Original Article

Aortic Pulse Wave Velocity and Carotid-Femoral Pulse Wave Velocity: Similarities and Discrepancies

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The objectives of this study were to determine the relationship between carotid-femoral (cfPWV) and aortic pulse wave velocity (aPWV) and to compare their modulators and association with coronary artery disease (CAD). We studied 107 consecutive patients (68 men) with a mean age of 60.49±8.31 years who had stable angina and had been referred for coronary angiography. cfPWV and aPWV were measured simultaneously during cardiac catheterization using the Complior® device and aortic pressure waveform recordings, respectively. Based on the presence or absence of significant coronary artery stenosis (CAS) patients were subdivided into a CAS+ or CAS– group. The mean values of cfPWV and aPWV were 10.65±2.29 m/s and 8.78±2.24 m/s, respectively. They were significantly higher in the CAS+ (*n*=71) compared with the CAS– (*n*=36) group and predicted significant CAS independently of cardiovascular risk factors and mean or systolic aortic blood pressure. aPWV and cfPWV were significantly correlated (*r*=0.70; *p*<0.001) but the degree of correlation differed significantly (*p*<0.03) between the CAS+ (*r*=0.74, *p*<0.001) and CAS– group (*r*=0.46, *p*=0.003). Age and mean aortic blood pressure were independent predictors for aPWV as well as cfPWV. In the receiver operating characteristic (ROC) analysis, aPWV and cfPWV had similar accuracy in identification of significant CAS (AUC [area under the ROC curve]=0.76 and 0.69, respectively; *p*=0.13). However, neither cfPWV nor aPWV was effective at differentiating the extent of CAD. In conclusion, aPWV and cfPWV are highly correlated parameters with similar determinants and comparable accuracy in predicting significant CAS. The strength of correlation between these two indices differed significantly between subjects with and those without CAS. (*Hypertens Res* 2007; 30: 1151–1158)

***Key Words*: aortic pulse wave velocity, carotid-femoral pulse wave velocity, stiffness, coronary artery disease**

Introduction

Carotid-femoral pulse wave velocity (cfPWV) is a commonly used index of aortic pulse wave velocity (aPWV). It has been shown to predict cardiovascular risk and all-cause mortality, particularly in elderly patients (*1*) and patients with end-stage renal failure (*2–4*), hypertension (*5*, *6*), and diabetes mellitus (*7*, *8*). It also appeared to be an independent predictor of coronary heart disease and stroke in a large population of apparently healthy adults (*9*). cfPWV is a marker of the presence and quantity of calcium in the coronary arteries of healthy subjects (*10*) and of coronary artery disease (CAD) severity in CAD patients with chronic kidney disease (*11*). Recently, the age-specific reference intervals for cfPWV have been determined (*12*). However, the relationship between aPWV and cfPWV is not known. Thus, the aim of this study was to 1) assess the correlation between cfPWV and aPWV, 2) com-

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Table 1. Clinical Characteristics of the Study Group

	All patients (n=107)	CAS– (n=36)	CAS+ (n=71)	p
Age (years)	60.49±8.31	58.11±8.19	61.70±8.17	0.03
Height (m)	1.69±0.09	1.67±0.09	1.70±0.08	0.07
aSBP (mmHg)	137.74±25.08	133.28±23.71	140.00±25.62	0.19
aDBP (mmHg)	71.67±10.98	71.55±9.51	71.73±11.72	0.94
aPP (mmHg)	65.84±22.08	61.05±22.41	68.27±21.66	0.12
aMBP (mmHg)	95.25±14.42	92.56±14.85	96.61±14.11	0.17
bSBP (mmHg)	126.21±16.51	128.47±18.24	125.07±15.57	0.33
bDBP (mmHg)	78.35±10.78	79.61±12.42	77.72±9.87	0.35
bPP (mmHg)	47.86±12.34	48.86±12.25	47.35±12.5	0.56
bMBP (mmHg)	94.31±11.58	95.89±13.43	93.50±10.54	0.31
HR (beats/min)	6.90±11.49	68.58±9.94	66.03±12.18	0.12
aPWV (m/s)	8.78±2.24	7.44±1.44	9.46±2.28	<0.0001
cfPWV (m/s)	10.65±2.29	9.58±1.54	11.19±2.42	0.001
Sex (men) (n (%))	68 (64)	16 (44)	52 (73)	0.004
Obesity (n (%))	36 (34)	15 (42)	21 (30)	0.21
Hyperlipidemia (n (%))	100 (93)	33 (92)	67 (94)	0.59
DM (n (%))	27 (25)	6 (17)	21 (30)	0.15
Smoking (current) (n (%))	12 (11)	3 (8)	9 (13)	0.73
Medication (n (%))				
β-Blockers	85 (79)	26 (72)	59 (83)	0.19
ACEI	90 (84)	28 (78)	62 (87)	0.20
Aspirin	107 (100)	36 (100)	71 (100)	—
Statins	86 (80)	26 (72)	60 (85)	0.13
Fibrates	4 (3.7)	0	4 (5.6)	0.37
Nitrates	51 (48)	17 (47)	34 (48)	0.95
Diuretics	41 (38)	17 (47)	24 (34)	0.09
Calcium antagonists	32 (30)	15 (42)	17 (24)	0.06

Continuous variables are reported as means±SD. Categorical variables are reported as counts (%). CAS– group, without significant coronary artery stenosis; CAS+ group, with significant stenosis in at least one coronary artery; aSBP (DBP, PP, MBP), aortic systolic (diastolic, pulse, mean) blood pressure; bSBP (DBP, PP, MBP), systolic (diastolic, pulse, mean) blood pressure measured with standard sphygmomanometer in resting conditions; aPWV, aortic pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; DM, diabetes mellitus; ACEI, angiotensin-converting enzyme inhibitor.

pare their risk factor profiles, and 3) assess their association with CAD.

Methods

Study Population

We studied 107 consecutive patients (68 men) with a mean age of 60.49±8.31 years who had stable angina and had been referred for coronary angiography. The characteristics of the study group are shown in Table 1. A history was obtained and physical examination and laboratory tests were performed in all the subjects. A blood sample was drawn after an overnight fast. Patients with irregular heart rhythm, heart failure and significant valvular heart disease were excluded from the study. The institutional ethics committee approved the study protocol, and informed consent was obtained from each patient before starting the study. The presence of type 2 diabetes mellitus was defined as a fasting blood glucose of ≥7.0 mmol/L confirmed on a different day; or a plasma glucose concentration of ≥1.0 mmol/L 2 h after a 75 g oral glucose load; or the use of blood glucose–lowering medication (*13*). Hyperlipidemia was defined as low-density lipoprotein (LDL) cholesterol >3.0 mmol/L, triglyceride >1.7 mmol/L, or the use of a lipid-lowering drug. Body mass index was calculated as weight divided by height raised to the second power and expressed as kg/m^2. Smoking status was classified as smoker (smoked in the last 6 months) or non-smoker (did not smoke for at least 6 months before the study). Before cardiac catheterization all the patients were taking cardiovascular medications with the following distribution in the study population: angiotensin-converting enzyme inhibitors (ACEIs) (n=90 patients), β-blockers (n=85), lipid-lowering drugs (n=86: 82 patients with statins alone and 4 patients

with statins + fibrates), nitrates ($n=51$), aspirin ($n=107$), calcium antagonists ($n=32$), and diuretics ($n=41$). All patients were taking at least one antihypertensive agent and thus all were classified as hypertensives.

Measurement of Pulse Wave Velocity

aPWV and cfPWV were recorded simultaneously with the patient in a supine position, in the catheterization laboratory, before coronary angiography.

cfPWV was measured using a semiautomatic computerized recorder and the results were analyzed using the Complior® program (Complior, Colson, Garges les Gonesse, France). TY-306–Fukuda pressure-sensitive transducers (Fukuda, Tokyo, Japan) were placed over the left carotid artery and left femoral artery. cfPWV was calculated by dividing the distance separating the two sensors by the time corresponding to the period separating the start of the rising phase of the carotid pulse wave and that of the femoral pulse wave. cfPWV was expressed in m/s. The pulse wave propagation distance was the total distance between the carotid and femoral sites measured with a tape measure over the surface of the body based on current guidelines (*14*). At least 10 correct single measurements were averaged to obtain the cfPWV. This method has been described in detail elsewhere (*15*).

Invasive measurements were made from the right femoral access. In order to assess aPWV we recorded pressure waveforms with a fluid-filled system (6 Fr right Judkins catheter) at an aortic bulb level and at the abdominal aorta just over the bifurcation. A hard copy was made of the pressure tracing using a chart recorder (Cathcor, Siemens, Erlangen, Germany; frequency response 500 Hz) at a paper speed of 200 mm/s. The level of the catheter was identified using fluoroscopy in an antero-posterior view. To calculate the aPWV we used the foot-to-foot velocity method as previously described and validated (*16*, *17*). The foot was identified as the beginning of the systole initial upstroke. A pulse wave propagation distance, the distance between the proximal and distal level of the pressure recording site, was measured as the difference between the lengths of the part of the catheter that extended out of the vascular sheath at both levels. The pulse wave propagation time was the difference between the R-to-foot times calculated at both levels of the aorta. The R-to-foot time was assessed using the pressure recordings as the time delay between the foot of the pressure wave and the preceding R wave in the ECG recording. aPWV was calculated as the pulse wave propagation distance divided by the pulse wave propagation time and expressed in m/s. For statistical analysis we used an average of three consecutive measurements, which has been shown to be highly reproducible. The correlation coefficients and p values for the relationship between the consecutive measurements were as follows: $r=0.93$, $p<0.0001$ for the first and second measurements; $r=0.95$, $p<0.0001$ for the second and third measurements; and $r=0.93$, $p<0.0001$ for the first and third measurements.

Table 2. Odds Ratio for the Association between Pulse Wave Velocity and Significant Coronary Artery Stenosis

	OR	95% CI	p
Regression model with aPWV			
aPWV (tertiles)	4.71	2.19–10.9	0.0001
Sex (0: female, 1: male)	5.86	1.96–17.51	0.0015
Regression model with cfPWV			
cfPWV (tertiles)	2.89	1.55–5.40	0.0009
Sex (0: female, 1: male)	4.34	1.63–11.59	0.0034

The initial model included cfPWV or aPWV and the following parameters: age, sex, height, obesity, diabetes, hyperlipidemia, smoking, aortic mean blood pressure, β-blockers, angiotensin converting enzyme inhibitors, calcium antagonists, nitrates, diuretics, statins, fibrates. The values did not change significantly when aortic systolic blood pressure was included instead of aortic mean blood pressure. OR, odds ratio; aPWV, aortic pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; CI, confidence interval.

Aortic blood pressure was measured in the ascending aorta. Aortic mean blood pressure (aMBP) was automatically calculated from the area under the pressure curve. Aortic pulse pressure (aPP) was calculated as the difference between aortic systolic blood pressure (aSBP) and aortic diastolic blood pressure (aDBP). Heart rate (HR) was read from the ECG recording.

Brachial artery blood pressure was measured with a standard sphygmomanometer at least twice. Phase I and V Korotkoff sounds were used to identify brachial artery systolic (SBP) and diastolic blood pressure (DBP), respectively, as previously recommended (*18*). Brachial pulse pressure (PP) was defined as PP = SBP – DBP, while brachial mean blood pressure (MBP) was defined as MBP = DBP + PP/3. Brachial artery pressure was measured bedside (bBP) a day before coronary angiography and during the invasive procedure.

Coronary Angiography

Cardiac catheterization was performed using a standard technique. The three major coronary vessels (left anterior descending artery, circumflex artery, and right coronary artery) were considered for evaluation of the extent of CAD. The degree of coronary artery stenosis (CAS) was assessed in the optimal view by comparing the minimal lumen diameter and the reference lumen diameter at end diastole. A significant CAS was defined as a reduction of the lumen diameter ≥50%. The CAS+ group was defined as having at least one significant CAS. The CAS– group had no coronary lesions or had non-significant stenosis. The extent of CAD was classified as 1 to 3, corresponding to a significant lesion in 1, 2 or 3 coronary arteries, respectively.

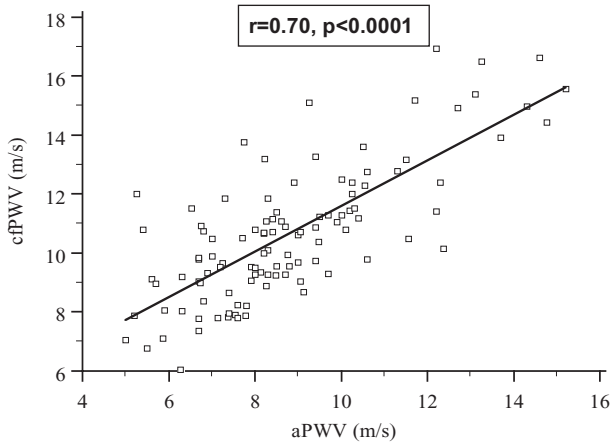

Fig. 1. *Correlation between aortic pulse wave velocity and carotid femoral pulse wave velocity. cfPWV, carotid-femoral pulse wave velocity; aPWV, aortic pulse wave velocity. aPWV and cfPWV are expressed in m/s.*

Table 3. Correlation Coefficients between Aortic Pulse Wave Velocity as Well as Carotid-Femoral Pulse Wave Velocity and Clinical and Hemodynamic Parameters*

	cfPWV (m/s)		aPWV (m/s)	
	r	*p*	*r*	*p*
Age (years)	0.52	<0.0001	0.54	<0.0001
BMI (kg/m^2)	−0.06	0.57	0.06	0.54
Height (m)	0.07	0.46	−0.06	0.54
aSBP (mmHg)	0.34	0.01	0.42	<0.0001
aDBP (mmHg)	−0.01	0.91	0.15	0.13
aPP (mmHg)	0.35	0.003	0.42	<0.0001
aMBP (mmHg)	0.27	0.01	0.33	0.001
HR (beats/min)	0.04	0.66	0.17	0.86

*Associations with categorical parameters are presented in the text. CAS– group, without significant coronary artery stenosis; CAS+ group, with significant coronary stenosis in at least one coronary artery; BMI, body mass index; aSBP (DBP, PP, MBP), aortic systolic (diastolic, pulse, mean) blood pressure; aPWV, aortic pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; HR, heart rate.

Statistical Analyses

Statistical analysis was performed with Statistica PL software (StatSoft, Inc. [2001] STATISTICA [data analysis software system], version 6.0, StatSoft Inc., Tulsa, USA) and MedCalc® Version 8.1.1.0. Continuous variables were reported using means and standard deviations. Categorical variables were described as counts and percentages. Continuous variables with normal distribution were compared using Student's *t*-test for comparison between two variables or analysis of variance (ANOVA) for comparisons among more than two variables. When the distribution of continuous variables was not normal the Mann-Whitney *U* test (for two variables) or Kruskal-Wallis test (for more than two variables) were used. Levene test was used to verify the equality of variances. The χ^2 test was used to compare categorical variables. The Pearson or Spearman tests were used to estimate correlations. To calculate the statistical significance of the difference between two independent correlation coefficients Fisher's *Z* test was used. The effects of classic risk factors on pulse wave velocity (PWV) were analyzed with multivariate regression analysis by stepwise selection. A stepwise logistic regression analysis was performed to identify independent predictors of significant CAS. Variables included in multivariate models were as follows: age, sex, height, obesity, diabetes, hyperlipidemia, smoking habits, the antihypertensive medications listed above, statins, fibrates and aSBP or aMBP. The receiver operating characteristic (ROC) curves with cutoff values of cfPWV and aPWV yielding the maximum sensitivity and specificity for predicting significant CAS were generated. The area under the ROC curve (AUC) was used as a measure of the test accuracy to discriminate between patients with and without significant CAS. A comparison between the two ROC curves was performed by calculating the statistical significance of the difference between their AUCs with the *z* test, as described by Park *et al*. (*19*). The significance level was set at $p<0.05$.

Results

The clinical characteristics of the study population and main differences between the CAS+ ($n=71$) and CAS– ($n=36$) groups are summarized in Table 1. Compared with the CAS– group, the CAS+ group had significantly higher values of both aPWV (9.46±2.28 *vs*. 7.44±1.44 m/s, $p<0.0001$) and cfPWV (11.19±2.42 *vs*. 9.58±1.54 m/s, $p=0.001$). Patients with 1-, 2-, or 3-vessel disease did not differ significantly with respect to cfPWV (10.58±1.82 *vs*. 10.87±2.32 *vs*. 11.95±2.79 m/s, respectively, $p=0.1$) and aPWV (9.19±1.76 *vs*. 8.95±2.18 *vs*. 10.08±2.65 m/s, respectively, $p=0.18$).

In a stepwise logistic regression analysis in which cfPWV or aPWV as well as main cardiovascular disease risk factors, height, medications, and aMBP or aSBP were used as independent variables, the only independent predictors of significant CAS were male sex and aPWV or cfPWV (Table 2).

The mean values of cfPWV and aPWV in the whole population were 10.65±2.29 m/s (median =10.50 m/s) and 8.78±2.24 m/s (median =8.3 m/s), respectively. Figure 1 depicts the correlation between these parameters ($r=0.70$; $p<0.0001$) in the study group. When the population was divided with respect to the presence of significant CAS, the correlation coefficient was significantly higher ($p=0.03$) for the CAS+ group than for the CAS– group ($r=0.74$, $p<0.0001$ and $r=0.46$, $p=0.003$, respectively).

Correlations between clinical and hemodynamic continuous variables and aPWV as well as cfPWV are presented in

Table 4. Variables Independently Associated with Increased aPWV or cfPWV in Multiple Regression Model

	β	SEM	p
Regression model for aPWV			
aMBP	0.04	0.01	0.0006
Age	0.14	0.02	<0.0001
Regression model for cfPWV			
aMBP	0.02	0.01	0.002
Age	0.14	0.02	<0.0001

The initial model included the following independent variables: age, sex, height, obesity, diabetes, hyperlipidemia, smoking, aortic mean blood pressure, β-blockers, angiotensin converting enzyme inhibitors, calcium antagonists, nitrates, diuretics, statins, fibrates. The values did not change significantly when aortic systolic blood pressure was included instead of aortic mean blood pressure. β, regression coefficient; SEM, standard error of β; aPWV, aortic pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; aMBP, aortic mean blood pressure.

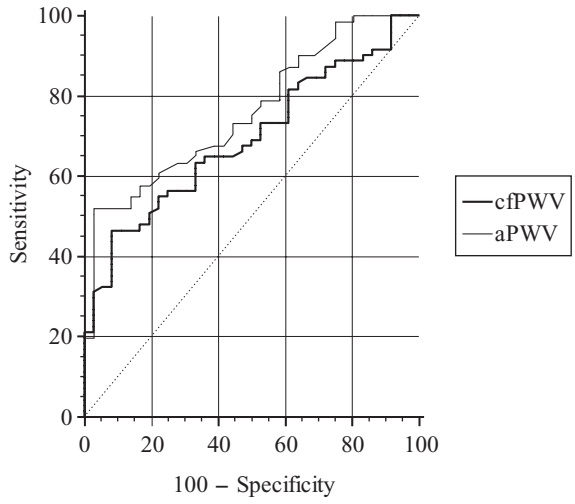

Fig. 2. *Receiver operating characteristic (ROC) analysis of aortic pulse wave velocity and carotid-femoral pulse wave velocity. aPWV, aortic pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity. The cutoff values of aPWV and cfPWV yielding the maximum sensitivity and specificity for predicting significant coronary artery stenosis were > 9.05 m/s and > 11.16 m/s, respectively. The area under the curve for aPWV (AUC = 0.76) and for cfPWV (AUC = 0.69) did not differ significantly (p = 0.13).*

Table 3. aPWV as well as cfPWV correlated well with age, aSBP, aMBP, and aPP. They did not differ significantly with respect to sex, diabetes, smoking, hyperlipidemia, obesity, and medication regimens. They also did not correlate with brachial blood pressure measured under resting conditions. However, the values of blood pressure at rest were significantly lower than those measured in stressful conditions during cardiac catheterization (SBP: 126.21±16.51 *vs.* 144.49±22.73 mmHg, $p<0.0001$; MBP: 94.31±11.58 *vs.* 102.57±16.44 mmHg, $p<0.0001$).

In multiple regression analysis, age and aMBP (or aSBP) were the only independent determinants of aPWV (adjusted $r^2=0.44$, $p<0.001$) as well as cfPWV (adjusted $r^2=0.33$, $p<0.001$) (Table 4).

In the ROC analysis (Fig. 2), aPWV >9.05 m/s predicted significant CAS with 52% sensitivity and 97% specificity, whereas cfPWV >11.16 m/s predicted significant CAS with 46.5% sensitivity and 92% specificity. There was no significant difference in the accuracy in identification of patients with significant CAS between aPWV and cfPWV (AUC =0.76 and 0.69, respectively; $p=0.13$).

Discussion

The development of noninvasive methods to assess aPWV has made this parameter an attractive tool for investigation. The most popular indices of aPWV are cfPWV and brachial-ankle PWV (baPWV), and their measurements have been shown to be highly reproducible (*15*, *20*). Their clinical utility arises from two main advantages. First, they correlate well with early markers of vascular damage such as intima-media thickness (*21*, *22*), microalbuminuria (*23*, *24*) and flow-mediated dilation of the brachial artery (*22*), and are also good indicators of advanced atherosclerotic lesions in the arterial tree (*11*, *25*). Secondly, they can be modified by non-pharmacological and pharmacological interventions (*26–30*). Interestingly, it has been suggested that increased aortic stiffness may enhance blood pressure reactivity to stress (*31*).

Munakata *et al*. showed that baPWV is greater than cfPWV in absolute values but the two indices are highly correlated in normotensive and untreated hypertensive individuals (*32*). baPWV has also recently been shown to correlate well with aPWV in patients with clinical presentation of CAD (*33*), although there is no available data on the association between cfPWV and aPWV in this group of patients.

The current study was thus designed to assess the relationship between cfPWV obtained by a semiautomatic, noninvasive method and aPWV measured directly during cardiac catheterization, and then to compare the clinical and hemodynamic determinants of these parameters as well as their association with coronary arterial lesions.

To the best of our knowledge, we are the first to show that cfPWV and aPWV are significantly and positively correlated, and that the degree of agreement between them differs significantly between groups with and without significant CAS. We have also shown for the first time that the noninvasive method of cfPWV measurement has similar accuracy in identification of patients with significant CAS as the invasive method of aPWV measurement, and that the main predictors of cfPWV and aPWV are similar.

The mean values of aPWV in our study were lower than

those presented in a recent work by Lim *et al*., in which a similar technical approach was used to estimate aPWV by using a fluid-filled system (*16*). In that study, however, aPWV was obtained from partly different arterial segment, that spanned from the descending aorta to the femoral artery, which may explain the different values of aPWV in these two studies. This assumption results from a classic work on aPWV with use of a specially designed catheter with six micromanometers equally spaced at 10 cm intervals, where aPWV rose in the direction from the aortic root to the distal part of the aorta and femoral artery (*34*).

With respect to cfPWV, to the best of our knowledge, there are no available data about cfPWV values in a general group of patients with coronary heart disease in relation to the presence of significant CAS. Such information is available only for a subset of patients with chronic kidney disease (*11*), but because different devices and different methods of measuring the pulse wave propagation distance were used in that study, it is difficult to compare the results with our present ones. In a recent meta-analysis (*12*), 223 studies on arterial stiffness from 1995 to 2004 were analyzed. In 25 of them the methodology of cfPWV measurement was the same as in our study, but only one paper referred to a high risk group, in which the impact of cfPWV on survival in end-stage renal disease was assessed (*2*).

When pressure waveforms are recorded on carotid and femoral arteries, the PWV is determined not only by aortic stiffness but rather from an admixture of data from two circulatory branches—the aortic-carotid and aortic-femoral—which represent different biophysical properties and are regulated separately (*35*). The current study showed that the strength of correlation between aPWV and cfPWV differed significantly between two analyzed groups. It was higher in a group of patients with significant CAS, which had a higher mean age and was predominantly male, than in a second group of patients who had symptoms of CAD but no significant CAS in angiography. The latter group was younger and predominantly female. Considering that there was no significant association between sex and PWV in the current study, we can assume that age and the advancement of atherosclerosis modulated the strength of correlation between aPWV and cfPWV in both groups. We must underscore here that as the number of patients in the CAS– group was smaller than in the CAS+ group and the standard deviations of cfPWV and aPWV differed between the two groups, we used a statistical approach to confirm that the correlation coefficients differed significantly.

This observed difference can probably be explained by variability in the rate of stiffening of various arterial segments during the process of atherogenesis and aging. The aorta has been shown to be the first arterial region to undergo pathological modifications in the presence of cardiovascular risk factors (*36*, *37*). In a recent work by Paini *et al*. (*38*), the correlation between carotid and aortic stiffness became weaker as the number of cardiovascular risk factors increased and was significantly higher in normotensives than in patients with hypertension or both hypertension and diabetes. It is likely that the discrepancies between aortic and carotid stiffness resulted from different influences of cardiovascular risk factors on the two parameters. In another work by Pannier *et al*. (*39*), carotid-femoral, but neither brachial nor femorotibial PWV, was able to predict cardiovascular outcome in patients with end-stage renal disease, which also reflects discrepancies in arterial stiffness at different stages of the process of atherogenesis.

It is thus possible that the difference in correlation between aPWV and cfPWV might result from a higher degree of discrepancy between the stiffness of aortic and other arteries included in the cfPWV measurement (carotid, iliac and femoral arteries) in the CAS– group compared with the CAS+ group. We can assume that in the CAS– group the process of stiffening of these arteries had not yet started or was at a much earlier stage than the process of aortic stiffening. In turn, in the CAS+ group, which was more advanced in the process of aging and atherogenesis, the discrepancies in stiffness between aortic and other large arteries were lower, and thus aPWV and cfPWV were highly related.

In our study the mean values of cfPWV were greater than those of aPWV. There are two possible explanations for this finding. First, as we underscored above, the territories covered by these two measurements differed to some extent. As distal arteries are stiffer than the aorta (*34*), the more peripheral the sites of pulse wave recording the greater the mean values of PWV. The same conclusion was reached by Munakata *et al*. (*32*), who showed that baPWV, which covers even more distal arterial territories, reaches higher values than cfPWV. Secondly, it was discussed previously (*40*) that the technical approach of measuring the pulse wave propagation distance between carotid and femoral sites over the body surface, although widely accepted, overestimates the values of cfPWV.

Such differences in absolute values as well as in the relationship between aPWV and cfPWV in different groups of patients led us to consider the use of separate terms for the aortic and carotid-femoral pulse wave velocity.

Because all patients in our study used several medications to treat hypertension and coronary heart disease, the cardiovascular risk factors were highly modified, which impeded conclusions about their impact on arterial stiffness. Nevertheless, it was still possible to compare the determinants of cfPWV and aPWV in the same group of patients. We showed that age and aMBP (or aSBP) were independent predictors of cfPWV as well as aPWV. There was no association between cfPWV and aPWV and resting brachial blood pressure, which probably resulted from significant differences between blood pressure measured bedside and under stressful conditions during invasive procedures when cfPWV and aPWV were measured

In our study cfPWV and aPWV had similar accuracy in predicting significant CAS, probably due to the fact that vari-

ability of both parameters reflects mainly age- and atherosclerosis-associated changes in the aorta. This observation reinforces the value of cfPWV as a marker of aortic stiffness. It appears that the differences in the absolute values of PWV between the carotid-femoral and aortic segment do not matter in clinical practice, where the prognostic role of parameters plays a pivotal role. However, to interpret the results appropriately, we must always consider the methodology used to measure them.

In the present study, cfPWV and aPWV had high specificity and rather low sensitivity in identifying patients with significant CAS. With respect to cfPWV these results are in concordance with the previously mentioned meta-analysis by Khoshdel *et al*. (*12*), where the sensitivity and specificity of this parameter in identifying high risk patients were 57.2% and 95.3%, respectively.

Some methodological aspects of PWV measurements in our study require additional comment. First, aPWV was measured invasively with an intraaortic catheter. Because the aorta becomes more tortuous and longer with age, such direct measurement provided us with more precise estimation of the pulse wave propagation distance than could be obtained from superficial measurements. Second, we did not record pressure waves at both levels of the aorta simultaneously, which means that aPWV was calculated from two separate pulse waves. This approach has been widely accepted and recommended for noninvasive PWV measurements using the SphygmoCo system, since the pulse waves are obtained at both sites a short time apart, and the changes in the isovolumic period of the left ventricle or heart rate variability have little or no effect on the measured pulse propagation time (*14*, *29*). Additionally, simultaneous recording of pressure waves at both sites in our study would require additional arterial access, which would be impractical from a clinical point of view and highly questionable ethically. One limitation of the current study is the use of a fluid-filled system to detect pressure waves. The use of a high-fidelity pressure transducer could increase the accuracy of the recorded pressure waveform. However, the fluid-filled system has been used commonly in clinical studies (*16*, *41*, *42*). In clinical practice, access to a high-fidelity pressure transducer is limited, and use of such a system requires additional procedures that prolong the already invasive measurement.

To compare aPWV and cfPWV we used the invasive method of aPWV measurement, which cannot be applied to large population studies. Recently, however, several new noninvasive techniques such as magnetic resonance imaging have been applied for measuring the PWV in inaccessible arteries such as the aorta (*43*).

Conclusions

The present study showed a good positive correlation between the results of a noninvasive measurement of cfPWV and invasively measured aPWV. Both parameters were similarly influenced by aortic blood pressure and the patient's age. They also had similar accuracy for identifying patients with significant CAS. The strength of correlation between cfPWV and aPWV differed significantly between patients with and those without significant CAS. Thus, the relationship between cfPWV and aPWV depends on the characteristics of the study population and the terms aPWV and cfPWV should not be used interchangeably.

References

1. Meaume S, Benetos A, Henry OF: Aortic pulse wave velocity predicts cardiovascular mortality in subjects >70 years of age. *Arterioscler Thromb Vasc Biol* 2001; **21**: 2046–2050.
2. Blacher J, Safar ME, Guerin AP, Pannier B, Marchais SJ, London GM: Aortic pulse wave velocity index and mortality in end-stage renal disease. *Kidney Int* 2003; **63**: 1852–1860.
3. Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM: Impact of aortic stiffness on survival in end-stage renal disease. *Circulation* 1999; **99**: 2434–2439.
4. Safar ME, Blacher J, Pannier B, *et al*: Central pulse pressure and mortality in end-stage renal disease. *Hypertension* 2002; **39**: 735–738.
5. Laurent S, Boutouyrie P, Asmar R, *et al*: Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 2001; **37**: 1236–1241.
6. Boutouyrie P, Tropeano AI, Asmar R, *et al*: Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients: a longitudinal study. *Hypertension* 2002; **39**: 10–15.
7. Shoji T, Emoto M, Shinohara K, *et al*: Diabetes mellitus, aortic stiffness, and cardiovascular mortality in end-stage renal disease. *J Am Soc Nephrol* 2001; **12**: 2117–2124.
8. Cruickshank K, Riste L, Anderson SG, Wright JS, Dunn G, Gosling RG: Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: an integrated index of vascular function? *Circulation* 2002; **106**: 2085–2090.
9. Mattace-Raso FUS, van der Cammen TJM, Hofman A, *et al*: Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study. *Circulation* 2006; **113**: 657–663.
10. Kullo IJ, Bielak LF, Turner ST, Sheedy PF, Peyser PA: Aortic pulse wave velocity is associated with the presence and quantity of coronary artery calcium: a community-based study. *Hypertension* 2006; **47**: 174–179.
11. Covic A, Haydar AA, Bhamra-Ariza P, Gusbeth-Tatomir P, Goldsmith DJ: Aortic pulse wave velocity and arterial wave reflections predict the extent and severity of coronary artery disease in chronic kidney disease patients. *J Nephrol* 2005; **18**: 388–396.
12. Khoshdel AR, Thakkinstian A, Carney SL, Attia J: Estimation of an age-specific reference interval for pulse wave velocity: a meta-analysis. *J Hypertens* 2006; **24**: 1231–1237.
13. American Diabetes Association: Diagnosis and classifica-

tion of diabetes mellitus. *Diabetes Care* 2006; **29** (Suppl 1): S43–S48.
14. Van Bortel L, Duprez D, Starmans-Kool MJ, *et al*: Clinical applications of arterial stiffness, Task Force III: recommendations for user procedures. *Am J Hypertens* 2002; **15**: 445–452.
15. Asmar R, Benetos A, Topouchian J: Assessment of arterial distensibility by automatic pulse wave velocity measurement. Validation and clinical application studies. *Hypertension* 1995; **26**: 485–490.
16. Lim HE, Park CG, Shin SH, Ahn JC, Seo HS, Oh DJ: Aortic pulse wave velocity as an independent marker of coronary artery disease. *Blood Pressure* 2004; **13**: 369–375.
17. Asmar R: Pulse wave velocity. Principles and measurements, in Asmar R (ed): Arterial Stiffness and Pulse Wave Velocity: Clinical Applications. Paris, Elsevier, 1999, pp 25–55.
18. European Society of Hypertension–European Society of Cardiology Guidelines Committee: 2003 European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens* 2003; **21**: 1011–1053.
19. Park SH, Goo JM, Jo CH: Receiver operating characteristic (ROC) curve: practical review for radiologists. *Korean J Radiol* 2004; **5**: 11–18.
20. Matsui Y, Kario K, Ishikawa J, Eguchi K, Hoshide S, Shimada K: Reproducibility of arterial stiffness indices (pulse wave velocity and augmentation index) simultaneously assessed by automated pulse wave analysis and their associated risk factors in essential hypertensive patients. *Hypertens Res* 2004; **27**: 851–857.
21. Munakata M, Sakuraba J, Tayama J, *et al*: Higher brachial-ankle pulse wave velocity is associated with more advanced carotid atherosclerosis in end-stage renal disease. *Hypertens Res* 2005; **28**: 9–14.
22. Kobayashi K, Akishita M, Yu W, Hashimoto M, Ohni M, Toba K: Interrelationship between non-invasive measurements of atherosclerosis: flow-mediated dilation of brachial artery, carotid intima-media thickness and pulse wave velocity. *Atherosclerosis* 2004; **173**: 13–18.
23. Munakata M, Nunokawa T, Yoshinaga K, Toyota T: Brachial-ankle pulse wave velocity is an independent risk factor for microalbuminuria in patients with essential hypertension—a Japanese Trial on the Prognostic Implication of Pulse Wave Velocity (J-TOPP). *Hypertens Res* 2006; **29**: 515–521.
24. Nakamura Y, Makino H: Brachial-ankle pulse wave velocity and microalbuminuria. *Hypertens Res* 2006; **29**: 469–470.
25. Imanishi R, Seto S, Toda G, *et al*: High brachial-ankle pulse wave velocity is an independent predictor of the presence of coronary artery disease in men. *Hypertens Res* 2004; **27**: 71–78.
26. Kita T, Suzuki Y, Eto T, Kitamura K: Long-term antihypertensive therapy with benidipine improves arterial stiffness over blood pressure lowering. *Hypertens Res* 2005; **28**: 959–964.
27. Matsui Y, Kario K, Ishikawa J, Hoshide S, Eguchi K, Shimada K: Smoking and antihypertensive medication: interaction between blood pressure reduction and arterial stiffness. *Hypertens Res* 2005; **28**: 631–638.
28. Nakamura T, Fujii S, Hoshino J, *et al*: Selective angiotensin receptor antagonism with valsartan decreases arterial stiffness independently of blood pressure lowering in hypertensive patients. *Hypertens Res* 2005; **28**: 937–943.
29. Laurent S, Cockcroft J, Van Bortel L, *et al*: Expert consensus document on arterial stiffness: methodogical issues and clinical applications. *Eur Heart J* 2006; **27**: 2588–2605.
30. Munakata M, Nagasaki A, Nunokawa T, *et al*: Effects of valsartan and nifedipine coat-core on systemic arterial stiffness in hypertensive patients. *Am J Hypertens* 2004; **17**: 1050–1055.
31. Tayama J, Munakata M, Yoshinaga K, Toyota T: Higher plasma homocysteine concentration is associated with more advanced systemic arterial stiffness and greater blood pressure response to stress in hypertensive patients. *Hypertens Res* 2006; **29**: 403–409.
32. Munakata M, Ito N, Nunokawa T, Yoshinaga K, *et al*: Utility of automated brachial ankle pulse wave velocity measurements in hypertensive patients. *Am J Hypertens* 2003; **16**: 653–657.
33. Yamashina A, Tomiyama H, Takeda K, *et al*: Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. *Hypertens Res* 2002; **25**: 359–364.
34. Latham RD, Westerhof N, Sipkema P, Rubal BJ, Reuderink P, Murgo JP: Regional wave travel and reflections along the human aorta: a study with six simultaneous micromanometric pressures. *Circulation* 1985; **72**: 1257–1269.
35. Izzo JL, Shykoff BE: Arterial stiffness: clinical relevance, measurement, and treatment. *Rev Cardiovasc Med* 2001; **2**: 29–40.
36. Lakatta EG, Levy D: Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part I: aging arteries: a "set up" for vascular disease. *Circulation* 2003; **107**: 139–146.
37. Lakatta EG, Levy D: Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part II: the aging heart in health: links to heart disease. *Circulation* 2003; **107**: 346–354.
38. Paini A, Boutouyrie P, Calvet D, Tropeano AI, Laloux B, Laurent S: Carotid and aortic stiffness: determinants of discrepancies. *Hypertension* 2006; **47**: 371–376.
39. Pannier B, Guérin AP, Marchais SJ, Safar ME, London GM: Stiffness of capacitive and conduit arteries: prognostic significance for end-stage renal disease patients. *Hypertension* 2005; **45**: 592–596.
40. Karamanoglu M: Errors in estimating propagation distances in pulse wave velocity. *Hypertension* 2003; **41**: e8.
41. Jankowski P, Kawecka-Jaszcz K, Bryniarski L, *et al*: Fractional diastolic and systolic pressure in the ascending aorta are related to the extent of coronary artery disease. *Am J Hypertens* 2004; **17**: 641.
42. Nakayama Y, Tsumura K, Yamashita N, Yoshimaru K, Hayashi T: Pulsatility of ascending aortic pressure waveform is a powerful predictor of restenosis after percutaneous transluminal coronary angioplasty. *Circulation* 2000; **101**: 470–472.
43. Mackenzie IS, Wilkinson IB, Cockroft JR: Assessment of arterial stiffness in clinical practice. *QJM* 2002; **95**: 67–74.