Pulse wave velocity and the second derivative of the finger photoplethysmogram in treated hypertensive patients: their relationship and associating factors

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Objectives To clarify the factors influencing two measures of arterial stiffness, pulse wave velocity (PWV) and the second derivative of the finger photoplethysmogram (SDPTG), and to evaluate their relationship in treated hypertensive subjects.

Subjects and methods The subjects were 294 hypertensive patients aged 32–91 years (mean, 61.4 ± 10.5 years). After blood pressure (BP) was measured, carotid-femoral PWV and SDPTG were recorded with the subjects in the supine position, with the aid of an automatic device. For assessing SDPTG, we focused mainly on the ratios of the absolute value of the height of the early negative 'b' wave (B) and that of the late re-decreasing 'd' wave (D) to that of the initial positive 'a' wave (A), namely the B : A and D : A ratios, and the aging index (AGI). Factors influencing PWV and SDPTG indices, and the relationship between PWV and SDPTG indices were evaluated by bivariate and multivariate analyses.

Results According to multiple linear regression analysis, age, systolic blood pressure (SBP), and heart rate (HR) were variables independently and positively correlated with PWV. The age and BP were significantly and independently related to SDPTG indices; there were positive correlations with the D : A ratio and AGI, and negative correlations with the B : A ratio. HR was correlated negatively with the D : A ratio and AGI, and positively with the B : A ratio. According to multiple logistic regression analysis, adjusted-odds ratios of high PWV, low B : A ratio, high D : A ratio, and high AGI were significantly elevated among the elderly and among the subjects with uncontrolled BP. Although PWV and the SDPTG indices were associated with common factors, including age and BP, bivariate analysis revealed that they were only weakly correlated with each other.

Conclusions The results suggest that in hypertensive patients, PWV and SDPTG provide different information about arterial properties at central and peripheral sites.
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Introduction

Arteriosclerosis is a main underlying cause of cardiovascular diseases, including coronary heart disease and stroke. Arteries stiffen progressively with age, and hypertension accelerates the progression of arteriosclerosis with aging [1]. To manage hypertension and prevent cardiovascular complications, the degree of arteriosclerosis must be assessed precisely [2,3].

One of the non-invasive methods of assessing arterial stiffness is the measurement of pulse wave velocity (PWV). It is thought that the PWV between the carotid artery and the femoral artery reflects the stiffness of the aorta. Previous studies have shown that the aortic PWV increases with increasing age and blood pressure (BP) in the general populations [4,5]. It has also been demonstrated that the PWV in hypertensive patients with well-controlled diastolic blood pressure (DBP) is higher than that in normotensive patients, indicating the presence of greater structural changes in arteries in hypertension [6]. A greater PWV leads to an earlier return of the reflected wave from the periphery, and augments systolic blood pressure (SBP) in the central arteries. It has been shown that increases in SBP and pulse pressure (PP), mediated partly through an increase in PWV, are strong risk factors of cardiovascular disease [7,8].

Another non-invasive method of evaluating arterial

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characteristics utilizes the finger photoplethysmogram (PTG) [9–11]. The PTG expresses blood volume changes in the fingertip as pulse waves, but the PTG itself is used only rarely in clinical fields. Instead, the second derivative of the PTG (SDPTG) has been developed for more accurate recognition of the inflection points of PTG. The SDPTG is a simple, convenient and non-invasive technique for pulse wave analysis, seemingly providing information about both central and peripheral arterial factors. In fact, there is a constant relationship between an index derived from SDPTG and the ascending aortic augmentation [9]. However, the clinical significance of SDPTG is not fully understood because of the lack of data on the factors that influence it. Furthermore, the relationship between PWV and SDPTG indices has not yet been examined, although it has been reported that both are closely related to arterial stiffness.

Therefore, we performed the present study in hypertensive subjects to clarify the factors influencing PWV and SDPTG indices and to evaluate the relationship between them.

Methods

Study subjects

Subjects were consecutive outpatients with hypertension at Kojinkai Central Hospital, Sendai, Japan. Verbal informed consent to participate was obtained from all of the subjects. For patients who were not taking medication for hypertension, high blood pressure (BP) was defined as a SBP $\geqslant$ 140 mmHg and/or DBP $\geqslant$ 90 mmHg, as measured in triplicate with the patient in the sitting position. Patients undergoing treatment with antihypertensive drugs were considered as hypertensives and were accepted into the study, regardless of whether their BP was well controlled. Patients with cancer or severe liver disease were not included in the study. The subjects thus enrolled into this study comprised 294 hypertensive patients (153 men and 141 women). Of these, 269 (91.4%) were undergoing treatment with antihypertensive drugs; the mean number of prescribed drugs was 2.7 ± 1.3 per patient. Of the treated patients, calcium channel blockers were prescribed in 234 patients (87.0%), β-blockers in 154 (57.2%), angiotensin-converting enzyme inhibitors in 116 (43.1%), central-acting agents in 64 (23.8%), diuretics in 53 (19.7%), α-blockers in 45 (16.7%), and angiotensin II receptor blockers in 37 (13.8%), either alone or in combination. Twenty-eight patients (9.5%) were being treated medically for diabetes mellitus, with either insulin or oral antidiabetic drugs such as sulfonylureas and α-glucosidase inhibitors. Seventy-nine patients (26.9%) were being treated medically for dyslipidemia, with statins or fibrates. Serum creatinine concentration, plasma total cholesterol and high-density lipoprotein (HDL) cholesterol were measured in each subject.

PWV and SDPTG measurements

All measurements were performed when the subject was resting in the supine position. Brachial SBP and DBP were measured using an automatic device based on the Korotkoff sound method (GP303S; Paramatec, Fukuoka, Japan). The PP and mean arterial pressure (MAP) were calculated according to the formulae: $PP = SBP - DBP$, and $MAP = [SBP + (DBP \times 2)]/3$, respectively. After measurement of BP, the carotid-femoral PWV was determined using an automatic device FCP-4731 with the aid of a pulse wave input box IB-70 (Fukuda Denshi, Tokyo, Japan), according to previous studies [12–15] as follows. The device utilized two transducers (TY-501A; Fukuda Denshi) to measure online pulse waves. One of the transducers was positioned at the base of the neck for the left common carotid artery and the other was placed over the left femoral artery. The device recorded simultaneously the electrocardiogram and phonocardiogram (PCG). Thus, the PWV was measured automatically according to the following equation: $PWV = D \times 1.3/(t + tc)$, where t is the time difference in foot between the carotid pulse wave and the femoral pulse wave, tc is the time interval from the beginning of the second cardiac sound on the PCG to the incisura of the carotid pulse wave, namely, the transmission time for pulse to reach the carotid site after opening of the aortic valve, and $t + tc$ indicates the time for the pulse wave to travel from the aortic orifice to the femoral site [12–15]. D is the superficially measured linear distance from the right parasternal margin of the second intercostal space to the position of the transducer over the left femoral artery. The actual intra-arterial curvilinear distance between the aortic orifice and the femoral site was estimated to be $D \times 1.3$ [13,16]. The correlation coefficients of t and tc, and PWV between two measurements were more than 0.93, and the automatic device based on this method has been validated [17]. The standardization of the measured PWV for DBP was not performed in the present study, because one of the purposes of the study was to clarify the relationship between PWV and BP. The mean PWV in each subject was determined from 4.2 ± 0.9 measurements.

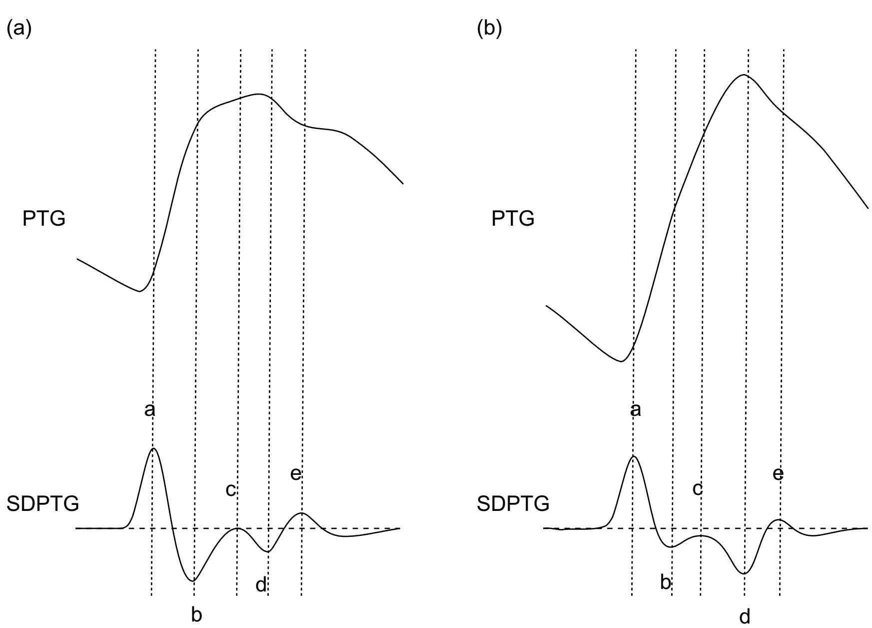
The finger PTG and SDPTG were then recorded by an FCP-4731 system with an IB-70, which contained a photoplethysmogram equipped with double-differentiation circuits. A transducer was placed on the cuticle on the second finger of the right hand, and the signal was fed to the FCP-4731. The details of the methodology for measurement of PTG and SDPTG are reported elsewhere [9,10]. The PTG expresses changes in the absorbance of hemoglobin using a waveform according to the Lambert–Beer law, thus reflecting changes in regional blood flow [11]. The SDPTG is, in general, obtained to specify inflection points on PTG waves. The SDPTG consists of 5 waves: the 'a' wave, which is the initial positive wave; the 'b' wave, which is an early negative wave; the 'c' wave, a re-increasing wave; the 'd' wave, a late re-decreasing wave; and the 'e' wave, which is a diastolic positive wave (Fig. 1). In the present study, absolute values for the height of the waves a, b, and d were referred to as A, B, and D, respectively. We calculated the B : A and D : A ratios, which correspond to the negative b : a and negative d : a ratios, respectively, reported in a previous study by Takazawa *et al.* [9]. The aging index (AGI), which is defined as (b−c−d−e)/a according to the previous study [9], was also obtained. The mean ratios and AGI of the SDPTG for each subject were determined 4.0 ± 1.1 times. The validation of this automatic device and its reproducibility have been reported previously, with an intra-observer repeatability (according to Bland and Altman [18]) of 8% [19].

Statistical analysis

Using bivariate regression analysis, we first assessed the linear relationships between PWV and its potentially related variables [i.e., age, gender, duration of hypertension, family history of hypertension (parental hypertension), current smoking status, body height, body mass index (BMI), SBP, DBP, MAP, PP, heart rate (HR), coexistence of diabetes mellitus, total cholesterol, and medication for hypertension, diabetes mellitus, and hyperlipidemia]. Thereafter, multiple stepwise linear regression analysis was performed using all variables that were found to be significantly associated with PWV according to the bivariate analysis. Among the components of BP, SBP was most closely related to PWV, and therefore SBP was entered into the model. Furthermore, we performed multiple stepwise logistic regression analysis to clarify the factors relating to high PWV. Based on the PWV data in 294 subjects, those subjects whose PWV exceeded the mean + SD were defined as having a high PWV. The adjusted-odds ratios (OR) and 95% confidence intervals (CI) of cases of high PWV were determined using possibly independent categorical variables [i.e., age: the young and middle-aged (< 60 years old), the elderly (≥ 60 years old); gender: male, female; obesity (BMI ≥ 25 kg/m^2): yes, no; supine BP: well-controlled (SBP < 140 mmHg and DBP < 90 mmHg), uncontrolled (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg); HR: lower (< 60/min), higher (≥ 60/min); use of antihypertensive drugs: yes, no; use of antidiabetic drugs: yes, no; use of lipid-lowering drugs: yes, no].

Similar analyses were carried out regarding SDPTG parameters, including the B : A and D : A ratios, and AGI. For multiple stepwise linear regression analysis, SBP was chosen among the components of BP as a

Fig. 1



Representative recordings of finger photoplethysmogram (PTG) and the second derivative of PTG (SDPTG). The SDPTG consists of five waves 'a–e'. (a) shows a recording in a 39-year-old male subject with a high B : A ratio (0.64), a low D : A ratio (0.28), and a low AGI (−0.54). (b) shows a recording in an 82-year-old male subject with a low B : A ratio (0.24), a high D : A ratio (0.62), and a high AGI (0.35).

determinant of the B : A ratio or AGI, while MAP was chosen as that of the D : A ratio, because of their best correlations. In multiple stepwise logistic regression analyses, we examined factors associating low B : A ratio, high D : A ratio, or high AGI. Based on the data on SDPTG indices in all subjects, those with a B : A ratio below the mean − SD, those with a D : A ratio above the mean + SD, and those with an AGI above the mean + SD, were considered to have a low B : A ratio, a high D : A ratio, and a high AGI, respectively. The possibly independent factors similar to those relating to high PWV were entered into the model. Finally, we used bivariate linear regression analysis to examine the correlation between PWV and SDPTG parameters.

Data are expressed as mean ± SD. Student's *t*-test was used for comparisons of the means of continuous variables between two groups. All statistical analyses were performed with SPSS software version 10.1 (SPSS Inc., Chicago, Illinois, USA). Statistical significance was accepted at a value of $P < 0.05$.

Results

The clinical characteristics of the subjects who participated in this study are given in Table 1. The mean age of the 294 hypertensive subjects was 61.4 ± 10.5 years (range, 32–91 years). The male subjects had a slightly higher DBP, a higher serum creatinine level, and lower total and high-density lipoprotein (HDL) cholesterol levels than the female subjects, but there were no gender differences in the other clinical characteristics. Table 2 shows the mean values of the PWV and SDPTG indices, including the B : A and D : A ratios, and AGI.

Factors influencing PWV

In bivariate analysis, the PWV was significantly and positively correlated with age (Table 3). There was no difference in PWV between male (8.50 ± 1.31 m/s) and female (8.63 ± 1.29 m/s) subjects. The PWV was significantly correlated with duration of hypertension, whereas it was not associated with family history of hypertension, smoking status, body height, or BMI. SBP, DBP, PP, and MAP were positively correlated with PWV; the strongest correlation was with SBP. HR was weakly but significantly associated with PWV. The PWV in those treated with antihypertensive drugs (8.57 ± 1.31 m/s) was similar to that in untreated subjects (8.52 ± 1.18 m/s). The subjects with diabetes ($n = 47$) tended to have a greater PWV than those without diabetes ($n = 247$), but the difference was insignificant (8.87 ± 1.23 versus 8.51 ± 1.31 m/s, $P = 0.08$). There was no significant difference in PWV between those treated medically for diabetes mellitus and the rest. The PWV was not correlated with total cholesterol level, but those treated medically for dyslipidemia had a significantly higher PWV than the rest of the subjects (8.85 ± 1.41 versus 8.46 ± 1.25 m/s, $P = 0.02$).

For multiple stepwise linear regression analysis, age, duration of hypertension, SBP, HR, and medication for dyslipidemia (no = 0, yes = 1) were entered into the model as potentially related variables. The multivariate analysis revealed that age, SBP, and HR were independently correlated with PWV, accounting for 34.4% of the variance (Table 4).

The multiple stepwise logistic regression analysis revealed that the adjusted OR of a high PWV

Table 2 **Cardiovascular parameters in the measurements of PWV and SDPTG ($n = 294$)**

SBP (mmHg)	132.1 ± 16.2
DBP (mmHg)	79.2 ± 9.7
PP (mmHg)	53.0 ± 14.6
MAP (mmHg)	96.8 ± 10.1
HR (bpm)	59.8 ± 10.4
PWV (m/s)	8.57 ± 1.30
B : A	0.419 ± 0.136
D : A	0.381 ± 0.109
AGI	−0.065 ± 0.279

PWV, pulse wave velocity; SDPTG, second derivative of finger photoplethysmogram; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure; HR, heart rate; B : A, the ratio of the absolute value of the height of 'b' wave (B) to that of 'a' wave (A) on SDPTG; D : A, the ratio of the absolute value of the height of 'd' wave (D) to A; AGI, aging index of SDPTG.

Table 1 **The clinical characteristics of the subjects**

	Male ($n = 153$)	Female ($n = 141$)	Total ($n = 294$)
Age (years)	60.4 ± 10.7	62.6 ± 10.2	61.4 ± 10.5
Duration of hypertension (years)	14.9 ± 11.0	15.6 ± 10.0	15.2 ± 10.5
Body height (cm)	166.2 ± 6.6	153.2 ± 5.0***	160.0 ± 8.8
Body mass index (kg/m^2)	25.1 ± 3.1	23.9 ± 3.1**	24.5 ± 3.1
Casual SBP (mmHg)	136.1 ± 16.8	139.8 ± 18.3	137.9 ± 17.6
Casual DBP (mmHg)	83.6 ± 10.7	80.0 ± 10.6**	81.9 ± 10.8
HR (bpm)	66.8 ± 11.0	69.5 ± 13.4	68.1 ± 12.3
Serum creatinine (mg/dl)	1.01 ± 0.31	0.81 ± 0.51***	0.91 ± 0.43
Total cholesterol (mg/dl)	194.7 ± 28.7	207.4 ± 27.1***	200.8 ± 28.6
HDL cholesterol (mg/dl)	52.7 ± 14.5	62.9 ± 16.4***	57.6 ± 16.3

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; HDL, high-density lipoprotein.
**$P < 0.01$, ***$P < 0.001$, versus male subjects.

Table 3 **Correlation coefficient between PWV or SDPTG indices and various parameters ($n = 294$)**

	PWV (m/s)		B : A		D : A		AGI	
	R	*P*	*R*	*P*	*R*	*P*	*R*	*P*
Age (years)	0.445	<0.001	−0.425	<0.001	0.196	0.001	0.418	<0.001
Duration of HT (years)	0.169	0.004	−0.160	0.006	0.119	0.04	0.188	0.001
Body height (cm)	−0.101	NS	0.227	<0.001	−0.008	NS	−0.207	<0.001
BMI (kg/m^2)	0.070	NS	0.228	<0.001	−0.090	NS	−0.183	0.002
SBP (mmHg)	0.405	<0.001	−0.275	<0.001	0.290	<0.001	0.230	<0.001
DBP (mmHg)	0.195	0.001	−0.045	NS	0.328	<0.001	0.072	NS
PP (mmHg)	0.319	<0.001	−0.275	<0.001	0.103	NS	0.207	<0.001
MAP (mmHg)	0.340	<0.001	−0.175	0.003	0.364	<0.001	0.168	0.004
HR (bpm)	0.146	0.01	0.203	<0.001	−0.175	0.003	−0.143	0.01

R, Pearson correlation coefficient; HT, hypertension; BMI, body mass index; NS, not significant; PWV, pulse wave velocity; SDPTG, second derivative of finger photoplethysmogram; B : A, the ratio of the absolute value of the height of ‘b’ wave (B) to that of ‘a’ wave (A) on SDPTG; D : A, the ratio of the absolute value of the height of ‘d’ wave (D) to A; AGI, aging index of SDPTG; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure; HR, heart rate.

Table 4 **Multiple stepwise linear regression analysis of pulse wave velocity ($n = 294$)**

	β	SE	*t*	*P*
Age (years)	0.052	0.006	8.719	<0.001
SBP (mmHg)	0.028	0.004	7.170	<0.001
HR (bpm)	0.015	0.006	2.510	0.01

β, partial regression coefficient; SE, standard error. Model $R^2 = 0.344$, $F = 50.66$, model probability $P < 0.001$. SBP, systolic blood pressure; HR, heart rate.

($\geqslant 9.9$ m/s) was 3.80 for elderly subjects (95% CI, range 1.75–8.24, $P = 0.001$), and 2.47 for the subjects with uncontrolled BP (95% CI, 1.30–4.70, $P = 0.006$). The high PWV was not significantly related to any other factors, including gender, obesity, HR, or medication for hypertension, diabetes or dyslipidemia.

Factors influencing SDPTG indices

Bivariate analysis showed that age was associated positively with the D : A ratio and AGI, and negatively with the B : A ratio (Table 3). Male subjects had a significantly lower AGI (-0.097 ± 0.301) and a higher B : A ratio (0.440 ± 0.138) compared with female subjects (-0.030 ± 0.250, $P = 0.04$; and 0.395 ± 0.129, $P = 0.004$, respectively), but there was no gender difference in the D : A ratio (male: 0.387 ± 0.113 versus female: 0.375 ± 0.104, $P > 0.05$). The SDPTG indices (the B : A and D : A ratios, and the AGI) were associated with duration of hypertension, but not with family history or smoking status. Body height and BMI were correlated only with the B : A ratio and AGI. The AGI and the B : A ratio were correlated most closely with SBP of all the BP components (Table 3); the former was positively and the latter was negatively associated with SBP. The D : A ratio was correlated most closely (and positively) with MAP of the BP components. Total cholesterol level was not significantly related to the SDPTG indices, but those treated with medication for diabetes had a significantly greater AGI (-0.058 ± 0.207) and a smaller B : A ratio (0.366 ± 0.101), compared with the rest of the subjects (-0.078 ± 0.238, $P = 0.01$ and 0.424 ± 0.138, $P = 0.03$, respectively). There was no relationship between medication for either hypertension or dyslipidemia and the SDPTG indices.

Using multiple linear regression analysis, we found that age, SBP, HR, BMI and gender were independent factors influencing the B : A ratio (Table 5). Independent factors influencing the D : A ratio were MAP, age, and HR, and those influencing AGI were age, SBP, HR, and BMI. Medical treatment for diabetes was not independently related to either AGI or the B : A ratio. HR had independent influences on SDPTG indices; the relationships between HR and the SDPTG indices were the inverse of those of age or BP.

According to multiple logistic regression analysis, the factors that were significantly related to a high AGI ($\geqslant 0.22$) were the elderly (OR, 2.27; 95% CI, 1.02–5.06; $P = 0.046$) and uncontrolled BP (OR, 2.44; 95% CI, 1.18–5.01; $P = 0.02$). Similarly, the adjusted OR of a high D : A ratio ($\geqslant 0.49$) was significantly high among

Table 5 **Multiple stepwise linear regression analysis of second derivative of the finger photoplethysmogram indices ($n = 294$)**

		β	SE	*t*	*P*
B : A	Age (years)	−0.0045	0.0006	−6.997	<0.001
	SBP (mmHg)	−0.0021	0.0004	−5.071	<0.001
	HR (bpm)	0.0032	0.0007	4.849	<0.001
	BMI (kg/m^2)	0.0062	0.0022	2.829	0.005
	Gender (F = 0, M = 1)	0.0279	0.0136	2.052	0.04
D : A	MAP (mmHg)	0.0047	0.0006	8.471	<0.001
	HR (bpm)	−0.0027	0.0005	−4.916	<0.001
	Age (years)	0.0024	0.0005	4.448	<0.001
AGI	Age (years)	0.0098	0.0014	7.031	<0.001
	SBP (mmHg)	0.0036	0.0009	3.987	<0.001
	HR (bpm)	−0.0043	0.0014	−3.072	0.002
	BMI (kg/m^2)	−0.0101	0.0047	−2.153	0.03

B : A, model $R^2 = 0.317$, $F = 26.70$, model probability $P < 0.001$; D : A, model $R^2 = 0.250$, $F = 32.30$, $P < 0.001$; AGI, model $R^2 = 0.245$, $F = 23.42$, $P < 0.001$. AGI, aging index; SBP, systolic blood pressure; HR, heart rate; BMI, body mass index; MAP, mean arterial pressure.

the elderly (OR, 2.24; 95% CI, 1.02–4.92; $P = 0.04$) and the subjects with uncontrolled BP (OR, 3.10; 95% CI, 1.57–6.34; $P = 0.002$); while it was significantly low among those treated with antihypertensive drugs (OR, 0.29; 95% CI, 0.10–0.81; $P = 0.02$) and among those with higher HR (OR, 0.41; 95% CI, 0.19–0.89; $P = 0.02$). The adjusted OR of a low B : A ratio (≤ 0.28) was significantly elevated among the elderly (OR, 2.24; 95% CI, 1.06–4.72; $P = 0.03$) and among uncontrolled hypertensives (OR, 2.54; 95% CI, 1.28–5.02; $P = 0.008$), while it was significantly lowered among those with a higher HR (OR, 0.36; 95% CI, 0.17–0.77; $P = 0.008$) and among obese subjects (OR, 0.48; 95% CI, 0.23–0.99; $P = 0.048$).

Relationship between PWV and SDPTG indices

Bivariate analysis revealed significant correlations between PWV and some of the SDPTG parameters (Table 6). PWV was correlated positively with the D : A ratio and AGI, and negatively with the B : A ratio. However, the correlation coefficients between PWV and these SDPTG indices were low, indicating only weak relationships between them. When adjusted by age, there was no significant correlation between PWV and AGI or the B : A ratio. A significant correlation between PWV and the D : A ratio was found even when adjusted by age (partial $r = 0.17$, $P = 0.003$), but it was not observed after further adjustment by MAP in addition to age.

Discussion

Factors influencing PWV

The present study demonstrated that carotid–femoral PWV was positively correlated with age in hypertensive subjects. The age-dependent increase in PWV has been shown in several populations [4,5,20], and has been observed among subjects with any BP level (i.e. normotensives, untreated hypertensives, and treated hypertensives) [6]. BP was positively correlated with PWV in the present study, which is consistent with the results of previous studies [6,21]. Of the BP components, SBP was most closely correlated with PWV. These results may be partly in agreement with the notion that the distensibility of large arteries is a major determinant of SBP [22]. In the present study, HR was a weak but significant independent determinant of PWV, although the underlying mechanism remains to be determined. The results of previous studies that have focused on the influence of HR on PWV have been controversial [23,24], but it is possible that the HR-dependent PWV increase as observed in the present and previous [24] studies might be partly due to a change in the distensibility of large elastic arteries with an elevation of HR [22].

Table 6 **Correlation coefficient between pulse wave velocity and second derivative of the finger photoplethysmogram indices**

	B : A	D : A	AGI
R	−0.164	0.239	0.205
P	0.005	<0.001	0.001

R, Pearson correlation coefficient. B : A, the ratio of the absolute value of the height of 'b' wave (B) to that of 'a' wave (A) on SDPTG; D : A, the ratio of the absolute value of the height of 'd' wave (D) to (A); AGI, aging index of SDPTG.

Factors influencing SDPTG indices

As noted earlier, SDPTG consists of five waves, labelled a–e. Although the clinical significance of the c and e waves has yet to be clarified, Takazawa *et al.* [9] reported that the b wave and the d wave are related to arterial stiffness. These authors also reported that the AGI would be useful for evaluation of vascular aging and for screening of arteriosclerosis. In the present study, the height of waves a, b, and d is represented as an absolute value, namely A, B, and D, respectively; we focused specifically on the B : A and D : A ratios and the AGI.

We have shown herein that the B : A ratio was independently associated with age, SBP, HR, BMI, and gender. In general, we found that A and B are included in the early systolic component, and are caused mainly by the first vascular response to the ejection of blood from the heart. Since the influence of wave reflection from the periphery on these waves in such an early phase is thought to be negligible, Takazawa *et al.* [9] claimed that the B : A ratio reflects the stiffness of the large arteries, without any influences of wave reflection. Therefore, the age-dependent decrease in the B : A ratio, as observed in the present study, may indicate a decrease in arterial distensibility with age. One of the more notable findings of the present study was that SBP was an independent factor relating to the B : A ratio in hypertensive subjects. The association between a decreased B : A ratio and BP in adult hypertensive patients may have occurred as a result of structural arterial alterations as well as a result of raised BP alone [10].

The D : A ratio was independently correlated with age, MAP, and HR. Takazawa *et al.* [9] also observed an age-dependent increase in the D : A ratio and claimed that this was attributable to an increased intensity of wave reflection from the periphery. The D component on the SDPTG corresponds to the late systolic component on the PTG, and the D : A ratio is closely related to the augmentation of BP in the aorta by wave reflection. It has been proposed that the aortic augmentation index, which is defined as the increment in pressure from the first systolic shoulder (inflection point) to the peak pressure of the aortic waveform, expressed as a percentage of the peak pressure [25], is an index of arterial stiffness [26]. It depends at least in part on aortic PWV; the faster the wave travels, the less the damping and the greater the intensity of reflected waves [1]. Since, as observed in the present study, PWV is closely related to age and BP, the aortic augmentation index, and hence the D : A ratio, might be influenced by the same factors.

In multivariate analysis, the AGI was independently correlated with SBP, HR, BMI, and age. It has been suggested that the AGI is useful for the evaluation of vascular aging [9], but factors other than age should be taken into account for its interpretation. It is noted that the HR was an independent determinant of the SDPTG indices including the AGI, and the influence of HR on the SDPTG indices was the inverse of that of age or BP.

Previous studies have postulated that a small B, a high D, and an elevated AGI might be signs of a reduction in arterial distensibility [9,27]. Multiple logistic regression analysis in the present study demonstrated that elderly and uncontrolled hypertensives had an elevated OR of the low B : A ratio, high D : A ratio, and high AGI, indicating an increased arterial stiffness in these hypertensives.

Relationship between PWV and SDPTG indices

In our study, PWV and the SDPTG indices (the B : A and D : A ratios and the AGI) were associated with common factors including age and BP. However, the correlations between PWV and these SDPTG indices were only weak. It is unlikely that the weak correlations might be due to poor reproducibility of PWV and SDPTG indices because the indices had sufficient repeatability [17,19]. Another preliminary study showed that the correlation coefficients of the B : A ratio, D : A ratio, and AGI were 0.85, 0.70, and 0.82, respectively (unpublished data), supporting the assumption. Therefore, this finding indicates that the two measures of arterial stiffness, namely PWV and SDPTG, are regulated at least in part through different mechanisms, and that the one is not capable of acting as a surrogate marker of the other. This may be explained partly by the hypothesis that PWV and SDPTG reflect different arterial properties at central and peripheral sites. The clinical usefulness of these markers remains to be evaluated comparatively by examining their associations with target organ damage or prognosis.

Study limitations

There are some limitations to the present study. Most of subjects included in the study were treated hypertensives. Further studies in untreated hypertensives or normotensives may be required for the establishment of the determinants of PWV and SDPTG indices. Some of the antihypertensive drugs as well as antidiabetic and antihyperlipidemic drugs may have influenced the structure and function of the central and peripheral arteries, thus modifying PWV and SDPTG indices. They may also have had some effects on cardiac function, including HR and contractility, and hence on the indices.

In conclusion, the PWV and SDPTG indices were associated with common factors including age and BP in hypertensive patients, but they were only weakly correlated with each other. These results suggest that the PWV and SDPTG are regulated at least in part through different mechanisms, and that they provide different information about arterial properties at central and peripheral sites.

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