Aortic–Brachial Pulse Wave Velocity Ratio
A Blood Pressure–Independent Index of Vascular Aging

Catherine Fortier, Aboubacar Sidibé, Marie-Pier Desjardins, Karine Marquis, Sacha A. De Serres, Fabrice Mac-Way, Mohsen Agharazii

Abstract—Aortic stiffness, a cardiovascular risk factor, depends on the operating mean arterial pressure (MAP). The impact of aortic stiffness on cardiovascular outcomes is proposed to be mediated by the attenuation or the reversal of the arterial stiffness gradient. We hypothesized that arterial stiffness gradient is less influenced by changes in MAP. We aimed to study the relationship between MAP and aortic stiffness, brachial stiffness, and arterial stiffness gradient. In a cross-sectional study of a dialysis cohort (group A, n=304) and a cohort of hypertensive or kidney transplant recipient with an estimated glomerular filtration rate of >45 mL/min/1.73 m² (group B, n=114), we assessed aortic and brachial stiffness by measuring carotid–femoral and carotid–radial pulse wave velocities (PWV). We used aortic–brachial PWV ratio as a measure of arterial stiffness gradient. Although there was a positive relationship between MAP and carotid–femoral PWV ($R^2=0.10$ and 0.08; $P<0.001$ and $P=0.003$) and MAP and carotid–radial PWV ($R^2=0.22$ and 0.12; $P<0.001$ and $P<0.001$), there was no statistically or clinically significant relationship between MAP and aortic–brachial PWV ratio ($R^2=0.0002$ and 0.0001; $P=0.8$ and $P=0.9$) in group A and B, respectively. Dialysis status and increasing age increased the slope of the relationship between MAP and cf-PWV. However, we found no modifying factor (age, sex, dialysis status, diabetes mellitus, cardiovascular disease, and class of antihypertensive drugs) that could affect the lack of relationship between MAP and aortic–brachial PWV ratio. In conclusion, these results suggest that aortic–brachial PWV ratio could be considered as a blood pressure–independent measure of vascular aging. (Hypertension. 2017;69:96-101. DOI: 10.1161/HYPERTENSIONAHA.116.08409.) • Online Data Supplement

Key Words: aorta • arterial pressure • arterial stiffness • hemodynamics • pulse wave velocity

Aortic stiffness, as measured by carotid–femoral pulse wave velocity (cf-PWV), has been associated with increased risk of cardiovascular events, mortality, and overall mortality in various groups of subjects.1–5 From a mechanistic point of view, although the impact of aortic stiffness on the myocardium is explained by increased cardiac workload and reduced coronary perfusion, the peripheral target organ damage is best explained by the arterial stiffness gradient hypothesis.6 Indeed, because of the heterogeneity of vascular wall composition and diameter, there is an increase in arterial stiffness (stiffness gradient) from the heart to the periphery. This gradient in arterial stiffness results in a gradual attenuation of forward pressure wave throughout its passage along the arterial tree down to the microcirculation, where the pulsatility is minimal. As aorta stiffness, there is attenuation and then reversal of the stiffness gradient, resulting in the lack of attenuation of the forward travelling wave pressure, and higher pulse pressure transmission into the microcirculation. This leads to vascular myogenic response, endothelial dysfunction, hypoperfusion, and organ damage.5–7 Indeed, recent studies underline the importance of vascular stiffness gradient on both blood flow and clinical outcomes.8–10

One of the limitations of aortic stiffness is that it is highly related to the operational mean arterial pressure (MAP). Although cf-PWV of a cohort could be adjusted for the group’s MAP by use of linear regression, there are limitations to such an approach. First, the pressure–diameter relationship is curvilinear. Second, the pressure–diameter curve differs among individuals because of variations in genetic background and exposure to environmental risk factors, which contribute to the cumulative changes in the arterial wall structure.

To study the impact of arterial stiffness gradient on mortality, we examined and found that aortic–brachial pulse wave velocity ratio (aortic–brachial PWV ratio) was better than cf-PWV in predicting mortality in a multivariable adjusted model in a dialysis population.11 Because both aortic and brachial stiffness are influenced in a similar manner with MAP, we hypothesized that aortic–brachial PWV ratio is not significantly affected by MAP and hence could be of additional value in clinical practice. Therefore, the
Objective of the present study was to examine the relationship between MAP and aortic stiffness, brachial stiffness, and arterial stiffness gradient as measured by aortic–brachial PWV ratio.

Methods

Study Design and Patient Population
This is a cross-sectional analysis of 2 cohorts of adult patients. The 2 cohorts were drawn from studies on vascular stiffness that were conducted at the CHU de Québec research center from 2006 to 2015. Group A (n=304) was composed of patients with end-stage renal disease treated by dialysis, and group B (114) was composed of all patients with an estimated glomerular filtration rate of >45 mL/min/1.73 m², who were either hypertensive patients (n=53) or kidney transplant recipient (n=61). For detailed Methods, please see online-only Data Supplement.

Hemodynamic Measurements
Hemodynamic measurements were performed after 15 minutes of rest in a supine position. Brachial artery blood pressure (BP) was recorded using an automatic oscillometric sphygmomanometer BPM-100 (BP-Tru, Coquitlam, Canada) by an experienced operator who was present in the room.11 Immediately after BP measurements, we determined cf-PWV and carotid–radial pulse wave velocity (cr-PWV) in triplicates.13,14 Aortic–brachial PWV ratio was calculated by the ratio of cf-PWV and cr-PWV (PWV ratio=cf-PWV/cr-PWV). For comparison, we also reported the standard cf-PWV, which was obtained taking into account differences in the transit time using the maximal upstroke algorithm and the overestimation of true distance obtained using the generalized transfer function.16 For detailed hemodynamic methods, please see online-only Data Supplement.

Statistical Analysis
Data are expressed as mean±SD, n (%), or median (25th–75th percentiles). t Test for independent samples and Mann–Whitney U test were used as appropriate to compare hemodynamic parameters between groups A and B. Linear and quadratic regressions were used to determine the relationship between PWVs, aortic–brachial PWV ratio, and age as appropriate. Linear regressions were used in univariate to assess the relationships between MAP and cf-PWV, cr-PWV, and aortic–brachial PWV ratio in each group of patients and in multivariate to adjust for potential confounders. Before combining the 2 groups, heterogeneity was examined by assessing the statistical significance of an interaction term between MAP and groups. Effect modification (departure from additivity) of sex, groups, and age in the relation between MAP and cf-PWV, cr-PWV, aortic–brachial PWV ratio was examined by introducing an interaction term between MAP and the variable under consideration in the linear regression models. The modification effect was tested in minimal adjusted models and fully adjusted models by assessing the significance of the interaction term described above. When applicable, MAP and age were used as continuous variables. The fully adjusted models include age, sex, groups, cardiovascular disease, and diabetes mellitus as covariates. Assumptions of linearity, colinearity, homoscedasticity, and outliers have been assessed in every model. The sandwich robust estimator (White) was used to correct the lack of homoscedasticity when needed. A quadratic trend was observed in all models assessing the association between MAP and cr-PWV or aortic–brachial PWV ratio, and in the minimal adjusted model testing the effect modification of sex in cf-PWV. Thus, a quadratic term (MAP squared) and its interaction with the variable of interest were used for correction. All statistical analyses were performed in SAS version 9.4. A 2-tailed P value <0.05 was considered to be statistically significant.

Results

Baseline Characteristics
Table 1 shows demographic, clinical, pharmacological, and biological characteristics of patients in groups A, B, and overall. Table 2 shows peripheral and central BP parameters, aortic

Table 1. Characteristics of Patients for Group A, Group B, and Overall

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A</th>
<th>Group B</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dialysis</td>
<td>eGFR &gt;45 mL/min/1.73 m²</td>
<td>Overall</td>
</tr>
<tr>
<td>Male sex</td>
<td>n=304</td>
<td>n=114</td>
<td>n=418</td>
</tr>
<tr>
<td>Age, y</td>
<td>65 (57–77)</td>
<td>53 (46–62)</td>
<td>64 (52–73)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>74.8±17.3</td>
<td>77.6±15.6</td>
<td>75.6±16.9</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.6±5.6</td>
<td>27.3±4.6</td>
<td>27.5±5.4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>277 (91)</td>
<td>96 (64)</td>
<td>373 (89)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>133 (44)</td>
<td>21 (18)</td>
<td>154 (37)</td>
</tr>
<tr>
<td>CVD</td>
<td>162 (53)</td>
<td>15 (13)</td>
<td>177 (42)</td>
</tr>
<tr>
<td>Dialysis vintage, y</td>
<td>1.5 (0.5–3.3)</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Dialysis modality*</td>
<td>63 (21)</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Peritoneal</td>
<td>241 (79)</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>130 (43)</td>
<td>68 (60)</td>
<td>198 (47)</td>
</tr>
<tr>
<td>Medication</td>
<td>104 (34)</td>
<td>62 (54)</td>
<td>166 (40)</td>
</tr>
<tr>
<td>ACEi/ARB</td>
<td>170 (56)</td>
<td>30 (26)</td>
<td>200 (48)</td>
</tr>
<tr>
<td>CCB</td>
<td>192 (63)</td>
<td>48 (42)</td>
<td>240 (57)</td>
</tr>
<tr>
<td>L–Blockers</td>
<td>190 (63)</td>
<td>64 (56)</td>
<td>254 (61)</td>
</tr>
<tr>
<td>Statins</td>
<td>3.87±0.96</td>
<td>4.73±1.08</td>
<td>4.10±1.06</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>0.99 (0.80–1.30)</td>
<td>1.34 (1.07–1.65)</td>
<td>1.06 (0.83–1.40)</td>
</tr>
<tr>
<td>HDL, mmol/L</td>
<td>1.93±0.75</td>
<td>2.51±0.90</td>
<td>2.08±0.83</td>
</tr>
<tr>
<td>LDL, mmol/L</td>
<td>1.65 (1.19–2.25)</td>
<td>1.49 (1.12–2.08)</td>
<td>1.58 (1.17–2.32)</td>
</tr>
</tbody>
</table>

Results are given as means±SD, n (%), or median (25th–75th percentiles). ACEi indicates angiotensin-converting enzyme inhibitors, ARB, angiotensin receptor blockers; ASA, acetylsalicylic acid; CCB, calcium channel blockers; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein, LDL, low-density lipoprotein; and TG, triglycerides.

*Percentage based on dialysis patients only.
stiffness, brachial stiffness, and aortic–brachial PWV ratio in each group and overall.

As presented in Figure 1, age was associated with a higher cf-PWV and a lower cr-PWV in group A. In group B, cf-PWV increased with age but with a smaller slope than that in group A. However, cr-PWV had a quadratic relationship with age and tended to decrease after the fifth decade. Overall, the relationship between aortic–brachial PWV ratio and age was linear in both groups, albeit with a steeper slope in group A. In group A, standardized β of age was 0.516 and 0.596 for cf-PWV and aortic–brachial PWV ratio, respectively (Table S1 in the online–only Data Supplement). In group B, standardized β of age was 0.514 for cf-PWV and 0.441 for aortic–brachial PWV ratio.

MAP Relationships With PWVs and Aortic–Brachial PWV Ratio

Figure 2 shows a significant positive relationship between cf-PWV, cr-PWV, and MAP in both groups. However, there were no clinically or statistically significant relationship between aortic–brachial PWV ratio and MAP in either group of patients.

Conditions Affecting MAP Relationship With PWVs and Aortic–Brachial PWV Ratio

Group A and age increased the effect of MAP on the cf-PWV but not on the cr-PWV and aortic–brachial PWV ratio (Table 3). The group– and age–interaction effect on cf-PWV remained significant in the fully adjusted model 2. We did not identify any modifying effect of cardiovascular disease, hypertension, or diabetes mellitus status on the relationship between MAP and cf-PWV and cr-PWV using various models. None of these factors affected the lack of relationship between MAP and aortic–brachial PWV ratio. We further examined and found no modifying effect of medication (angiotensin-converting enzyme inhibitors/angiotensin receptor blockers or calcium channel blockers) on the absence of relationship between MAP and aortic–brachial PWV ratio.

Discussion

This study shows that aortic–brachial PWV ratio, which is a measure of arterial stiffness gradient, is independent of MAP, potentially making it an ideal indicator of vascular aging and risk stratification. Contrary to cf-PWV, clinical conditions such as group of patients and age did not have a significant impact on the lack of relationship between MAP and aortic–brachial PWV ratio. Various sensitivity analyses showed that cardiovascular disease, hypertension, diabetes mellitus status, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and calcium channel blockers did not affect the lack of relationship between aortic–brachial PWV ratio and MAP. Furthermore, the extent of the association between age and aortic–brachial PWV ratio were similar to the association of age with cf-PWV, in both groups of patients.

The relationship between arterial stiffness and MAP is indeed complex. Increase in MAP results in an increase in vessel diameter and puts the blood vessel in a less optimal pressure–diameter relationship, where the energy is transferred from the elastic elastin lamella to the stiffer collagen, and smooth muscle cells. Using reference pressure and diameter, Hayashi et al17 proposed stiffness index β0, which is considered to reflect a pressure-independent local stiffness index. However, the clinically derived stiffness β is slightly different than β0, as the reference pressure and diameter are replaced by diastolic pressure and diameter, and instantaneous pressure change is replaced with systolic pressure. Stiffness index β is, therefore, a relatively good approximation for the blood pressure–independent arterial stiffness in the assessment of local stiffness of superficial vessels, where pressure and diameter can be assessed by arterial tonometry and ultrasound. Building on these assumptions, cardio–ankle vascular index has been proposed as a pressure-independent stiffness index over the vascular tree from the heart to the ankle.18 The calculation of cardio–ankle vascular index incorporates both systolic and diastolic brachial blood pressures in a similar manner as in calculation of β. However, there are some limitations because arterial stiffness is heterogeneous, and there is an amplification of systolic blood pressure from heart to the periphery. To

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**Table 2. Hemodynamic Parameters**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A</th>
<th>Group B</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=304</td>
<td>n=114</td>
<td>n=418</td>
</tr>
<tr>
<td><strong>Peripheral hemodynamic parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg*</td>
<td>131.2±25.7</td>
<td>123.3±16.7</td>
<td>129.0±23.8</td>
</tr>
<tr>
<td>DBP, mm Hg*</td>
<td>70.5±13.1</td>
<td>74.2±10.7</td>
<td>71.5±12.6</td>
</tr>
<tr>
<td>MAP, mm Hg†</td>
<td>91.6±14.7</td>
<td>90.8±12.5</td>
<td>91.2±15.7</td>
</tr>
<tr>
<td>PP, mm Hg*</td>
<td>60.6±21.2</td>
<td>49.1±12.3</td>
<td>57.5±19.9</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>68.6±10.7</td>
<td>68.6±12.2</td>
<td>68.6±11.1</td>
</tr>
<tr>
<td><strong>Central hemodynamic parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cSBP, mm Hg*</td>
<td>120.7±25.1</td>
<td>111.3±16.9</td>
<td>118.2±23.5</td>
</tr>
<tr>
<td>cDBP, mm Hg*</td>
<td>71.5±13.3</td>
<td>79.1±10.6</td>
<td>72.6±12.8</td>
</tr>
<tr>
<td>cPP, mm Hg*</td>
<td>49.2±20.2</td>
<td>36.0±12.0</td>
<td>45.6±19.3</td>
</tr>
<tr>
<td>AIX@75, %*</td>
<td>26.7±11.0</td>
<td>16.7±12.8</td>
<td>24.0±12.3</td>
</tr>
<tr>
<td>SEVR, %*</td>
<td>135.5±31.1</td>
<td>154.0±31.2</td>
<td>140.4±32.2</td>
</tr>
<tr>
<td><strong>Pulse wave velocities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cf-PWV, m/s*</td>
<td>13.58±4.06</td>
<td>10.84±1.98</td>
<td>12.83±3.81</td>
</tr>
<tr>
<td>cr-PWV, m/s*</td>
<td>8.67±1.64</td>
<td>9.05±1.19</td>
<td>8.78±1.54</td>
</tr>
<tr>
<td>Aortic–brachial PWV ratio*</td>
<td>1.61±0.51</td>
<td>1.21±0.23</td>
<td>1.50±0.49</td>
</tr>
</tbody>
</table>

Results are given as means±SD or median (25th–75th percentiles). t Test and Mann–Whitney U test were used as appropriate. Significant if P<0.01. AIX@75 indicates augmentation index adjusted for heart rate; cDBP, central diastolic blood pressure; cf-PWV, carotid–femoral pulse wave velocity; cPP, central pulse pressure; cr-PWV, carotid–radial pulse wave velocity; cSBP, central systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; PWV, pulse wave velocity; SBP, systolic blood pressure; and SEVR, subendocardial viability ratio.

*Difference between groups A and B statistically different with P<0.01.†MAP was obtained by radial artery tonometry after calibration for peripheral SBP and DBP.
circumvent this problem for aortic stiffness, the Reference Values for Arterial Stiffness’ Collaboration has taken into account the hypertension stage and the age of subjects.15 Although aortic stiffness is generally the driving force in the attenuation and reversal of arterial stiffness gradient, as the stiffness of muscular conduit arteries are less affected by age, studies suggest that stiffness of medium-sized muscular conduit vessels may decrease with age and in conditions of accelerated vascular aging, such as in chronic kidney disease and diabetes mellitus.13,19–21 In the present study, we showed a negative linear relationship between brachial stiffness and age in the dialysis group. This is in line with the findings of a repeated measurement study in a dialysis cohort, where cr-PWV decreased despite a progression of aortic stiffness.13 However, in the group with estimated glomerular filtration rate >45 mL/min/1.73 m², the relationship with age was quadratic, declining slightly after the fifth decade. Indeed, the arterial tree’s response to aging and accelerated aging conditions is not uniform and depends on sex, exposure to specific risk factors, and the vascular territory.19 For example, aorta and carotid become stiff at an earlier age, whereas femoral stiffness is more sex dependent and remains relatively stable until the fifth or sixth decade of life.22

In the present study, we explored this heterogeneous nature of arterial stiffness, which also integrates the physiological concept of arterial stiffness gradient. The lack of relationship between MAP and aortic–brachial PWV ratio was tested in

![Figure 1. Relationship between vascular stiffness parameters and age. The figure shows the relationship between age and (A) carotid–femoral pulse wave velocity (cf-PWV), (B) carotid–radial pulse wave velocity (cr-PWV), and (C) aortic–brachial pulse wave velocity ratio (PWV ratio) as measured by the cf-PWV/cr-PWV ratio in a group of patients on dialysis (n=304, open circles) and a group of patients with an estimated glomerular filtration rate of >45 mL/min/1.73 m² (n=114, filled circles).](image)

![Figure 2. Relationships between mean arterial pressure (MAP), aortic stiffness, brachial stiffness, and arterial stiffness gradient. In a group of patients with end-stage renal disease on dialysis (group A, n=304), there is a positive relationship between MAP and carotid–femoral pulse wave velocity (cf-PWV; A) and carotid–radial pulse wave velocity (cr-PWV; B) but no relationship with aortic–brachial pulse wave velocity ratio (PWV ratio; C). Similar findings are shown for a group of patients with an estimated glomerular filtration rate of >45 mL/min/1.73 m² (group B, n=114) in panels D through F.](image)
2 different cohorts that were completely different in terms of age, renal function, and comorbidities. The various modeling and sensitivity analyses make a strong case about the robustness of our findings. However, there are some limitations that need to be addressed. First, because major reflecting sites originate from the lower part of the body, the absolute hemodynamic impact of aortic–brachial PWV ratio is believed to be relatively limited. Second, the measurements of aortic and brachial PWV were performed while patients were taking their usual antihypertensive drugs. Although we sought to examine the modifying effect of major classes of drugs on the lack of relationship between MAP and aortic–brachial PWV ratio, the impact of antihypertensive drugs on aortic–brachial PWV ratio was beyond the scope of the present study. Finally, our conclusions are based on the observations from a cohort of mostly middle-aged to elderly subjects who were treated with antihypertensive drugs.

**Perspectives**

We have previously shown that aortic–brachial PWV ratio was a better predictor of overall mortality than aortic stiffness alone.\(^1^1\) In this study, we show that aortic–brachial PWV ratio is independent of blood pressure, which is a major advantage over the classical aortic PWV. Whereas other BP-independent or BP-adjusted parameters, such as stiffness index $\beta$ and cardio-ankle vascular index, are based on complex mathematical analysis that are less intuitive for clinician and have the inherent limitations that have been discussed above. In this context, aortic–brachial PWV ratio is possibly more suitable as a blood pressure–independent parameter of vascular aging. However,
the impact of arterial stiffness gradient using muscular vascular bed and its impact on microcirculatory forward pressure and flow pulsatility, with or without antihypertensive drugs, need to be assessed in future studies. Finally, these findings need to be confirmed in a younger population without antihypertensive drugs.

Acknowledgments

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Disclosures

None.

References


Novelty and Significance

What Is New?

Aortic stiffness is a cardiovascular risk factor. This study shows that, contrary to aortic stiffness, aortic–brachial stiffness ratio, which is related to arterial stiffness gradient, is independent of blood pressure.

What Is Relevant?

Aortic–brachial stiffness ratio could potentially be used as a blood pressure-independent index of vascular aging.

Summary

Although aortic stiffness is a cardiovascular risk factor, its effect is partly driven through its impact on the attenuation or reversal of arterial stiffness gradient and its subsequent pulse pressure transmission into the microcirculation. However, aortic stiffness is blood pressure dependent. In this study, we show that the ratio between aortic and brachial stiffness, which explores arterial stiffness gradient, is independent of blood pressure. This lack of relationship was tested in 2 distinct groups, and multiple sensitivity analysis demonstrated the robustness of this finding.
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TITLE: AORTIC-BRACHIAL PULSE WAVE VELOCITY RATIO: A BLOOD PRESSURE INDEPENDENT INDEX OF VASCULAR AGING.

Running title: PWV ratio and blood pressure

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SUPPLEMENTAL METHODS

Study design and patient population
This is a cross-sectional analysis of two cohorts of adult patients. The two cohorts were drawn from studies on vascular stiffness that were conducted at the CHU de Québec research center from 2006-2015. Group A was composed of patients with end-stage renal disease treated by dialysis, and Group B was composed of all patients with an estimated eGFR of > 45ml/min/1.73m². These studies had been approved by the comité d’éthique de la recherche du CHU de Québec and were conducted in accordance with the Declaration of Helsinki. All procedures followed were in accordance with institutional guidelines and each patient had provided informed written consent. The inclusion criteria were adult patients with stable blood pressure medication. In Group A, additional inclusion criteria were chronic dialysis (>3 months), stable dry weight, single-pool KT/V >1.4. In group B, additional inclusion criteria were an eGFR of > 45ml/min/1.73m² from either hypertension clinic (n=53) or kidney transplant clinic (n=61, approximately 6 months following a kidney transplantation). Patients were excluded if they had an acute episode of illness (infection, recent cardiovascular events or acute rejection) or unreliable or unavailable measurements of either aortic or brachial stiffness (16 from Group A and 2 from Group B (transplant recipients).

Hypertension was defined as blood pressure ≥140/90 mm Hg or the use of antihypertensive medications in patients with a history of hypertension. Cardiovascular disease was defined as myocardial infarction, coronary artery revascularization or ischemic heart disease as shown by either a treadmill, echo or thallium stress tests, myocardial infarction, lower extremity amputation or revascularization.

Hemodynamic measurements
Hemodynamic measurements were performed after 15 minutes of rest in a supine position prior to the mid-week dialysis session in group A. In case of an arterio-venous fistula, measurements were performed on the contralateral arm. Brachial artery blood pressure (BP) was recorded using an automatic oscillometric sphygmomanometer BPM-100 (BP-Tru, Coquitlam, Canada) by an experienced operator who was present in the room. BP was recorded 6 times, with a 2-minutes interval between each measurement, and the average of the last 5 measurements was used to determine the brachial systolic blood pressure (SBP) and diastolic blood pressure (DBP) 1. Immediately after BP measurements, we determined carotid-femoral pulse wave velocity (cf-PWV) and carotid-radial pulse wave velocity (cr-PWV) in triplicates by Complior® SP (Artech Medical, Pantin - France), using the maximal upstroke algorithm as previously described 2,3. Aortic-brachial PWV ratio was calculated by the ratio of cf-PWV and cr-PWV (PWV ratio = cf-PWV/cr-PWV). In tables, we have also reported the standard cf-PWV, which was obtained taking into account differences in the transit time using the maximal upstroke algorithm and the overestimation of true distance by multiplying direct distance by 0.8 4. MAP was obtained by applanation tonometry of the radial artery after calibration with brachial SBP and DBP (SphygmoCor system®, AtCor Medical Pty. Ltd., Sydney, Australia). Central systolic pressure (cSBP), central diastolic pressure (cDBP), central pulse pressure (cPP), augmentation index adjusted for heart rate (AIx@75), and subendocardial viability ratio (SEVR) of the central pulse wave profile were obtained using the generalized transfer function 5.
SUPPLEMENTAL REFERENCES


### SUPPLEMENTAL TABLE

#### Table S1: Relationship between vascular stiffness parameters and age

<table>
<thead>
<tr>
<th>Dependant variables</th>
<th>Groups</th>
<th>Independent variables</th>
<th>Slope (95% CI)</th>
<th>Standardized β</th>
<th>Model R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>cf-PWV</td>
<td>Group A</td>
<td>Age</td>
<td>0.144 (0.117 – 0.172)</td>
<td>0.516</td>
<td>0.266</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>Age</td>
<td>0.076 (0.053 – 0.100)</td>
<td>0.514</td>
<td>0.264</td>
</tr>
<tr>
<td>cr-PWV</td>
<td>Group A</td>
<td>Age</td>
<td>-0.027 (-0.040 – -0.015)</td>
<td>-0.243</td>
<td>0.059</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>Age</td>
<td>-0.024 (-0.057 – 0.009)</td>
<td>-0.267</td>
<td>0.068</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Age²</td>
<td>-1.24 x10⁻³ (-2.30 x10⁻³ – -1.81 x10⁻⁴)</td>
<td>-0.430</td>
<td></td>
</tr>
<tr>
<td>PWV ratio</td>
<td>Group A</td>
<td>Age</td>
<td>0.021 (0.018 – 0.024)</td>
<td>0.596</td>
<td>0.356</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>Age</td>
<td>0.008 (0.005 –0.011)</td>
<td>0.441</td>
<td>0.195</td>
</tr>
</tbody>
</table>

Univariate regressions (linear or quadratic) with robust estimator.

cf-PWV: carotid-femoral pulse wave velocity, cr-PWV: carotid-radial pulse wave velocity,
Group A: on dialysis (N=304), Group B: with an eGFR>45ml/kg/1.73m² (N=114), PWV ratio: aortic-brachial pulse wave velocity ratio.