

Heart-to-Brachium Pulse Wave Velocity as a Measure of Proximal Aortic Stiffness: MRI and Longitudinal Studies

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BACKGROUND

Stiffening of the proximal aorta is associated with heightened cardiovascular disease risks but can be quantified by limited methodologies (e.g., magnetic resonance imaging [MRI]). As an initial step to evaluate the emerging technique to assess proximal aortic stiffness *via* pulse wave velocity from the heart to the brachium (hbPWV), we determined the influences of aging on pulse wave velocity (PWV) and aortic hemodynamics.

METHOD

Using the cross-sectional and follow-up study designs, hbPWV was compared and evaluated in relation to other PWV in various arterial segments. Arterial path lengths were measured by the 3-dimensional arterial tracing of MRI.

RESULTS

In the cross-sectional study including 190 subjects (aged 19–79 years), hbPWV exhibited one of the largest age-related increases and a stronger correlation with age ($r = 0.790$) compared with the other

measures of PWV including carotid-femoral PWV, brachial-ankle PWV, and PWV of muscular arteries ($r = 0.445$ – 0.688). In addition, hbPWV was correlated with aortic systolic blood pressure (BP) and augmentation index ($r = 0.380$ and 0.433 , respectively) after controlling for brachial systolic BP. These results were confirmed by the 10-year follow-up study involving 84 individuals (53 years at baseline). The decadal changes in hbPWV were significantly correlated with the corresponding changes in several aortic hemodynamic variables (e.g., aortic systolic BP, augmentation pressure, and augmentation index) ($r = 0.240$ – 0.349).

CONCLUSIONS

The present findings indicate that hbPWV is a potential marker of proximal aortic stiffening that reflects age-related changes and aortic hemodynamics.

Keywords: arterial stiffness; blood pressure; hypertension; magnetic resonance imaging; pulse wave analysis; pulse wave velocity.

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Large elastic arteries (e.g., aorta and carotid arteries) dampen cyclic mechanical forces of cardiac pulsations by extending and recoiling against intermittent cardiac blood flow ejection. This function commonly referred to as the “Windkessel” function acts to attenuates left ventricular (LV) afterload, preserves coronary perfusion, and protects vulnerable microvasculature such as the brain and kidneys.¹ The proximal aorta (e.g., the ascending aorta and aortic arch) makes the greatest contribution to Windkessel function because of the prominent elasticity and the anatomical location closest to LV. Large cohort studies indicated that deteriorated proximal aortic Windkessel function is associated with heightened cardiovascular disease (CVD) risks, cardiovascular events, and all-cause mortalities.^{2–5}

Currently, carotid–femoral pulse wave velocity (cfPWV) is considered to be the reference standard technique as recently described in the consensus statements on arterial stiffness.^{6,7} In addition, there is a growing recognition that brachial-ankle pulse wave velocity (baPWV) could be a surrogate index for cfPWV as it is one of few measures of arterial stiffness that have been incorporated in the routine clinical settings.^{8,9} A recent meta-analysis using individual participant data from prospective cohort studies indicates baPWV could be an independent predictor of the risk of the development of CVD in adults without preexisting CVD.⁸ However, these measures do not involve the segment of the proximal aorta because the segments from the ascending aorta to the carotid artery and to the brachium are omitted

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from the effective path lengths used for cfPWV and baPWV calculations.¹⁰ Some methodologies such as phase contrast magnetic resonance imaging (MRI) can quantify proximal aortic stiffness, but the expense and technical expertise limit the use of such techniques. Therefore, very little information is available as to how aging and other relevant factors would influence proximal aortic stiffness.^{4,11,12}

One of the promising methodologies to evaluate the stiffness of the proximal aorta is heart-to-brachium pulse wave velocity (hbPWV).^{13,14} Its measurement includes the segment of the proximal aorta and does not require the technical placement of transducers. Pulse transit time for hbPWV can be evaluated fairly easily by simultaneous recordings of the heart sound or electrocardiograph and brachial arterial pulse waves recorded with the high-fidelity sensor (e.g., air-plethysmography) embedded in the blood pressure (BP) cuff. We have recently proposed a validated estimation formula for arterial path length from the heart to the brachium using MRI.¹⁵ In the present study, we evaluated the influence of aging and aortic hemodynamic factors on hbPWV. To determine whether hbPWV provides unique and distinct information from other pulse wave velocity (PWV), hbPWV was compared and evaluated in relation to other PWV in various arterial segments. In addition, the analyses were conducted using the cross-sectional and longitudinal study designs.

METHODS

Subjects

This study consisted of 2 investigations of different nature: a cross-sectional (study 1) and a 10-year longitudinal follow-up (study 2) study. A total of 190 adults (100 men, 19–79 years) participated in study 1. Twenty-seven participants were taking prescribed antihypertensive ($n = 15$), cholesterol lowering ($n = 7$), diabetic ($n = 4$), and other (e.g., anticoagulation, thyroid hormone) ($n = 14$) medications. For the reason of MRI scanning, exclusion criteria included pregnancy or patients with electrically, magnetically, or mechanically active implants, intracranial aneurysm clips, prior CVD, epileptic seizures, or claustrophobic symptoms.

In study 2, we studied 84 volunteers (51 men, 63 ± 14 years) who were followed up for approximately 10 years.¹⁶ Smokers and pregnant women were excluded at the premeasurement. No one took any medication at the time of premeasurement, whereas some patients were taking prescribed antihypertensive ($n = 19$), cholesterol lowering ($n = 6$), and diabetic ($n = 3$) medications at the postmeasurement. Women had not taken any hormone replacement therapy during the follow-up period. All experimental procedures and protocols conformed to the Declaration of Helsinki and were approved by the institutional review board. All subjects provided written informed consent to participate.

Experimental protocol

Subjects abstained from alcohol intake and strenuous physical activity for at least 24 hours. Furthermore, all measurements were performed after 3 hours of fasting and an abstinence from caffeine. Upon arrival, subjects underwent

body height and weight assessments, which were followed by supine rest for more than 10 minutes and cardiovascular measurements. Cardiovascular measurements were performed under supine resting conditions in a quiet, temperature-controlled room (24–26 °C).

PWV measurement

Heart rate, BP, and pulse wave velocity (PWV = arterial path length/arterial pulse transit time) were measured noninvasively with the automated cardiovascular screening device (VP-1000plus; Omron Healthcare, Kyoto, Japan) equipped with an electrocardiogram, a phonocardiogram, 4-extremity BP cuffs involving air-plethysmographic sensors, and 2 applanation tonometry sensors. Carotid and femoral artery pulse waves were obtained using arterial applanation tonometry incorporating an array of 15 micro-piezoresistive transducers placed on the carotid and femoral arteries.^{15,17,18} The applanation tonometry sensors were not used in study 2 as the premeasurements did not include such setups. Bilateral brachial and posterior-tibial arterial pressure waveforms were recorded by extremities cuffs connected to air-plethysmographic sensors wrapped on both arms and ankles. Heart sound was recorded by a phonographic sensor that was placed on the chest. Pulse transit times were determined from the time delay between the second heart sound and diastolic notch on the right brachial arterial waveforms or between the proximal and distal “foot” waveforms. As shown in [Supplementary Figure 1](#), the “foot” (i.e., the commencement of the sharp systolic upstroke) and the diastolic notch were automatically detected by a band-pass filter (5–30 Hz)¹⁹ using a LabVIEW-based software provided by Colin AT company (Komaki, Japan). The validity of determination from the time delay (T_{cb}) between the second heart sound and diastolic notch was confirmed in the subanalyses. In randomly selected 100 subjects (50 men), pulse transition time between carotid and brachial arterial pulse waves was obtained by the foot-to-foot method (the carotid “foot” to the brachial “foot”) and the diastolic notch method (the second heart sound to the diastolic notch of brachial arterial waveform).

Arterial path lengths were obtained by 2 different ways as follows: In study 1, arterial path lengths were computed by the 3-dimensional artery tracing of transverse MRI with ImageJ (1.45s; NIH, Bethesda, MD, USA). Transverse MRI was taken at end diastole (gradient echo method, echo time/repetition time 11.0/4.2 millisecond, flip angle 258°, field of view 400 mm, slice thickness 5 mm, interslice gap 0 mm) by a 1.0 T MRI system (Magnetom Impact, Siemens Japan, Tokyo, Japan).¹⁷ The accuracy of the 3-dimensional artery tracing was verified as previously reported.²⁰ In study 1, PWV was evaluated at the following segments from the MRI-derived arterial path lengths: between the carotid and femoral sites (cfPWV), from the heart (e.g., the aortic root) to the right brachium (hbPWV), between the right carotid and the right brachium (cbPWV), from the right femoral artery to the right ankle (faPWV), and between the right brachium and the right ankle (baPWV).¹⁷ Arterial path lengths for cfPWV were measured by the body surface distance, and those for hbPWV (Lhb)¹⁵ and baPWV (Lba)^{19,21,22} were derived from the following equations:

$$\text{Lhb (mm)} = 37.9 \times \text{sex (male = 1; female = 0)} \\ + 0.9 \times \text{height (cm)} + 316.5$$

$$\text{Lba (mm)} = 5.934 \times \text{Height (cm)} + 144.01$$

In study 2, hbPWV and baPWV were evaluated using the height-based equations above.

Aortic hemodynamics

Using the generalized transfer function-based central BP measurement system (SphygmoCor; AtCor Medical, Sydney, Australia), aortic BP was synthesized from carotid arterial BP waveform.²³ Synthesized aortic BP waveform was calibrated by equating the aortic mean and diastolic BP to the brachial artery values acquired with the vascular screening system. Brachial mean BP was calculated by the following equation: mean BP = (systolic BP–diastolic BP) / 3 + diastolic BP. The pressure height of the peak above the shoulder of the wave was defined as augmentation pressure (AP). The AP by aortic pulse pressure (PP) was calculated as the augmentation index (AIx).²⁴

Statistical analyses

Relationships between age and measurements of interests were determined by one-way analysis of variance. Regarding PWV, the interaction between age and the arterial segment

was determined by the two-way repeated-measures analysis of variance. Multiple comparisons were performed with Scheffé's *post hoc* test in the case of significant *F* value. Paired *t* test was applied for pre- and postmeasurements comparisons in study 2. Simple and partial correlation analyses were performed to determine relations of interests. Differences in correlation coefficients were evaluated with the Fisher *r*-to-*z* transformation. To validate the determination from the time delay between the second heart sound and diastolic notch, the regression analysis and Brand and Altman's plot were used. All data are reported as mean ± SD. Statistical significance was set *a priori* at *P* values less than 0.05.

RESULTS

Subjects' characteristics and results of validation study are presented in [Supplementary Table 1](#) and [Supplementary Figure 2](#). In comparison with the foot-to-foot method, the diastolic notch method exhibited a strong correlation ($r = 0.902$, $P < 0.0001$; [Supplementary Figure 2](#)) though it was significantly shorter (45.4 ± 5.3 vs. 48.7 ± 5.8 millisecond, $P < 0.001$). The difference between these methods significantly correlated with age ($r = 0.343$, $P < 0.001$), heart rate ($r = 0.331$, $P < 0.001$), and diastolic BP ($r = 0.232$, $P = 0.034$), but not with systolic ($r = 0.023$, $P = 0.823$) and mean BP ($r = 0.133$, $P = 0.187$).

Study 1: [Table 1](#) presents subject characteristics in study 1. Brachial and aortic systolic BP were greater with increasing age categories. Aortic PP, AP, and AIx were significantly

Table 1. Subject characteristics in study 1

Variables	Age category			
	< 35 years	35–49 years	50–64 years	≥ 65 years
<i>N</i> , men/women	20/16	16/17	35/42	21/23
Age, years	27.0 ± 4.6	43.3 ± 4.8*	59.9 ± 3.1*†	69.2 ± 3.2*†‡
Height, cm	166.2 ± 8.3	165.2 ± 8.1	160.4 ± 8.1*	158.0 ± 8.6*†
Body weight, kg	61.7 ± 11.9	63.2 ± 11.5	59.1 ± 9.3	56.8 ± 8.7
BMI, kg/m ²	22.2 ± 3.1	23.0 ± 3.0	22.9 ± 2.6	22.7 ± 2.2
Heart rate, bpm	58.1 ± 8.8	60.1 ± 8.4	60.4 ± 7.5	60.1 ± 7.2
Brachial SBP, mm Hg	112 ± 15	119 ± 14	126 ± 16*	130 ± 16*†
Brachial DBP, mm Hg	65 ± 10	74 ± 10*	78 ± 10*	79 ± 10*
Brachial PP, mm Hg	47 ± 7	45 ± 7	48 ± 10	50 ± 10
Aortic SBP, mm Hg	99 ± 14	110 ± 15*	120 ± 16*†	123 ± 15*†
Aortic MBP, mm Hg	65 ± 10	74 ± 10*	78 ± 10*	79 ± 10*
Aortic DBP, mm Hg	65 ± 10	74 ± 10*	78 ± 10*	79 ± 10*
Aortic PP, mm Hg	33 ± 7	35 ± 8	41 ± 10*†	43 ± 9*†
Aortic AP, mm Hg	6.2 ± 3.7	8.8 ± 4.3	14.9 ± 6.0*†	16.3 ± 6.3*†
Aortic AIx, %	18.8 ± 10.4	24.3 ± 9.3	35.7 ± 8.9*†	37.0 ± 8.8*†

Abbreviations: AIx, augmentation index; AP, augmentation pressure; BMI, body mass index; DBP, diastolic blood pressure; MBP, mean blood pressure; PP, pulse pressure; SBP, systolic blood pressure.

Data are mean ± SD. “**”, “†”, and “‡” indicate significant differences from <35 years, 35–49 years, and 50–64 years, respectively (by Scheffé *post hoc* test).

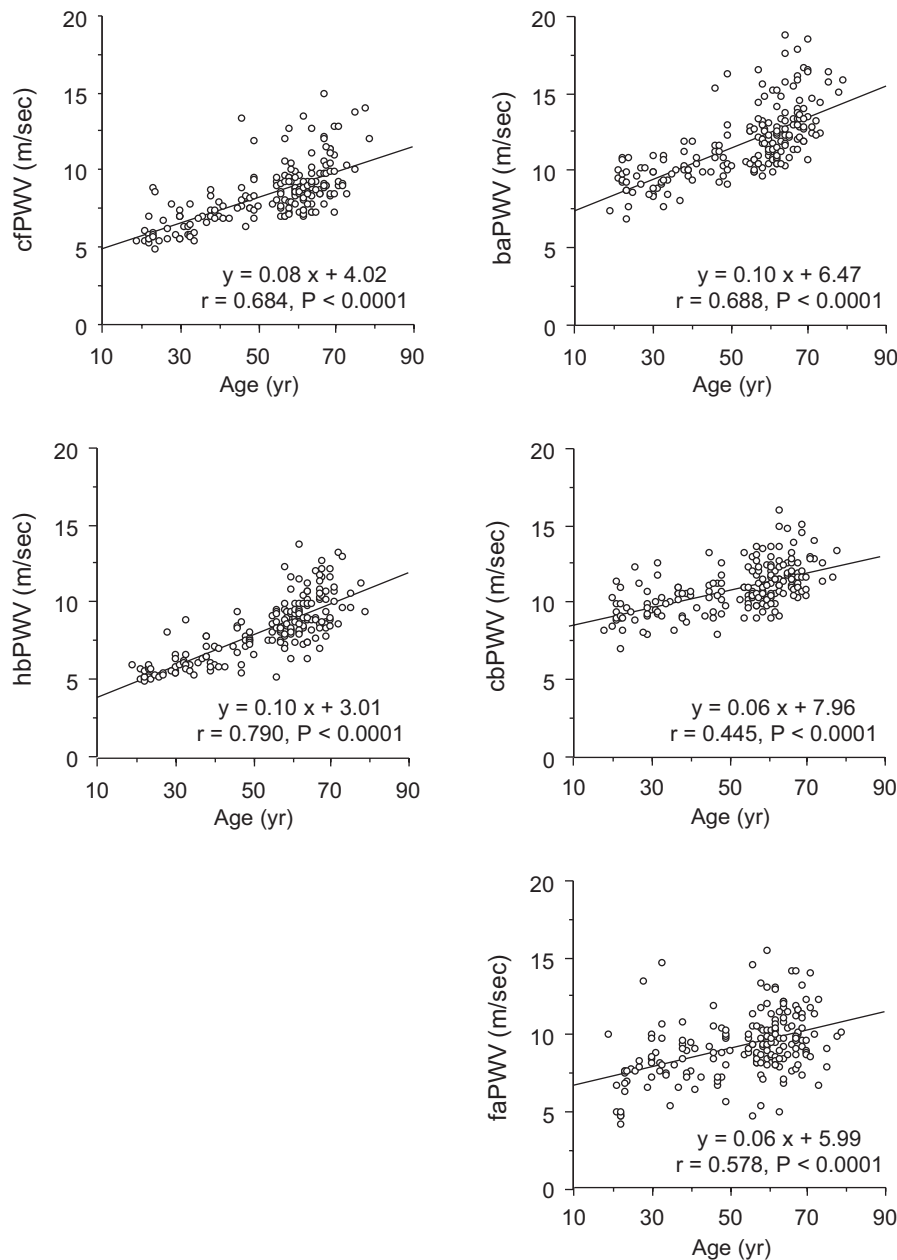


Figure 1. Scatter plots between age and pulse wave velocity (PWV) of various arterial segments in study 1. Abbreviations: baPWV, brachial-ankle PWV; cbPWV, carotid-brachial PWV; cfPWV, carotid-femoral PWV; faPWV, femoral-ankle PWV; hbPWV, heart-brachial PWV.

higher in 2 older age categories than in 2 younger age categories. Heart rate and brachial PP were not different among the age categories.

As shown in [Figure 1](#), all the MRI-based PWV measures displayed were significantly correlated with age ($r = 0.445$ – 0.790 , $P < 0.0001$ for all). Correlation coefficient with age was significantly greater in hbPWV compared with those of other PWVs ($P < 0.05$ for all). Similar results were observed in PWVs calculated from body surface and height-based arterial path lengths ([Supplementary Table 2](#)).

[Figure 2](#) shows a comparison of hbPWV and cbPWV in each age category. Both PWV measures increased gradually throughout the age range. Notably, there were significant

differences between hbPWV and cbPWV in the 2 younger age categories, but these measures were comparable after 50 years of age.

[Figure 3](#) presents correlations between MRI-based PWVs. baPWV was strongly correlated with cfPWV ($r = 0.869$, $P < 0.0001$), whereas hbPWV exhibited modest correlations with cfPWV ($r = 0.686$, $P < 0.0001$) and baPWV ($r = 0.663$, $P < 0.0001$). [Table 2](#) presents simple and partial correlational analyses between selected PWV and aortic hemodynamics. All the selected PWVs were correlated with all the hemodynamic variables in simple correlational analyses. hbPWV had the stronger correlations with aortic systolic BP and AIx after controlling for brachial systolic BP. Similar

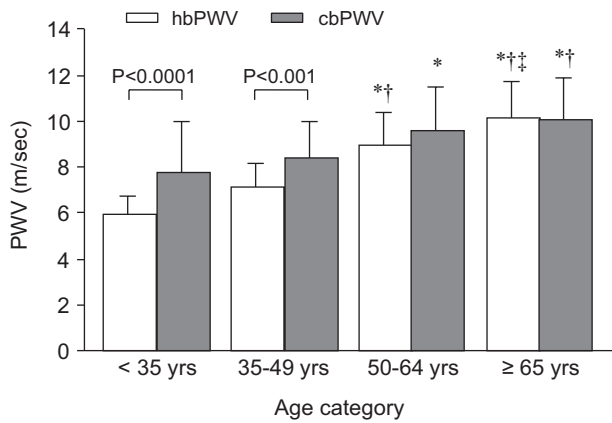


Figure 2. Comparison of heart-brachial pulse wave velocity (hbPWV) and carotid-brachial PWV (cbPWV) in each age category in study 1. Data indicate mean \pm SD. “*”, “†”, and “††” indicate significant differences from <35 years, 35–49 years, and 50–64 years, respectively (by Scheffe *post hoc* test).

results were obtained in PWVs calculated from body surface and height-based arterial path lengths (Supplementary Table 2).

Study 2: Selected characteristics of subjects in study 2 are summarized in Table 3. Height decreased whereas body mass index, heart rate, systolic BP, PP, baPWV, and hbPWV increased after the 10-year follow-up period. Body weight, brachial diastolic BP, aortic AP, and AIx did not change significantly.

The magnitudes of decadal changes in hbPWV and baPWV were similar ($P = 0.994$; Figure 4, top). However, changes in hbPWV were not associated with changes in baPWV ($r = 0.173$, $P < 0.05$; Figure 4, bottom). As summarized in Table 4, decadal changes in aortic systolic BP were correlated with corresponding changes in baPWV ($r = 0.228$, $P < 0.05$) and hbPWV ($r = 0.349$, $P < 0.05$). Decadal changes in aortic AP and AIx were correlated with corresponding changes in hbPWV but not with those in baPWV.

DISCUSSION

Salient findings of this study were as follows. Among all the PWV measures, hbPWV exhibits one of the largest age-related increases and significantly stronger correlation with age. In addition, there were significant differences between hbPWV and cbPWV in the 2 younger age categories, but these measures were comparable after 50 years of age. hbPWV demonstrated significant correlations with aortic hemodynamic variables such as aortic systolic BP and aortic AIx. These correlations remained significant even after controlling for brachial systolic BP. Even in the 10-year follow-up study, decadal change in hbPWV was significantly associated with the corresponding changes in aortic hemodynamic variables. These results suggest that hbPWV is an index of arterial stiffness that displays pronounced age-associated changes and reflects hemodynamic factors in the aorta. Our present findings provide evidence that hbPWV is a potential marker of subclinical stiffening of the proximal aorta and call for further clinical evidence.

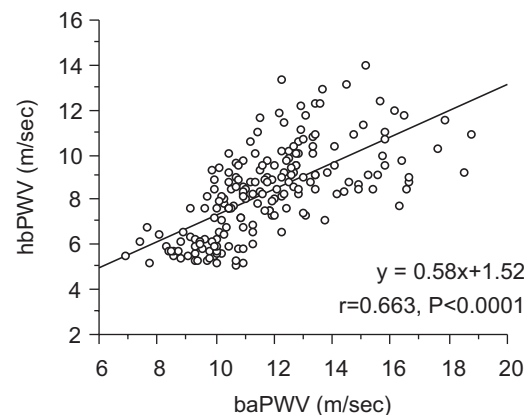
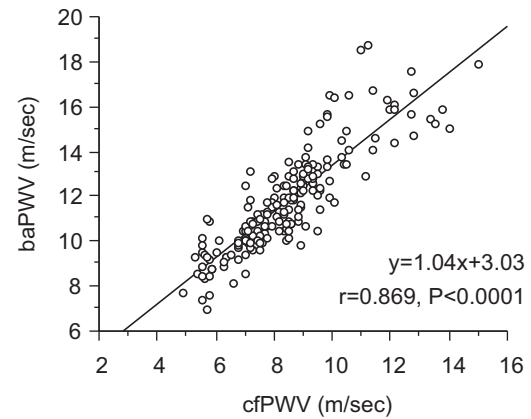
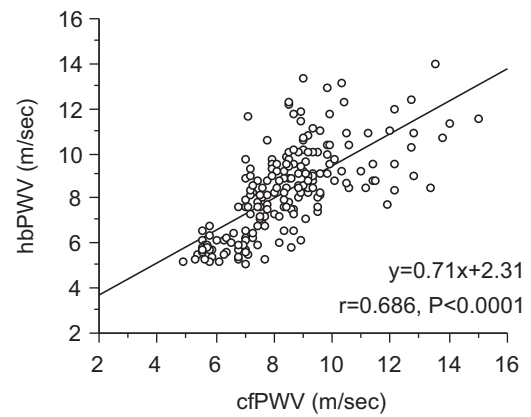


Figure 3. Relationships among carotid-femoral pulse wave velocity (cfPWV), heart-brachial PWV (hbPWV), and brachial-ankle PWV (baPWV) in study 1.

Age-related changes

Our cross-sectional investigation revealed that hbPWV exhibits the strongest correlation with age among selected measures of PWV. Age-related stiffening is remarkable in elastic artery than muscular artery.^{25,26} The projected arterial tree evaluated by hbPWV includes both the proximal aorta and muscular arteries (e.g., subclavian and brachial arteries), but the proximal aorta part seems to occupy <20%.¹⁷ Nevertheless, the extent of increase in hbPWV was modestly larger than that of cfPWV (+0.10 m/s/decade vs. +0.08 m/s/decade evaluated

Table 2. Results of simple and partial correlation analyses between selected magnetic resonance imaging (MRI)-based pulse wave velocity (PWV) and aortic hemodynamic variables in study 1

	cfPWV	baPWV	hbPWV
Simple correlation coefficient			
Aortic SBP	0.632	0.700	0.629
Aortic MBP	0.591	0.654	0.610
Aortic DBP	0.554	0.609	0.606
Aortic PP	0.510	0.570	0.444
Aortic AP	0.552	0.582	0.533
Aortic Alx	0.472	0.469	0.503
Partial correlation coefficient (controlling for age)			
Aortic SBP	0.444	0.552	0.417
Aortic MBP	0.434	0.531	0.463
Aortic DBP	0.360	0.445	0.432
Aortic PP	0.353	n.s.	0.227
Aortic AP	0.246	0.295	n.s.
Aortic Alx	n.s.	n.s.	n.s.
Partial correlation coefficient (controlling for brachial SBP)			
Aortic SBP	0.306	0.311	0.380
Aortic MBP	n.s.	n.s.	0.280
Aortic DBP	n.s.	n.s.	0.281
Aortic PP	n.s.	n.s.	n.s.
Aortic AP	0.339	0.350	0.324
Aortic Alx	0.393	0.390	0.432

Abbreviations: Alx, augmentation index; AP, augmentation pressure; baPWV, brachial-ankle pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; DBP, diastolic blood pressure; hbPWV, heart-brachial pulse wave velocity; MBP, mean blood pressure; n.s., non significant; PP, pulse pressure; SBP, systolic blood pressure.

Numbers are significant Pearson’s *r* values.

by the slope of regression line with age). On the other hand, cbPWV, which omits the section of the proximal aorta from the arterial path of hbPWV, showed a much smaller increase (+0.06 m/s/decade). For example, Figure 1 suggests that a subject aged 50 years exhibits 12.5 % and 5.5 % of decadal increases in hbPWV and cbPWV, respectively. Here, assuming that subject’s body height does not change much for a decade as seen in study 2 (~1 cm) and that the ascending aortic length corresponds 20% of the arterial path length for hbPWV, the ascending aortic PWV would increase by approximately 16% for a decade. Taken together, these results suggest that hbPWV undergoes marked age-related increases presumably as it reflects the aging-induced stiffening of the proximal aortic region.

Currently, very little information is available regarding the age-related changes in the proximal aortic properties despite the recognition that it is the most important arterial segment for buffering and cushioning cardiac pulsations.^{4,11,12} A study using MRI technique¹² reported similar PWV values among the proximal- (including the aortic root, the ascending aorta, and proximal descending aorta), mid- (including the proximal and

Table 3. Subjects characteristics in study 2

	Before	After
Age, years	53 ± 14	63 ± 14
Height, cm	163.7 ± 8.7	162.7 ± 9.3*
Body weight, kg	60.9 ± 11.1	61.0 ± 9.8
BMI, kg/m ²	22.6 ± 3.1	23.0 ± 2.8*
Heart rate, bpm	59.2 ± 6.8	61.4 ± 9.4*
Brachial SBP, mm Hg	121 ± 16	126 ± 15*
Brachial DBP, mm Hg	75 ± 12	77 ± 11
Brachial PP, mm Hg	46 ± 8	49 ± 11*
Aortic SBP, mm Hg	111 ± 16	118 ± 16*
Aortic MBP, mm Hg	91 ± 13	94 ± 11*
Aortic DBP, mm Hg	75 ± 12	77 ± 11
Aortic PP, mm Hg	36 ± 7	41 ± 12*
Aortic AP, mm Hg	10.7 ± 6.9	10.1 ± 10.9
Aortic Alx, %	29.1 ± 16.0	25.8 ± 22.2
baPWV, m/s	13.4 ± 2.6	14.9 ± 3.2*
hbPWV, m/s	9.4 ± 1.7	10.7 ± 1.8*

Abbreviations: Alx, augmentation index; AP, augmentation pressure; baPWV, brachial-ankle pulse wave velocity; BMI, body mass index; DBP, diastolic blood pressure; hbPWV, heart-brachial pulse wave velocity; MBP, mean blood pressure; PP, pulse pressure; SBP, systolic blood pressure.

Data are mean ± SD. *significant difference (vs. before, by paired *t* test).

mid-descending thoracic aorta), and distal- (including the mid-thoracic and abdominal aorta) sections in individuals <55 years of age, whereas the remarkable aortic stiffness gradient from the proximal to the distal region in individuals ≥55 years of age. In another study using phase-contrast MRI, aortic arch PWV increased dramatically after 50 years of age.¹¹ The present comparisons of PWV among age categories indicate that hbPWV demonstrated significantly lower values than cbPWV in younger age categories, whereas the difference gradually diminished with increasing age categories and abolished at older age categories. These results suggest that stiffness of the proximal artery reaches to that of muscular arteries (e.g., subclavian and brachial arteries) after 50 years of age. In our 10-year follow-up study, hbPWV increased by 14% for a decade in apparently healthy individuals 53 years of age at baseline (from 9.4±1.7 to 10.7±1.8 m/s). This extent of elevation was similar to the difference in hbPWV between the 2 oldest age categories in the cross-sectional comparison (9.0 ±1.4 vs. 10.2±1.5 m/s). In this context, a large cohort study demonstrated a 18% increase in aortic arch PWV over the 10-year follow-up period.⁴ Thus, the age-related changes in hbPWV observed in the present study are consistent with previous studies using different modalities that assessed the stiffness of the proximal aorta.

Relationship with aortic hemodynamics

The proximal aorta, the most elastic segment of the blood vessel directly connected to LV, would strongly

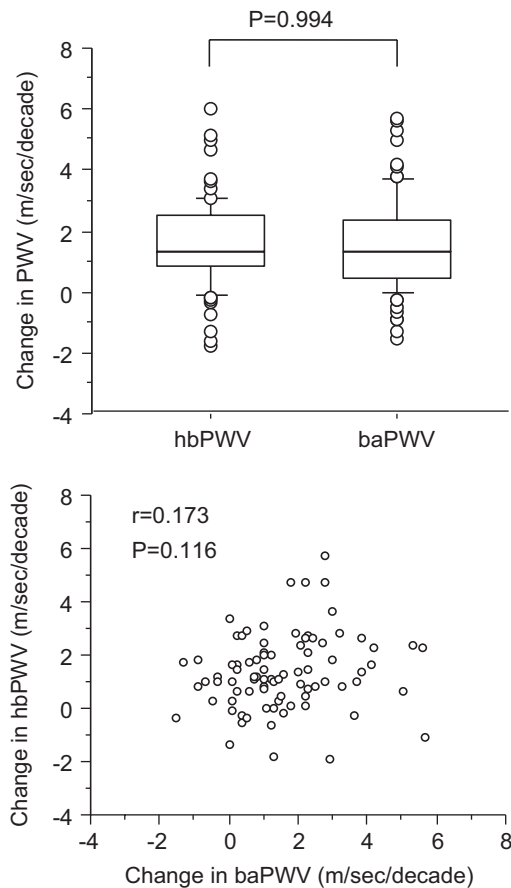


Figure 4. Comparison between decadal changes in heart-brachial pulse wave velocity (hbPWV) and brachial-ankle PWV (baPWV) in study 2: the box and whisker plot (top); the scatter plot (bottom).

contribute to dampening cyclic mechanical forces of cardiac pulsations. Accordingly, it is plausible to hypothesize that the age-related aortic stiffening of the proximal region possesses stronger interaction with aortic hemodynamics compared with that of the distal aortic region evaluated by other PWV measures. hbPWV was modestly correlated with most of the selected aortic hemodynamic variables as cfPWV and baPWV did. However, the 10-year follow-up data indicated that decadal changes in hbPWV were more strongly correlated with corresponding changes in aortic hemodynamic variables. It should be emphasized here that aortic hemodynamic indices such as aortic systolic BP, PP, and AIx, are independent predictors of future CVD events and all-cause mortality.^{27–30} Therefore, our findings strongly suggest that hbPWV is a potential marker of subclinical arterial stiffening. Prospective data linking hbPWV to clinical endpoints are warranted.

Study limitations

There are some drawbacks of this study that should be mentioned. First, arterial path lengths were directly measured by MRI in the cross-sectional investigation but not in the follow-up study. However, the estimation equation

Table 4. Results of simple correlation analyses between changes in pulse wave velocity (PWV) and corresponding changes in aortic hemodynamic variables in study 2

	Δ hbPWV	Δ baPWV
Δ Aortic SBP, mm Hg	0.349	0.228
Δ Aortic MBP, mm Hg	0.471	0.272
Δ Aortic DBP, mm Hg	0.439	n.s.
Δ Aortic PP, mm Hg	n.s.	n.s.
Δ Aortic AP, mm Hg	0.289	n.s.
Δ Aortic AIx, %	0.240	n.s.

Abbreviations: AIx, augmentation index; AP, augmentation pressure; baPWV, brachial-ankle pulse wave velocity; DBP, diastolic blood pressure; hbPWV, heart-brachial pulse wave velocity; MBP, mean blood pressure; n.s., non significant; PP, pulse pressure; SBP, systolic blood pressure.

Numbers are significant Pearson's *r* values.

for hbPWV has been validated by comparison with those obtained with 3-dimensional MRI.¹⁵ Second, we conducted the 10-year follow up study but could not evaluate clinical events or end point because the sample size was relatively small and the participants were apparently healthy at baseline. Third, we evaluated the longitudinal change of baPWV instead of cfPWV, the reference standard of central arterial stiffness assessment. However, baPWV has been recognized as a useful predictor of risk of total cardiovascular events and all-cause mortality as a surrogate of cfPWV.³¹ Finally, in study 2, as arterial path lengths were estimated by functions of height not by MRI, the age-related elongation of arterial lengths could not be accounted for in the analysis. A cross-sectional study with large sample size³² demonstrated that the path length for invasive aortic PWV was relatively constant across all age groups although body heights were shorter with advancing age of groups. These results may indicate that body surface measurement and height-based estimation of arterial path length could be a potential confounding artifact for the comparison of aortic PWV between younger and older populations. In our longitudinal observation, however, individual shrinkage of body height was very slight (~1 cm). Furthermore, its impact might be negligible because age-related change in PWV could be mainly attributed to the shorten pulse transition time.¹⁸

CONCLUSION

As an initial step to evaluate the emerging technique to assess proximal aortic stiffness *via* hbPWV, we determined the influence of aging on PWV and aortic hemodynamic measures. hbPWV exhibits a stronger correlation with age and aortic hemodynamic factors such as aortic systolic BP and AIx. Our present findings demonstrate that hbPWV is a potential marker of subclinical arterial stiffening.

PERSPECTIVES

In this study, using both cross-sectional and longitudinal follow-up studies, we demonstrated that

hbPWV increases markedly with advancing age and is associated with aortic hemodynamic factors. Given the simplicity of the technique, hbPWV assessment has the potential to be a promising technique that is suitable for routine clinical settings. However, in order for hbPWV to be recognized as an important clinical tool, a more thorough analysis that links this PWV measure to clinical outcomes is needed.

SUPPLEMENTARY DATA

Supplementary data are available at *American Journal of Hypertension* online.

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DISCLOSURE

The authors declared no conflict of interest.

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