes. Oscillometric measurement of the pulse volume was recorded with a volume-plethysmographic apparatus (Colin Co. Ltd., Komaki, Japan), that simultaneously recorded brachial-ankle PWV (baPWV) and blood pressure (BP). The baPWV and BP were measured preoperatively and six months postoperatively. We also measured the abdominal aortic calcification index (ACI) calculated by abdominal CT scan preoperatively. We divided the CT scan images of the aorta in all slices from the diaphragm to the aortic bifurcation into 12 deltaic sectors and counted the number of calcified sectors. Then we calculated the ACI using the formula: ACI (%)=sum total of calcified sectors/sum total of all sectors.

Biochemical parameters

Data for total cholesterol (TC), triglyceride (TG), hemoglobin A1c (HbA1c), serum calcium (Ca) and serum phosphorus (P) were obtained at the time of the preoperative baPWV examination.

Statistical Analysis

Statistical analysis was performed with Prism (version 5). Continuous data were summarized as mean ± standard deviation. All tests were two-sided and $P < 0.05$ was considered statistically significant.

Results

The clinical characteristics and biochemical parameters of the subjects are shown in Table 1. The mean baPWV was 15.9 ± 4.5 m/s in all patients. First, we investigated the relationship between the preoperative baPWV and the parameters related to arterial stiffness (AS), such as age, body mass index (BMI), BP, duration of pre-transplant dialysis, lipid profile (TC, TG), HbA1c, Ca, P, Ca x P and ACI. PWV showed significant positive correlations with age (P<0.001), dialysis period (P<0.05), systolic BP (P<0.001), diastolic BP (P<0.001) and ACI (P<0.001). The other parameters did not correlate with PWV. (Fig. 1)

Second, we studied the difference between pre- and post-transplant vascular parameters, including baPWV, BP and ACI, to evaluate the amelioration of AS after successful kidney transplantation. After successful kidney transplantation, baPWV significantly decreased in all patients (P<0.01). In addition, systolic and diastolic BP significantly decreased (P<0.01 and P<0.05, respectively). However, ACI did not change after kidney transplantation. (Table. 2)

Discussion

Successful kidney transplantation ameliorates arterial stiffness and reduces cardiovascular risk.

However, there is little information on the amelioration of AS after transplantation. In this study, using noninvasive baPWV, we demonstrated the amelioration of arterial stiffness six months after successful KTx.

It has previously been shown that aortic PWV, measured between the carotid and femoral arteries, is an independent predictive parameter for overall and cardiovascular mortality in patients with ESRD.[8] Several studies examined the change of aortic PWV after KTx. Covic et al. found significant improvement of aortic PWV after transplantation.[9] In contrast, another studies reported that KTx did not decrease aortic PWV.[10,11] Recently, brachial-ankle PWV, which can be measured easily and noninvasively, was described. baPWV is also a useful parameter to estimate aortic damage, like aortic PWV.[12,13] Therefore, we used noninvasive baPWV in this study as a parameter of arterial stiffness and demonstrated improvement after KTx. Similarly, in a cohort of 36 transplant recipients, Zoungas et al. investigated the reduction of peripheral PWV one year after KTx. They described that the difference of improvement between aortic and peripheral PWV may reflect the propensity of distal muscular arteries to be more responsive to changes in volume state, sympathetic innervation and neurohumoral-mediated vasomotor tone.[14]

There are several reports to evaluating the amelioration of arterial stiffness after KTx using other parameters. Hornum et al reported that the aortic augmentation index (AIX) and nitroglycerin-induced vasodilation were improved one year after KTx.[15] Similarly, Zoungas et al.

also suggested that KTx significantly reduced the AIX.[14] These data suggested that successful KTx ameliorated arterial stiffness in ESRD patients.

In contrast, several studies reported no reduction of arterial stiffness after KTx. Zoungas et al. examined the change of carotid artery intima-media thickness (IMT). However, there was no significant change in it at one year after KTx.[14] In this study, we examined the aortic calcification in 29 KTx recipients. There was no significant change in the ACI six months after KTx. Sharon et al. also reported that there was no amelioration of coronary artery calcification (CAC) after KTx. However, they found that KTx appeared to slow down or arrest CAC, whereas CAC progressed in hemodialysis patients.[16] Larger numbers of patients and a longer period of observation will be needed to confirm the improvements of these variables; however, it is at least clear that KTx does not cause severe arterial damage to progress.

In conclusion, using noninvasive baPWV, we demonstrated that successful KTx ameliorates arterial stiffness. This might explain the improved cardiovascular prognosis of ESRD patients who undergo kidney transplantation.

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Figure legend

Fig 1. Correlation between brachial-ankle pulse wave velocity (PWV) and the parameters rerated to arterial stiffness. baPWV show significant positive correlations with age ($P<0.001$), dialysis period ($P<0.05$), systolic BP ($P<0.001$), diastolic BP ($P<0.001$) and abdominal aortic calcification index (ACI) ($P<0.001$).

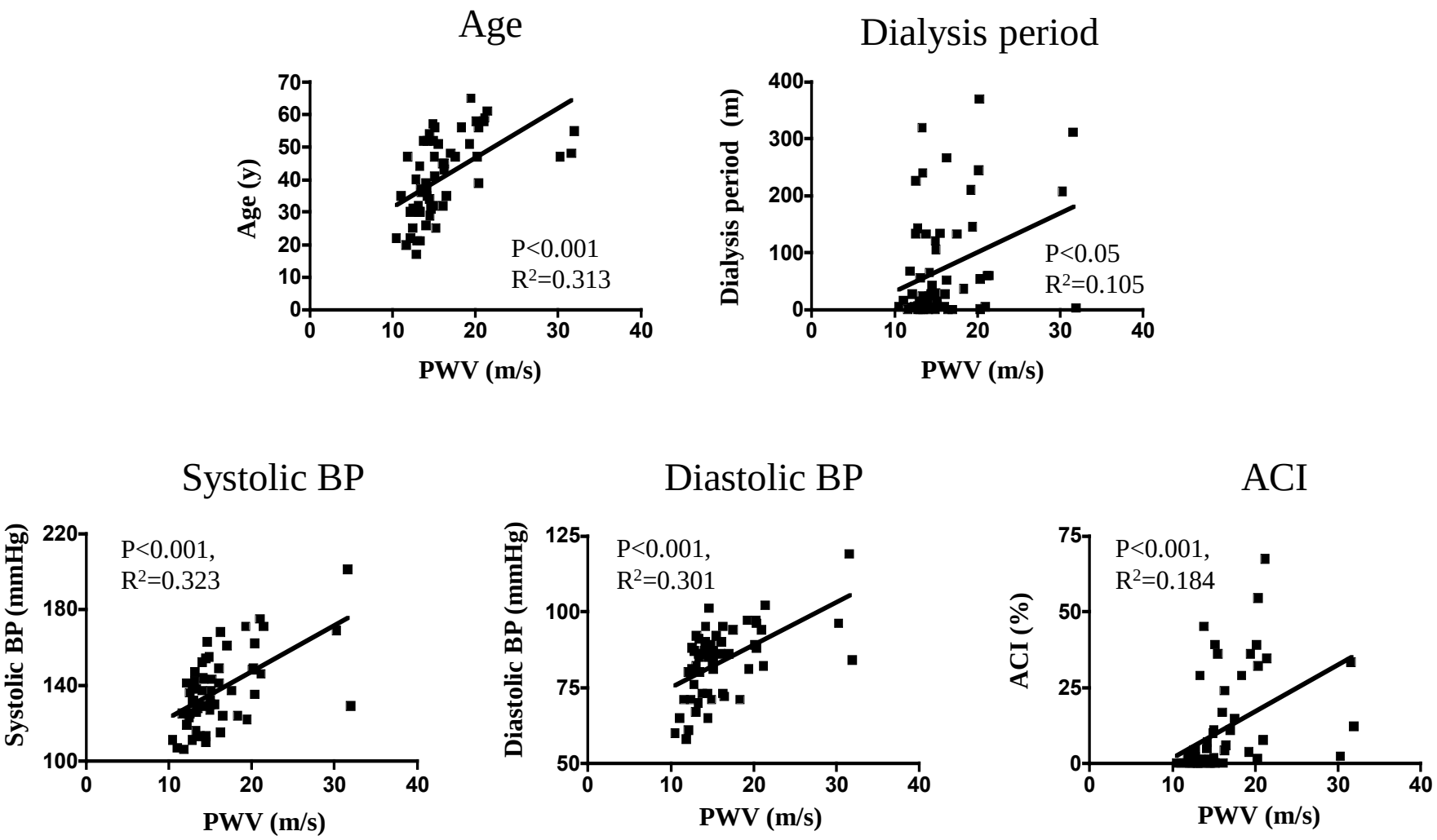
Age
Age (y)
PWV (m/s)
P<0.001
R2=0.313
Dialysis period
Dialysis period (m)
PWV (m/s)
P<0.05
R2=0.105
Systolic BP
Systolic BP (mmHg)
PWV (m/s)
P<0.001,
R2=0.323
Diastolic BP
Diastolic BP (mmHg)
PWV (m/s)
P<0.001,
R2=0.301
ACI
ACI (%)
PWV (m/s)
P<0.001,
R2=0.184

Fig 1

Table 1. The clinical characteristics and biochemical parameters in 58 transplant recipients

	n = 58
Age	40.5 ± 12.3
Male gender	34 (59%)
Dialysis duration (months)	73.1 ± 95.8
Body mass index (Kg/m^2)	21.0 ± 3.3
Systolic BP (mmHg)	134.4 ± 19.4
Diastolic BP (mmHg)	83.4 ± 11.5
Hemoglobin A1c (%)	4.9 ± 0.5
Total cholesterol (mg/dl)	162.2 ± 37.7
Triglyceride (mg/dl)	118.6 ± 81.6
Ca (mg/dl)	9.3 ± 1.0
P (mg/dl)	5.4 ± 1.7
Ca × P	50.6 ± 17.5
Aortic calcification index (%)	10.9 ± 16.3
Pulse wave velocity (m/sec)	15.9 ± 4.5

BP: blood pressure, Ca: serum calcium
P: serum phosphorus

Table 2. Comparison of vascular parameters pre- and post transplantation

	n	Pre KTx	Post KTx	P value
PWV (m/sec)	58	15.9 ± 4.5	14.3 ± 2.6	P<0.01
SBP (mmHg)	58	137.4 ± 19.4	127.6 ± 26.9	P<0.01
DBP (mmHg)	58	83.4 ± 11.5	79.5 ±12.4	P<0.05
ACI (%)	29	10.1 ± 13.8	10.37 ± 14.9	NS

KTx: kidney transplantation, PWV: pulse wave velocity,
SBP: systolic blood pressure, DSP: diastolic blood pressure
ACI: aortic calcification index