Aortic Stiffness, Living Donors, and Renal Transplantation

Sola Aoun Bahous, Antoine Stephan, Jacques Blacher, Michel E. Safar

Abstract—In subjects with renal disease, reduced renal function and increased arterial stiffness are significantly associated in cross-sectional studies. The relationship is independent of age, blood pressure (BP), and atherosclerosis. Because both variables are independent predictors of cardiovascular risk, time-dependent relationships between them are important to determine. Aortic pulse wave velocity was measured noninvasively by comparison with healthy volunteers in 101 living kidney donors and their 101 corresponding recipients. Healthy volunteers were divided into 2 groups: one was recipient related through familial links and the other was nonrecipient related. Independently of age, gender, and BP, pulse wave velocity was significantly elevated in donors and recipients by comparison with the 2 groups of healthy volunteers. Pulse wave velocity was significantly higher in the recipient-related than in the nonrecipient-related group. Whereas in healthy volunteers, pulse wave velocity was exclusively related to age, gender, and BP, in donors and recipients, it was rather associated with a cluster of cardiovascular risk factors, including smoking habits and plasma glucose. Major factors related to pulse wave velocity were renal: time since nephrectomy (donation date) in donors, in whom pulse pressure was specifically associated with proteinuria, and renal rejection in recipients. Plasma creatinine doubling secondary to chronic allograft nephropathy was significantly associated with renal rejection and donor pulse wave velocity, independent of age. Our findings strongly suggest consistent interactions (including familial factors) between kidney function and arterial stiffness. Assessment of cause–effect relationships and implication of biochemical and/or genetic factors warrant additional studies. (Hypertension. 2006;47:216-221.)

Key Words: transplantation, renal ◼ kidney ◼ arteries ◼ pulse ◼ risk factors

Cross-sectional studies in chronic renal failure have shown a significant negative association between increased arterial stiffness and decreased kidney function. The relationship, which is independent of age, mean arterial pressure (MAP), and presence of atherosclerosis, is found in both mild-to-moderate and advanced renal failure. Because aortic stiffness and renal failure are each significant and independent predictors of cardiovascular (CV) risk, and because the age-related increase in arterial stiffness is consistently related to baseline creatinine clearance, there is reason to suspect a cause–effect relationship between renal structure and function and the elastic properties of large arteries.

We recently reported a significant increase in recipient aortic stiffness after living donor renal transplantation, determined primarily by graft rejection; this was the first evidence that renal damage might increase aortic stiffness during long-term follow-up in a time-dependent relationship that was independent, not only of age and MAP, but also of atherosclerosis, drug treatment, and even the presence of the recipient’s native kidneys. However, the study left several unanswered questions regarding the pretransplant and posttransplant periods. First, living donors undergo unilateral nephrectomy and, thus, develop renal adaptive mechanisms, which may eventually modulate arterial stiffness. Second, vascular elasticity in the recipients may be influenced by that in their donors, given the identical renal structure, function, and genotype in both after transplantation. Such questions, which may have important consequences on CV risk, have been poorly investigated in the literature.

The goal of the present study was 2-fold: (1) to discover whether there is a consistent difference in the factors associated with aortic stiffness in kidney donors and their matched controls; and (2) to determine whether the determinants of recipient aortic pulse wave velocity (PWV) include not only the renal immunologic conflict because of transplantation but also other unidentified factors related to donor arterial structure and function.

Methods

Populations

The study population consisted of 3 groups: renal graft recipients (n=101), living kidney donors (n=101), and 2 healthy volunteer populations (n=263; see below). All provided their informed consent, and the protocol was approved by the local Institutional Review Board. For the 3 populations, all of the measurements were done at the same time period between July 2003 and February 2004 at Rizk Hospital, Beirut, Lebanon.
### Table 1. Living Donor Population (n=101): Clinical and Laboratory Parameters Prekidney vs Postkidney Donation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Prekidney</th>
<th>Postkidney ≥ 3 y</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>40.5±11.2</td>
<td>49.7±11.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>35 (34.7%)</td>
<td>...</td>
</tr>
<tr>
<td>Body mass index (Kg/m²)</td>
<td>26.0±3.9</td>
<td>27.8±3.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BP (mm Hg)</td>
<td>Systolic 114.0±17.6</td>
<td>129.6±20</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>69.1±9.4</td>
<td>81.6±11.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pulse</td>
<td>44.9±13.2</td>
<td>48±14</td>
<td>0.039</td>
</tr>
<tr>
<td>MAP</td>
<td>84.1±11.1</td>
<td>97.6±13.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>80.5±12.5</td>
<td>74.6±11.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Plasma glucose (mg/dL)</td>
<td>93.4±9.9</td>
<td>100±11</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Plasma creatinine (mg/dL)</td>
<td>0.79±0.16</td>
<td>0.91±0.17</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calculated creatinine clearance (ml/min/1.73 m²)</td>
<td>107.5±19.6</td>
<td>86.2±17.9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

All values: mean±SD, except gender and drug therapy: n (%).

### Donors (Table 1)
Between January 1985 and December 1999, 273 renal transplantations were performed at Rizk Hospital; 25 kidneys were harvested from cadaver donors, 156 from living-related donors, and 92 from living-unrelated donors. All of the donors were contacted, and 101 participated in the study. Their age was 49.7±11.9 years (±1 SD) at inclusion and 40.5±11.2 years at donation; 90% were first-degree relatives to their recipients, and 10% were living-unrelated donors; the time elapsed since donation was 111±42.2 months (range, 43 to 219 months). All had been carefully evaluated before donation; the exclusion criteria had been composed of old age (>60 years), history of hypertension, diabetes mellitus, CV, renal or connective tissue disease, any systemic illness, and cancer. After donation, 6 donors (5.9%) developed diabetes, defined by a fasting blood sugar >7 mmol/L, and/or antidiabetic medication (sulfonylurea, biguanide, and/or insulin). At the time of the study, 48 donors (47.5%) were hypertensive (defined by a total cholesterol/high-density lipoprotein ratio >5 and/or statin therapy), and 5 (4.9%) were taking a statin; 29 (28.7%) had metabolic syndrome, defined by the presence of 3 of the 5 criteria of the National Cholesterol Education Program’s Adult Treatment Panel III report. Nineteen donors (18.8%) had developed hypertension, defined by systolic blood pressure (BP) >140 mm Hg, or diastolic BP >90 mm Hg, on ≥3 casual measurements by mercury sphygmomanometer in the supine position in the previous month or by antihypertensive therapy for previously diagnosed hypertension; 18 (17.8%) were taking antihypertensive therapy at the time of the study. Five donors (4.9%) developed ≥1 CV event (total, 7), whether coronary, cerebral, aortic, or peripheral.

### Recipients
At the same time of the donor study, the 101 corresponding recipients, 70.3% of whom were males, were aged 42.2±12.6 years. Their clinical, biological, and therapeutic characteristics have been recently detailed elsewhere and are summarized in Table 2. BP, plasma glucose, and cholesterol were in the normal range. Graft age was 111±42.2 months. Acute rejection was observed in 47% of patients. Three recipients had returned to dialysis, and the remainders were still dialysis free. Plasma creatinine doubling was observed in 25 recipients at 63±40 months of follow-up, with etiologies that included chronic allograft nephropathy (n=13), recurrent underlying renal disease (n=4), cyclosporine toxicity (n=3), infection (n=1), de novo glomerulonephritis (n=2), and discontinuation of immunosuppressive drugs (n=2). All but the latter etiology were biopsy proven and read by the same renal histopathologist using the Banff working classification available at the time of the biopsy.

### Healthy Volunteers
Two groups of healthy volunteers were recruited at the same time as donors and recipients for hemodynamic and laboratory measurements. The first one was composed of an unselected population, as described in our previous works, and, thus, included nonrecipient-related (NRR) healthy volunteers. The second one was composed of recipient-related (RR) healthy volunteers who were recruited from the family of recipients, which was also the family of the related living donors. Clinical characteristics of both populations are indicated in Table 3. None of the NRR and RR healthy volunteers had a clinical or biological history of CV disease, chronic smoking habits, hypertension, diabetes mellitus, dyslipidemia, renal disease, connective tissue disease, or cancer, and they were not receiving any specific treatment at inclusion.

### Methods
Methods for the study of biological and hemodynamic parameters, including PWV measurement, have been published in detail else-
TABLE 3. Comparison of NRR Healthy Volunteers to the RR Healthy Volunteers

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NRR Healthy Volunteers (n=134)</th>
<th>RR Healthy Volunteers (n=129)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>43.8±13</td>
<td>43±8.2</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>74 (55.2%)*</td>
<td>46 (35.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>60 (44.8%)*</td>
<td>83 (64.3%)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.5±3.3†</td>
<td>27.5±4</td>
</tr>
<tr>
<td>BP (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>125.2±9.5</td>
<td>123.2±15.1</td>
</tr>
<tr>
<td>Diastolic</td>
<td>75.7±6.1†</td>
<td>78.5±10.6</td>
</tr>
<tr>
<td>Pulse</td>
<td>49.5±7.2†</td>
<td>44.7±10</td>
</tr>
<tr>
<td>MAP</td>
<td>92.2±7.2†</td>
<td>93.4±11.3</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>76.4±12</td>
<td>75.6±9.7</td>
</tr>
</tbody>
</table>

All values: mean±SD, except gender: n (%).
*P<0.001; †P<0.0001; ‡P<0.05.

where. Renal ultrasounds before nephrectomy and at the time of the study were performed by the same radiologist with an intraobserver repeatability coefficient of 0.91. Renal length was taken as the maximal bipolar measurement using real-time ultrasound scan. Hemodynamics were measured by a trained physician in the afternoon in the supine position. Each individual, the living donor, recipient, or healthy volunteer had a single hemodynamic determination. Aortic PWV was measured using a validated and highly reproducible automatic device (Complior, Colson), which calculates PWV from 2 transducers, one over the common carotid artery at the base of the neck and the other over the femoral artery. The distance covered between the 2 transducers was estimated as the direct distance over the skin between the 2 middle-transducer skin traces using a measuring tape. Because the pulse wave propagates in opposite directions at the carotid and femoral sites, superficial measurement of the distance causes an overestimation of true PWV in all of the subjects approximating 0.91±0.23 m/s. Comparisons of parameters among healthy volunteers, donors, and recipients were adjusted for age, sex, and MAP. All of the donor and recipient medical records were consulted, and preoperative parameters were obtained. Morning BP measurements (by the same registered nurse) for the last 3 preoperative days were averaged. Renal outcome was determined from recipient charts: acute rejection, doubling of serum creatinine, resumption of dialysis, and graft biopsy results, using parameters predefined elsewhere.

Statistical analysis was performed using NCSS 6.0.21 software (NCSS Statistical Software). Descriptive statistics were used to evaluate donor, recipient, and healthy volunteer characteristics. Simple regression was performed to evaluate linear associations between hemodynamic parameters, such as PWV and PP, renal function parameters, and other biological, morphological, and therapeutic variables. An evaluation of the nonlinearity of the age–PWV relationship was explored by introducing standardized age and the square of age in the various regressions: this research was constantly negative. All of the variables showing significant correlation with PWV, PP, and/or renal parameters, and those theoretically or historically related to these parameters, were integrated in a stepwise regression analysis with backward elimination to identify those independently associated with significant change in these parameters. The renal end point in the recipient population was the doubling of serum creatinine during posttransplant follow-up, as described previously; its determinants were assessed by multivariate logistic regression, taking as prior hypothesis that only subjects with chronic allograft nephropathy would have significant results.

Predonation versus postdonation donor parameters were compared using the paired Student t test. The unpaired 2-sided Student t test was used to compare normally distributed variables between donors and their controls and between donors and their recipients. Dummy variables were compared using the χ² test. A value of P≤0.05 was considered significant.

Results

For donors and recipients, clinical and biological parameters are presented in Tables 1 and 2. The corresponding drug therapy is indicated in a supplemental file.

Donor Parameters

Body mass index, systolic BP, diastolic BP, MAP, and, to a lesser extent, PP, showed significant increase at follow-up compared with predonation levels (Table 1). Plasma glucose and creatinine also increased significantly (P<0.0001). Heart rate decreased. The only significant change in antihypertensive therapy was in β-blocker use (P<0.028), corresponding to the mean reduction in hazard ratio; 4.9% of subjects were taking a calcium channel blocker at the time of the study. The mean size of the remaining kidney was 9.4% higher than the initial size. Aortic PWV was significantly higher in donors than in healthy volunteers, even after adjustment on age, gender, and MAP (Figure). PWV was, in RR volunteers, significantly higher than in NRR volunteers and lower than in living donors.

Factors Related to Donor Aortic PWV and PP at End of Follow-Up

The factors related to donor aortic PWV, evaluated at end of follow-up, were donor age, MAP, plasma glucose, smoking habits, and time since kidney donation (Table 4). Thus, age and time since donation were 2 independent factors to consider. Only age, gender, and MAP were associated with aortic PWV in RR and NRR healthy volunteers (data not shown).

![Figure 1. Aortic PWV (±SD) in living kidney donors and recipients by comparison with RR and NRR healthy volunteers (ANOVA adjusted on age, gender, and MAP). Comparisons between groups were all statistically (P<0.01) significant (NRR<RR<donors<recipients).](image-url)
In multiple regression analysis, the factors associated with donor PP evaluated at end of follow-up were exclusively PWV, and the presence of proteinuria and/or microalbuminuria ($R^2=32\%$; Table III, available online at http://hyper.ahajournals.org). On the other hand, analysis of proteinuria and/or microalbuminuria as a dependent variable revealed that their presence was related, not only to the end of follow-up PP, but also to time since donation (19% of total variance; Table IV, available online at http://hyper.ahajournals.org). MAP had no influence in this regard.

**Aortic PWV in Donors Versus Recipients**

There was a positive and significant univariate correlation ($r=0.30$; $P<0.003$) between aortic PWV within each donor versus recipient pair for the same kidney graft (data not shown). Recipients had significantly higher PWV ($11.4\pm2.4$ versus $10.3\pm2.5$ m/s; $P=0.001$) despite younger age ($42.2\pm12.6$ versus $49.7\pm12$ years; $P<0.0001$) and lower MAP ($84.5\pm11.6$ versus $97.7\pm13.5$ mm Hg; $P<0.0001$). After adjusting for age and MAP, the significance of the correlation between the donor and recipient’s PWV disappeared. Compared with RR and NRR healthy volunteers, PWV was increased ($P<0.0001$) in recipients after adjustment for age, sex, and MAP. PWV in recipients was significantly higher ($P<0.0001$) than in donors. Again, PWV was significantly higher in RR than in NRR healthy volunteers (Figure 1).

The factors related to recipient PWV were age, MAP, and smoking habits (as in donors), but also graft rejection, a factor obviously not shared by donors (Table 5). Nonsignificant in this regard were donor PWV and date of nephrectomy.

In recipients with chronic allograft nephropathy ($n=13$), doubling of the plasma creatinine at follow-up (renal end point) was associated with 2 factors (after adjustment on age; Table V, available online at http://hyper.ahajournals.org): acute rejection ($P=0.004$) and donor aortic PWV ($P=0.03$). This result was not observed when the totality of patient ($n=25$) doubling plasma creatinine was studied or when only subjects without allograft nephropathy ($n=12$) were studied.

**Discussion**

The salient findings of this study refer to living kidney donors and recipients, in that order. In donors at the end of the follow-up, the factors associated with PWV and PP were specifically of renal origin: time since donation, in the case of PWV, and presence of proteinuria and/or microalbuminuria, in the case of PP. In recipients, PWV was significantly increased, with graft rejection as a significant determinant. There were also 2 main factors related to the serum creatinine doubling at follow-up: graft rejection and donor aortic PWV. Taken together, such findings strongly suggest consistent interactions between kidney function and arterial tissue elasticity.

In the present investigation, PWV was used as a marker of large artery stiffness, because this parameter is related to the square root of the aortic elasticity modulus and to the corresponding arterial thickness/radius ratio. Repeatability studies, checks made with Bland and Altman diagrams, and modern computer technology have now made PWV a feasible parameter for epidemiologic investigation of aortic stiffness.

Because, in the present study, the main determinants were age

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**TABLE 4. Living Donor Population (n=101): Determinants of Aortic PWV**

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\beta$ Coefficient±SE of $\beta$</th>
<th>$P$ Value</th>
<th>Individual Contribution to Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor age (y)</td>
<td>0.09±0.015</td>
<td>&lt;0.0001</td>
<td>32.6%</td>
</tr>
<tr>
<td>Time postdonation (months)</td>
<td>0.01±0.004</td>
<td>0.02</td>
<td>6.4%</td>
</tr>
<tr>
<td>Smoking (dummy variable)</td>
<td>0.7±0.3</td>
<td>0.03</td>
<td>2%</td>
</tr>
<tr>
<td>MAP2 (mm Hg)</td>
<td>0.07±0.012</td>
<td>&lt;0.0001</td>
<td>13.6%</td>
</tr>
<tr>
<td>Plasma glucose 2 (mg/dL)</td>
<td>0.07±0.015</td>
<td>&lt;0.0001</td>
<td>8.3%</td>
</tr>
</tbody>
</table>

MAP2 indicates mean arterial pressure at end of follow-up; Plasma glucose 2, fasting blood sugar at end of follow-up; $R^2$, total contribution to variance. Univariate correlations showed that donor PWV: (1) did not correlate significantly with sex and lipid profile, but sex was included in the final model; and (2) did correlate significantly with the presence of proteinuria and/or microalbuminuria, antihypertensive treatment, statin therapy, waist/hip ratio, plasma creatinine, and recipient aortic PWV, but all this significance disappeared in multiple regression analysis.

**TABLE 5. Recipients (n=101): Determinants of Aortic PWV**

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\beta$ Coefficient±SE of $\beta$</th>
<th>$P$ Value</th>
<th>Individual Contribution to Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>0.08±0.015</td>
<td>&lt;0.0001</td>
<td>25%</td>
</tr>
<tr>
<td>MAP at time of study (mm Hg)</td>
<td>0.056±0.013</td>
<td>&lt;0.0001</td>
<td>12.5%</td>
</tr>
<tr>
<td>Acute rejection (dummy variable)</td>
<td>1.2±0.5</td>
<td>0.01</td>
<td>5%</td>
</tr>
<tr>
<td>Smoking (pack/y)</td>
<td>0.01±0.008</td>
<td>0.02</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

$R^2$ indicates total contribution to variance. Univariate correlations showed that recipient PWV: (1) did not correlate significantly with sex, transplant age, and lipid profile, but sex was included in the final model; and (2) did correlate significantly with the presence of proteinuria and/or microalbuminuria, antihypertensive treatment, dialysis duration, waist/hip ratio, plasma creatinine, and donor aortic PWV, but the significance of correlations disappeared in multiple regression analysis.
and MAP and never involved the square meter of age, we constantly adjusted for both of these parameters in our study. Because living donors were mainly composed of women (Table 1), all of the results were adjusted to gender. The statistical analysis revealed smoking and plasma glucose as significant determinants in both donors and recipients. Thus, a cluster of CV risk factors involving age, smoking habits, diabetes, and MAP were combined to determine PWV in both these groups. This profile differed consistently from that in healthy controls. In particular, in donors investigated ≥3 years after nephrectomy, the combined variance because of smoking and plasma glucose was ≈10% (Table 4).

Because, as is commonly observed in the Middle East countries, living donors and recipients had frequently a familial heredity, and because this heredity was mainly transmitted by women (Table 1), the role of familial factors in the mechanism of increased PWV was important to discriminate. For this purpose, PWV was measured in 2 populations of healthy volunteers, one being RR and the other NRR. We identified that both living donors and recipients had a significant increase in PWV by comparison with healthy volunteers but also that RR volunteers had a significantly higher value of PWV by comparison with NRR volunteers, on one hand, and a significantly lower value by comparison with donors or recipients, on the other hand. These findings suggest that familial factors, either genetic or environmental in origin, might play a role in the mechanism of the PWV level. Because in recipients, donor aortic PWV was associated with the doubling of plasma creatinine in subjects with chronic allograft nephropathy, the role of hereditary factors seems likely. Transmitted genetic factors have been widely described after either experimental or human transplantation.

A dominant finding of this study was that, in the donor population, aortic PWV correlated positively and independently with the interval between donation and end of follow-up. A contributory factor is that, in both animals and humans, kidney size increases significantly, and preglomerular arteriolar resistance decreases in response to unilateral nephrectomy, resulting in greater fractional transmission to the kidney of ambient systemic BP. In most cases, arteriolar vasodilatation is not accompanied by substantial impairment of renal autoregulation, severe hypertension, or an age-related loss of kidney function. Under these conditions, only modest renovascular impairment is expected. Such a slight change may account for the largely benign outcome in most uninephrectomized individuals, as those in the present study. Indeed, our donors were, by definition, in excellent health, with even the prospect of a longer life span. However, it is worth noting that in some uninephrectomized subjects, additional factors may accelerate glomerular transmission of ambient systemic BP. In the present study, most such factors are accounted for by the cluster of age, diabetes (5.6% of subjects), clinical or biochemical markers of metabolic syndrome (28.7% of subjects), smoking habits, or even arteriolar preglomerular vasodilatation because of chronic administration of calcium channel blockers (4.9% of subjects; Table 1). These changes appeared after nephrectomy at long-term follow-up. Their gradual development explains the significant and positive association between PWV and the “age” of unilateral nephrectomy and, finally, the increased values by comparison with age, sex, and MAP-adjusted healthy volunteers. These simple observations point to a possible link between the kidney and arterial tissue elasticity, particularly in subjects with uninephrectomy.

Another result provided an even more consistent link between renal function and conduit artery stiffness: the positive, independent, and significant relationship between PP and macroalbuminuria and/or microalbuminuria. In uninephrectomized subjects, the transmission of cyclic BP to the glomerulus is a dynamic process, which, by definition, is frequency dependent. In the presence of reduced preglomerular arteriolar resistance, fluctuations of microvascular pressure and, particularly, PP have a greater pathophysiologic role than sustained and steady MAP. The recent demonstration in animals of unusually rapid activation kinetics of the different arteriolar myogenic responses of the kidney is consistent with this simple observation. A similar finding between PP and proteinuria is observed in subjects with essential hypertension and mainly in subjects with systolic hypertension in the elderly.

In this study, aortic PWV was investigated in 3 different populations: normotensive healthy controls, living donors, and transplanted patients. The latter 2 cohorts were investigated on the basis of the presence of renal transplantation and, therefore, of quite similar renal structure, function, and genotype in donors and recipients. Thus, the present study cannot be described as totally cross-sectional. Aortic PWV was increased in donors and recipients compared with healthy volunteers, even after adjustment on confounders. In the 3 populations, the main determinants of PWV were age and MAP. However, in both donors and recipients, smoking was an additional factor compared with controls, and constituted, in association with age, MAP and possibly diabetes, a cluster of CV risk factors, which have been consistently identified as associated with PWV. But we also discovered renal factors related to PWV. These had never been observed previously in large unselected epidemiologic populations. They consisted of proteinuria and/or time since donation in donors and graft rejection, hence, renal damage, in recipients. Because graft rejection and donor PWV were independent determinants of renal failure progression in recipients, all of these results taken together suggest possible genetic links between arterial status in donors and vascular and renal changes in recipients. The arterial elasticity-mediated changes in kidney function may be either intrinsic to the arteries and/or related to metabolic or hormonal disorders associated with increased arterial stiffness. Because CV events currently represent a dominant risk in long-term renal graft survival and because increased PP is an independent CV risk factor in these patients, clinical, experimental, and genetic studies are needed to identify the precise links between such factors and large artery pathophysiology.

Perspectives

The present results involve 2 different perspectives: the first one is related to recipients of kidney graft and the second one to living donors. It seems likely that in patient survival, not
only the kidney is important but also the vascular system. Whether the changes in the large arterial system in kidney recipients are because of the immunologic conflict, the drug treatment, or one or several particularities of the living donors remains to be established and may play an important role in CV risk. Regarding the living donors, for a long time their survival was considered comparable to, if not better than, that of subjects with 2 kidneys. This study is the first to show that increased PWV, a marker of CV risk, may be elevated along the life of donors by comparison with healthy controls. This finding will have to be verified by long-term follow-up. The environmental and genetic relationship between the recipient and the donor on the kidney and the CV system should be studied together prospectively.

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**References**


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