Utility of Automated Brachial Ankle Pulse Wave Velocity Measurements in Hypertensive Patients

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Background: We examined whether pulse wave velocity (PWV), determined by brachial ankle arterial pressure wave measurements, using a newly developed, fully automated device could be a surrogate measure for carotid femoral PWV.

Methods & Results: This device (AT-form PWV/ABI, Nippon Colin, Komaki, Japan) can simultaneously monitor bilateral brachial and ankle pressure wave forms using the volume plethysmographic method, with two optional tonometry sensors for carotid and femoral arterial wave measurements. We examined the right brachial–right ankle PWV and left carotid–left femoral PWV in 89 normotensive and untreated hypertensive patients. The brachial ankle PWV correlated well with carotid femoral PWV ($r = 0.755$, $P < .00001$). The Bland-Altman plots of the two variables, however, showed a significant difference exists between the two techniques over the range of measurement. The within-observer and between-observer coefficients of variation of the brachial ankle PWV were 6.5% ± 4.1% and 3.6% ± 3.9%, respectively. To determine the factors affecting brachial ankle PWV, we studied treated and untreated hypertensive patients with World Health Organization stage I ($n = 146$), stage II ($n = 74$), or stage III ($n = 54$). In multiple regression analysis, age, brachial ankle PWV, and the presence of diabetes were significant predictors of the severity of hypertensive organ damage. Age, systolic blood pressure, and the stage of hypertensive organ damage were major determinants of brachial ankle PWV.

Conclusions: Although the brachial ankle PWV does not agree with the carotid femoral PWV, this parameter may yet become a new, useful measure for arterial stiffness. Further longitudinal studies are necessary to confirm the clinical significance of the brachial ankle PWV. Am J Hypertens 2003;16:653–657 © 2003 American Journal of Hypertension, Ltd.

Key Words: Pulse wave velocity, hypertension, arteriosclerosis, arterial stiffness.

Epidemiologic and clinical studies have shown that increased aortic stiffness, determined by the measurement of aortic pulse wave velocity (PWV), is an independent predictor of cardiovascular risk in the general population[1–3] and an independent predictor of cardiovascular mortality in patients with either essential hypertension or end-stage renal failure.[4,5] Recently, Guerin et al[6] have shown that a lack of change in the PWV in response to decreased blood pressure (BP) is an independent predictor of mortality in the setting of end-stage renal failure. Therefore, it is important not only to lower BP but also to reduce aortic stiffness to improve prognosis in patients with hypertension. Traditionally, the carotid femoral PWV has been used to evaluate aortic stiffness because 1) the pressure wave can easily be recorded at these two sites and 2) the distance between these two sites is great enough to allow an accurate calculation of the time interval between the two waves.[7] Manual detection of the pressure wave form, however, requires specific training and subsequent certification.[8] To generalize the evaluation of arterial stiffness among primary care physicians, a fully automated device that requires no specialized technical skill seems to be desirable.

Recently, the AT form device (Nippon Colin, Komaki, Japan) to measure PWV was developed.[9] This device monitors arterial pressure waves in the arm and ankle using volume plethysmographic method. The PWV is calculated from measurements of pulse transit time and path length between the brachial and ankle sites. Obtaining the PWV measurement using this device is easy and time

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saving because no specialized skills are needed to use the probe. Recently, Yamashina et al[10] have shown that brachial ankle PWV correlated well with aortic PWV examined by an invasive method. However, it remains to be clarified if the brachial ankle PWV could substitute for the carotid femoral PWV as a cardiovascular risk measure. The aims of this study were 1) to evaluate the validity and reliability of the brachial ankle PWV in comparison with carotid femoral PWV and 2) to identify the major determinants of brachial ankle PWV by measuring this variable in a large population of hypertensive patients.

Methods

AT Form PWV/ABI

The new device, the AT form PWV/ABI (Nippon Colin), simultaneously measures bilateral brachial and tibial arterial pressure wave forms, the lead I electrocardiogram, and the phonocardiogram. Occlusion cuffs, which were connected to both plethysmographic and oscillometric sensors, were placed around both arms and ankles with the subject in the supine position. All cuffs were inflated until the brachial and tibial arteries were completely occluded and then deflated. The arterial pressure waveforms were digitized at 1200 Hz for the brachial arterial waves and at 240 Hz for the tibial arterial wave. The signals were low-pass filtered at 50 Hz to remove high frequency noise.

The pulse transit time between the right brachial arterial wave and both tibial arterial waves (ΔTa) were determined by the foot-to-foot method. The foot was determined based on phase velocity theory. It has been shown that a mean phase velocity $>$2.5 Hz is constant and coincides with the wave front velocity.[11] Therefore, we can use the high frequency components of the arterial wave as a marker of phase shift. The high frequency components of the arterial wave are derived mainly from the "foot" and "notch" and are about 30 Hz. Accordingly, we used a band-pass filter with a lower cut-off frequency of 5 Hz and higher cut-off frequency at around 30 Hz to extract the high frequency components.[12] The foot can be identified using the R wave from the simultaneously recorded electrocardiogram as a reference. The plethysmographic sensor has bandwidth up to 30 Hz with 1200 Hz or 240 Hz sampling. In the frequency range from 5 to 30 Hz, the delay is devised to be within 0.8333 μsec. Therefore, an error should not seriously harm the reliability of measurement of PWV using the plethysmographic signal above 5 Hz.

The path length between the right arm and ankle was determined according to the patient's height and anthropomorphic data for the Japanese population.[13]

The path lengths from the suprasternal notch to the arm (ΔDa), from the suprasternal notch to the femur (ΔDb), and from the femur to the ankle (ΔDc) were calculated as $0.2195 \times H - 2.0734$, $0.5643 \times H - 18.381$, and $0.2486 \times H + 30.709$, respectively, where H is the patient's height in centimeters. The brachial ankle PWV was calculated by the following formula: $(\Delta Db + \Delta Dc - \Delta Da)/\Delta Ta$.

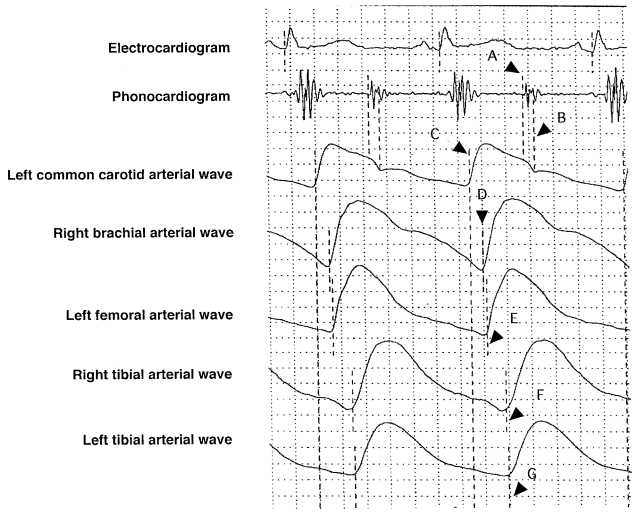

FIG. 1. Simultaneous recordings of the electrocardiogram, phonocardiogram, and arterial waves at left common carotid, right brachial, left femoral, and bilateral tibial sites in a 24-year-old woman. Lines A, B, C, D, E, F, and G indicate the starting point of second cardiac sound, the notch of the left common carotid arterial wave, the foot of the right brachial arterial wave, the foot of the left femoral arterial wave, the foot of the right tibial arterial wave, and the foot of the left tibial arterial wave, respectively.

There are several established devices for the measurements of carotid femoral PWV.[14] In this study, we used multielement tonometry sensors equipped with this device for the measurement of carotid femoral PWV.

The validity and reliability of this tonometry sensor has been published previously.[15] Therefore, we were able to compare the brachial ankle PWV directly with the carotid femoral PWV for the same cardiac cycles (Fig. 1). The carotid and femoral arterial waves were also digitized at 1200 Hz, and the pulse transit time between the carotid and femoral sites (ΔTb) was also determined by phase velocity theory. The path length from the suprasternal notch to the carotid site (ΔDd) was calculated as $\Delta Dd = 0.2437 \times H - 19.0$. The carotid femoral PWV was calculated by the following formula: $(\Delta Db - \Delta Dd)/\Delta Tb$. All reported PWV values represent the mean values obtained from a 10-sec recording.

Study Design

Two separate studies were conducted, each including different subjects. Approval was obtained from the Ethics Committee of Tohoku Rosai Hospital and informed consent was obtained from each participant.

Study I: Validity and Reproducibility of the Brachial Ankle PWV Eighty-nine normotensive and untreated hypertensive individuals participated in the study (60 ± 14 SD years, 37 men). The brachial ankle PWV and the left carotid–left femoral PWV were studied in those subjects. The agreement of the brachial ankle PWV and the carotid

Table 1. Demographic and cardiovascular variables for each group

Variable	WHO Stage I	WHO Stage II	WHO Stage III	*P*
Age (y)	56 ± 12	58 ± 12	71 ± 9‡¶	<.000001
Gender (male, %)	30	54†	35§	
Current smoker (%)	22	46‡	28§	
Diabetes (%)	3.4	6.7*	16.7#	
Dyslipidemia (%)	10	12	24†§	
Systolic blood pressure (mm Hg)	136 ± 16	143 ± 18†	145 ± 19‖	<.001
Diastolic blood pressure (mm Hg)	84 ± 10	88 ± 18†	81 ± 11¶	<.0005
Fasting blood glucose (mg/dL)	106 ± 20	106 ± 20	106 ± 16	ns
Total cholesterol (mg/dL)	211 ± 39	203 ± 39	212 ± 35	ns
HDL cholesterol (mg/dL)	57 ± 14	58 ± 16	59 ± 13	ns
Pulse wave velocity (cm/sec)	1525 ± 245	1627 ± 238†	1880 ± 398¶	<.000001

WHO = World Health Organization; ns = not significant.
* $P < .05$; † $P < .01$; ‡ $P < .001$ *v* WHO I; § $P < .05$; ‖ $P < .01$; ¶ $P < .001$ *v* WHO II.

femoral PWV were studied by the correlation analysis and the Bland-Altman plots.[16] Interobserver and intraobserver variability of the brachial ankle PWV was assessed for 47 healthy individuals, 39 to 81 years old (mean, 64 ± 11 years, 20 men) and 52 subjects, 31 to 83 years old (mean, 61 ± 14 years, 16 men), respectively. Measurements were repeated at the same time by two different observers to determine interobserver reproducibility. Intraobserver reproducibility was assessed by obtaining measurements from 2 different days under the same conditions by a single observer. Data were analyzed using Bland-Altman plots and reproducibility is expressed in terms of the mean difference ± SD between paired measurements.

Study II: Clinical Application We measured the brachial ankle PWV in treated ($n = 153$) or untreated ($n = 124$) patients with essential hypertension. In those patients, dyslipidemia was defined as a total cholesterol concentration >240 mg/dL or the use of a hypocholesterolemic drug. Diabetes mellitus was defined as a fasting blood glucose >126 mg/dL or the use of oral hypoglycemic agents. Patients with secondary hypertension, cancer, insulin-dependent diabetes, or renal insufficiency (plasma creatinine concentration >3.0 mg/dL) were not included in the study. Patients with peripheral arterial disease with ankle pressure index below 0.9 were excluded because precise measurement of the tibial arterial pressure wave was difficult in those patients. The cohort included a group with no organ damage (World Health Organization [WHO] stage I, $n = 146$), with mild organ damage (WHO stage II, $n = 74$), and with overt organ damage group (WHO stage III, $n = 54$). The WHO stage III group included 38 patients with cerebrovascular diseases, 13 patients with ischemic heart disease, and 3 patients with mild chronic renal failure due to nephrosclerosis. The clinical characteristics of each group are summarized in Table 1. Venous blood samples were obtained from all participants after an overnight fast for the study of glucose and lipid profiles.

Statistical Analysis

Data are expressed as the mean ± SD. Analysis of variance was used to test for differences in the mean values of several parameters based on the stage of hypertensive organ damages. Student *t* test was used to compare normally distributed continuous variables. Differences in frequency were determined by the χ^2 test. Multiple regression analysis was used to identify which parameters predicted the severity of hypertensive organ damage. We also examined the determinants of brachial ankle PWV. All statistical analyses were performed using commercially available software (Stat Flex version 5.0 for Windows, Artec, Osaka, Japan). A value of $P < .05$ was considered as statistically significant.

Results

Validity of the Brachial Ankle PWV By the AT Form PWV/ABI Device

The brachial ankle PWV (right:1553 ± 264 cm/sec, left: 1578 ± 305 cm/sec) was significantly greater than the carotid femoral PWV (1066 ± 249 cm/sec, $P < .000001$ for both). The mean differences were 488 ± 180 and 512 ± 192 cm/sec, respectively. The carotid femoral PWV correlated well with both the right brachial–right ankle PWV ($r = 0.755$, $P < .000001$; Fig. 2a) and the right brachial–left ankle PWV ($r = 0.778$, $P < .000001$). The Bland-Altman plots of the right brachial–right ankle PWV and the carotid femoral PWV showed that the significant difference exists over the range of measurement (Fig. 2b).

The intraobserver and interobserver differences for the right brachial–right ankle PWV were −22 ± 111 and −1 ± 83 cm/sec, respectively. The corresponding variation coefficients were 6.5% ± 4.1% and 3.6 ± 3.9%, respectively. Fig. 2c,d shows Bland-Altman plots for intraobserver and interobserver reproducibilities for the right brachial–right ankle PWV. There was no trend for the reproducibility for the measurement to vary with the un-

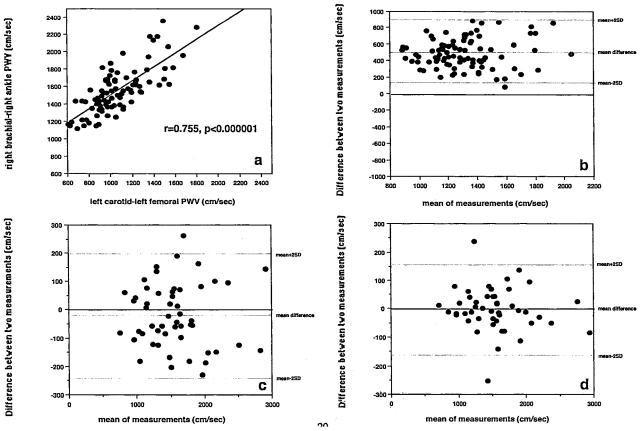

FIG. 2. a) Relationship between the left carotid–left femoral pulse wave velocity and the right brachial–right ankle pulse wave velocity in 89 subjects. **b**) Bland-Altman plots of the data of **a**. The **vertical** and **horizontal axes** indicate the difference between the brachial ankle pulse wave velocity (PWV) and the carotid–femoral PWV, and the mean of the two variables, respectively. **c, d**) Bland-Altman plots showing the relationship between intraobserver differences in measurements of the right brachial–right ankle PWV and the mean, and between interobserver differences in measurements and the mean value, respectively.

derlying value in any of the analyses. In addition, there was no evidence of systematic bias.

Table 1 summarizes the demographic and cardiovascular variables for each group. Patients with WHO stage III were older than patients in the other two groups ($P < .001$). Systolic BP increased with increasing hypertensive organ damage ($P < .001$). Diastolic BP was higher in patients with WHO stage II group than in those with stage I group ($P < .01$). However, patients with WHO stage III group had a lower diastolic BP than patients with WHO stage II group ($P < .001$). Sixty-three percent of patients with stage I, 59% with stage II, and 86% with stage III had received antihypertensive medications. The treatment rates for diabetes and dyslipidemia increased with increasing hypertensive organ damage. The fasting blood sugar, total cholesterol, and HDL concentrations did not differ among the three groups. The right brachial–right ankle PWV increased with increasing hypertensive organ damage ($P < .000001$). On the basis of stepwise linear regression analysis, the factors influencing the severity of hypertensive organ damage were age ($P = .0004$), right brachial–right ankle PWV ($P = .02$), and the presence of diabetes ($P = .04$). If the right brachial–right ankle PWV was made a dependent variable, age ($P < .00001$), brachial systolic BP ($P < .00001$), and the severity of hypertensive organ damage ($P = .01$) were major determining factors.

Discussion

We examined the usefulness of a new PWV measurement based on the analysis of brachial and ankle arterial pressure waves. The right brachial–right ankle PWV correlated well with the left carotid–left femoral PWV ($r = 0.755$, $P < .00011$). The Bland-Altman plots, however, showed that the brachial ankle PWV was significantly greater than the carotid femoral PWV over the range of measurement. This means that the brachial ankle PWV reflects not only aortic stiffness but also the stiffness of the peripheral muscular artery.

The higher values for the brachial ankle PWV were independently associated with more severe stages of hypertensive organ damage in a large cohort of hypertensive patients. Moreover, considering the brachial ankle PWV as a dependent variable, age, systolic BP, and the severity of hypertensive organ damage were major determining factors. Therefore, our data are consistent with previous findings that carotid femoral PWV is strongly related to age, BP, and the presence of atherosclerotic alterations in treated or untreated patients with essential hypertension.[17] These data suggest that the brachial ankle PWV has a possibility to become a new, useful measure for arterial stiffness, although it does not agree with the carotid femoral PWV.

There are two methodologic characteristics that deserve mention. First, the time difference between the carotid and femoral arterial waves has previously been determined by performing a correlation analysis of the two waves. With our new device, it was determined based on the wave front velocity theory.[11] It has been shown that variations in the phase velocity of the arterial pulse wave are large in the low frequency range but small and constant above 2.5 Hz. The mean value of the velocities of harmonics >2.5 Hz has been shown to coincide with the wave front velocity. Because the high frequency components of the arterial wave are derived mainly from the foot and notch, we used the foot wave, which was extracted by band-pass filtering as a marker of time shift. Second, we used the path length determined from the patient's height and anthropomorphic data for a large population instead of actual measurement. In fact, arteries become longer and more tortuous with age, and therefore the path length determined from superficial linear measurements is often underestimated. Because the structure of the arterial tree largely depends on patient height, it seems reasonable to estimate the path length based on the patient's height. We found an independent association between the brachial ankle PWV and the degree of organ damage in hypertensive patients. Moreover, the factors modulating the brachial ankle PWV determined by our new methodology are similar to those for the carotid femoral PWV determined by traditional methods. These data support the notion that our new methodologies are as reliable as traditional ones.

The brachial ankle PWV measurement by this new device seems to possess several practical benefits. First, no special skill is required to obtain brachial ankle PWV measurements in contrast to carotid femoral PWV measurements. This can reduce observer bias and could save time during studies. In fact, the intraobserver and interobserver differences for the brachial ankle PWV were -22 ± 111 and -1 ± 83 cm/sec, respectively. Therefore, the

brachial ankle PWV had better intraobserver and interobserver reproducibilities than carotid femoral PWV.[18] Moreover, the time needed to obtain a brachial ankle PWV measurement was less than half that needed for a carotid femoral PWV measurement.[9] Second, the brachial ankle PWV measurement does not require exposure of the inguinal region, which could eliminate the offensive feeling associated with the femoral artery examination. These practical advantages may be important in using the PWV measurements in general populations.

However, two important issues remain to be addressed. First, there are no data on the prognostic significance of brachial ankle PWV. Because the brachial ankle PWV examines more global arterial stiffness than carotid femoral PWV, the prognostic significance of brachial ankle PWV may differ from that of carotid femoral PWV. To confirm the clinical significance of the brachial ankle PWV as a predictor of cardiovascular risk, we need to perform a prospective, longitudinal study in a large population. Second, the formula used for calculating path length is based on anthropometric data from a Japanese population. We, therefore, must examine whether these formulas could extrapolate to other populations to establish a worldwide usefulness of the fully automated brachial ankle PWV measurement device.

In summary, the brachial ankle PWV measurement determined by the new device does not agree with the carotid femoral PWV. However, this parameter has a possibility to be used as a new useful measure for arterial stiffness. This novel method needs no specialized skills, enabling general physicians to evaluate arterial stiffness in daily practice. To confirm further the clinical significance of brachial ankle PWV measurements, we need to perform a longitudinal study in a large group of individuals.

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