Original Article

Pulse Wave Velocity as a Marker of Arteriosclerosis and Its Comorbidities in Chinese Patients

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To obtain reliable data on the epidemiology of arteriosclerosis and the comorbidities in patients with hypertension (HP), coronary heart disease (CHD), type 2 diabetes mellitus (T2DM) and stroke, we evaluated the clinical significance of pulse wave velocity (PWV) as an indicator of arteriosclerosis and its comorbidities in Chinese patients. A total of 910 subjects, including 748 Chinese patients with one or more cardiovascular risk factors (80.2% male, mean age 73.69±5.03 years) and 162 healthy volunteers (78.4% male, mean age 73.60±5.32 years) were recruited into the study. PWV was measured in 910 subjects, and large artery arteriosclerosis was defined as PWV ≥12 m/s. Multivariable logistic regression analyses were performed to identify risk factors associated with arteriosclerosis. The prevalence of large artery arteriosclerosis in the patients overall was 67.4%, and the prevalence was higher in patients with than in those without HP (63.3% *vs.* 34.0%; odds ratio [OR]: 3.451), T2DM (24.8% *vs.* 11.1%; OR: 2.854), CHD (56.1% *vs.* 45.1%; OR: 1.246) and stroke (26.6% *vs.* 19.2%; OR: 1.236), but the OR values of CHD and stroke did not differ significantly ($p>0.05$). After multiple logistic regression analysis, female sex, older age, HP and T2DM were risk factors for large artery arteriosclerosis. In conclusion, PWV can be used as a routine measurement to scan arteriosclerosis in patients with HP or T2DM. (*Hypertens Res* 2007; 30: 237–242)

***Key Words*: pulse wave velocity, arteriosclerosis, cardiovascular risk factors**

Introduction

Arteriosclerotic diseases are a main cause of mortality worldwide. Coronary heart disease (CHD) and stroke are important manifestations of systemic atherosclerosis. Moreover, arteriosclerosis leads to the degeneration of arterial elasticity. Elasticity is an important characteristic of the arteries and is a direct reflection of their condition (*1*). It has been reported that pulse wave velocity (PWV) is an independent predictor of cardiovascular and cerebrovascular mortality in hypertensive patients (*2*). The aims of the present study were to evaluate the relationship between PWV and hypertension (HP), CHD, type 2 diabetes mellitus (T2DM) and stroke, and to determine whether noninvasive measurement of PWV can be a useful approach to screening Chinese patients who are at high risk for generalized arteriosclerosis.

Methods

Subjects

This investigation was based on a large-scale epidemiological study in China with cross-sectional parts conducted from August 2004 to February 2005. Enrolled in the study were 910 subjects, including 748 patients with one or more cardiovascular risk factors who were registered as outpatients at the Department of Geriatrics of Qi-Lu Hospital of Shandong University and 162 healthy volunteers who were examined in the Center of Health Examination of Qi-Lu Hospital of Shandong University. The risk factors of the 748 patients included a previous diagnosis of HP, T2DM, CHD or stroke according to

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Table 1. Baseline Characteristics of Healthy Subjects and Patients

Risk factors	Healthy subjects (N=162)	Patients (N=748)	p value
Age (years)	73.60±5.32	73.69±5.03	0.838
Gender (male)	127 (78.4%)	600 (80.2%)	<0.001
Female	35 (21.6%)	148 (19.8%)	
BMI (kg/m^2)	24.88±2.98	25.29±3.05	0.120
SBP (mmHg)	123.77±15.34	144.63±18.63	<0.001
DBP (mmHg)	73.23±8.66	79.68±10.04	<0.001
MAP (mmHg)	94.17±12.13	109.36±14.17	<0.001
PP (mmHg)	50.53±10.72	64.94±14.13	<0.001
HR (bpm)	70.53±11.27	71.13±11.84	0.556
PWV(m/s)	11.82±2.77	14.20±3.58	<0.001

Mean±SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate; PWV, pulse wave velocity.

the 1999 diagnostic guidelines of the World Health Organization (WHO); in all cases, the diagnoses were made no later than 1999. As for the healthy volunteers, selection criteria were generated before the trial began, based on the records of participating health care providers. The inclusion criteria were general good health and mobility and agreement to conform with the trial guidelines or provide notification of noncompliance. They had no medical history of atherogenic diseases, cardiovascular diseases, renal insufficiency or other diseases requiring medical treatment. A "healthy subject" was defined by the following criteria: blood pressure <140/90 mmHg, fasting blood glucose <110 mg/dl, total cholesterol <240 mg/dl, triglycerides <150 mg/dl, uric acid <7.5 mg/dl, body mass index (BMI) <25 kg/m^2, and no history of smoking. Exclusion criteria were any recent history of acute or chronic debilitating illness or any record of HP, DM, CHD, stroke, peripheral vascular disease or hyperlipemia, according to the 1999 WHO diagnostic guidelines. All subjects gave informed written consent. All subjects and all clinical data were collected cross-sectionally from medical records. The study protocol was approved by the Ethics Board of Qi-Lu Hospital of Shandong University.

Medical History and Examinations

All participants were administered a standardized questionnaire that obtained information about their occupation, medical history, drug use, smoking, personal habits, and family medical histories. Risk factors included obesity, HP, T2DM, CHD and stroke. The subjects' weight and height were measured while they were wearing light clothes without shoes. BMI was calculated as the weight in kg divided by the square of the height in m.

Hypertension was defined as a systolic blood pressure (SBP) of ≥140 mmHg, a diastolic blood pressure (DBP) of ≥90 mmHg or the current use of antihypertensive drugs (according to 1999 WHO criteria). T2DM was diagnosed by 1) a fasting plasma glucose concentration of >7.0 mmol/l in the absence of treatment; 2) a plasma glucose concentration of ≥11.0 mmol/l, 2 h after a 75 g oral glucose load; or 3) current treatment with glucose-lowering drugs. None of the subjects had a history of ketoacidosis. The presence of underlying CHD was defined as a history of a physician-diagnosed heart attack, evidence of prior myocardial infarction by electrocardiogram or self-reporting of a prior coronary revascularization procedure (percutaneous coronary artery intervention [PCI] or coronary-artery bypass surgery [CABG]).

PWV Measurement

Carotid-femoral PWV was measured in a temperature-controlled room at 24°C. This method, including the use of an automatic device (Complior, Artech, France) has been extensively applied. Briefly, two pressure waves were recorded transcutaneously at the base of the neck for the right common carotid artery and over the right femoral artery. PWV was determined as the foot-to-foot velocity. Pulse transit time was determined as the average of 10 consecutive beats. The distance traveled by the pulse wave was measured over the body surface as the distance between the two recording sites. Aortic PWV was calculated as the ratio of distance to transit time. The validation of this automatic method and its reproducibility have been previously published, with an intraobserver repeatability coefficient of 0.93 and an interobserver reproducibility coefficient of 0.89 (*3–5*). R. Asmar proposed a PWV cutoff level of 12 m/s at the 15th Great Wall International Congress of Cardiology. Subjects were assigned to one of two groups according to their PWV level, as follows: PWV ≥12 m/s and PWV <12 m/s.

Statistical Analysis

All data were analyzed by SPSS 10.0 for Windows (SPSS, Chicago, USA). Continuous variables were given as means±SD. The variables included in the analysis were age, gender, BMI, and the presence of HP, T2DM, CHD and

Table 2. PWV Values of Healthy Subjects and Hypertension, Diabetics, Coronary Heart Disease and Stroke Patients

Groups	*N*	PWV (m/s)
Healthy subjects	162	11.82±2.77
HP patients	121	14.24±2.94$^{\#}$
T2DM patients	31	13.64±2.60$^{\#}$
CHD patients	120	12.95±2.89$^{\#,\ddagger}$
Stroke patients	28	12.71±3.53†
HP+T2DM patients	30	15.31±4.38$^{\#,\flat}$
HP+CHD patients	166	14.53±3.51$^{\#,\S}$
HP+Stroke patients	30	14.30±3.47$^{\#}$
T2DM+CHD patients	20	13.91±5.00$^{\#}$
T2DM+Stroke patients	30	13.57±2.49*
CHD+Stroke patients	30	13.16±3.15
HP+T2DM+CHD patients	40	15.47±3.16$^{\#}$
HP+T2DM+Stroke patients	68	14.58±4.16$^{\#}$
HP+T2DM+CHD+Stroke patients	34	16.90±5.65$^{\#}$

Mean±SD. PWV, pulse wave velocity; BMI, body mass index; HP, hypertension; T2DM, type 2 diabetes mellitus; CHD, coronary heart disease. *p* value for the PWV values by one-way ANOVA for cardiovascular risk factors. *$p<0.05$, $^{\#}p<0.01$, healthy subjects *vs*. others; $^{\dagger}p<0.05$, $^{\ddagger}p<0.01$, HP patients *vs*. T2DM, CHD or Stroke patients; $^{\S}p<0.05$, $^{\flat}p<0.01$, CHD + Stroke patients *vs*. HP + T2DM, HP+Stroke, T2DM+CHD, T2DM+Stroke or HP+CHD patients.

stroke. Comparisons between means were evaluated by unpaired *t*-test or one-way ANOVA for continuous variables. Stepwise logistic regression analysis, which included variables identified as statistically significant in the univariate analysis, was used to assess the independence of the association with arteriosclerosis, and the corresponding odds ratios (ORs) and/or their 95% confidence intervals (CI) were calculated. The results were compared between the PWV <12 m/s group and the PWV ≥12 m/s group. Values of $p<0.05$ were considered statistically significant.

Results

Baseline Characteristics of Healthy Subjects and Patients

Table 1 shows the baseline characteristics of the healthy subjects and the patients. Age, BMI and heart rate showed no significant difference ($p>0.05$) between the groups, but the patients had higher blood pressure ($p<0.001$). The PWV values are shown in Table 2. These values were significantly higher in patients with HP, T2DM, CHD or stroke than in healthy subjects (14.24±2.94 m/s, $n=121$; 13.64±2.60 m/s, $n=31$; 12.95±2.89 m/s, $n=120$; 12.71±3.53 m/s, $n=28$; *vs*. 11.82±2.77 m/s, $n=162$; $p<0.05$), and those of patients with HP were significantly higher than those of patients with CHD or stroke ($p<0.05$). The PWV values of HP complicated with T2DM and HP complicated with CHD were significantly higher than that of CHD complicated with stroke (15.31±4.38, $n=30$; 14.53±3.51 m/s, $n=166$; *vs*. 13.16±3.15 m/s; $p<0.05$). The PWV values of HP complicated with T2DM, CHD and stroke were the highest among all subjects (16.90±5.65 m/s, $n=34$).

Arteriosclerosis and Its Prevalence in Different Comorbidities

Table 3 lists the baseline characteristics of patients with and without increased PWV, the results of the univariate analysis of arteriosclerosis and its comorbidities, and the levels of statistical significance. Of the 910 subjects were included in the study, 25.7% were female, and the mean age and mean BMI were 73.67±5.08 years and 25.21±3.08 kg/m^2, respectively. More than half (53.7%) of the patients had HP, 20.3% had T2DM, 52.5% had CHD and 24.2% had stroke. Moreover, 613 (67.4%) of patients whose PWV ≥12 m/s had large artery arteriosclerosis. The mean value of PWV was 13.78±3.48 m/s in all patients, 15.41±3.03 m/s in the arteriosclerosis group and 10.41±1.28 m/s in the non-arteriosclerosis group. The difference was significant between the latter two groups. The patients with arteriosclerosis were older (74.49±4.66 years *vs*. 72.00±5.48 years, $p<0.05$). The proportion of patients in the arteriosclerosis group with concomitant clinical HP, T2DM, CHD and stroke was also higher (Table 3).

Risk Factors and Comorbidity

Table 4 shows the adjusted ORs of arteriosclerosis and the comorbidities. The prevalence of large artery arteriosclerosis was higher in females than in males (76.1% *vs*. 64.3%; OR: 1.465). Patients with arteriosclerosis were older than those without (74.49±4.66 years *vs*. 72.00±5.48 years; OR: 1.111) and more frequently had HP (63.3% *vs*. 34.0%; OR: 3.451), T2DM (24.8% *vs*. 11.1%; OR: 2.854), CHD (56.1% *vs*.

Table 3. Baseline Characteristics and Univariate Analysis of Patients

Risk factors	PWV≥12 m/s (n=613)	PWV<12 m/s (n=297)	Total (n=910)	p value
PWV (m/s)	15.41±3.03	10.41±1.28	13.78±3.48	<0.001
Age (years)	74.49±4.66	72.00±5.48	73.67±5.08	<0.001
Gender (male)	435 (71.0%)	241 (81.1%)	676 (74.3%)	<0.001
Female	178 (29.0%)	56 (18.9%)	234 (25.7%)	
BMI (kg/m^2)	25.31±3.02	24.99±3.09	25.21±3.08	0.137
SBP (mmHg)	147.00±19.00	125.29±14.67	136.28±20.14	<0.001
DBP (mmHg)	80.48±9.99	73.63±8.80	77.10±10.00	<0.001
MAP (mmHg)	110.06±15.12	96.34±12.09	103.29±15.30	<0.001
PP (mmHg)	66.51±14.49	51.66±10.47	59.18±14.66	<0.001
HR (bpm)	72.79±13.56	68.94±9.27	70.89±11.58	<0.001
HP history	388 (63.3%)	101 (34.0%)	489 (53.7%)	<0.001
T2DM history	152 (24.8%)	33 (11.1%)	185 (20.3%)	<0.001
CHD history	344 (56.1%)	134 (45.1%)	478 (52.5%)	0.002
Stroke history	163 (26.6%)	57 (19.2%)	220 (24.2%)	0.015

Mean±SD. PWV, pulse wave velocity; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate; HP, hypertension; T2DM, type 2 diabetes mellitus; CHD, coronary heart disease.

Table 4. Risk Factors and Arteriosclerosis in Multiple Logistic Regression Analysis

Risk factors	OR	95% CI	p value
Women	1.465	1.056–2.156	0.024
Age	1.111	1.084–1.154	<0.001
BMI	1.001	0.936–1.036	0.553
HP	3.451	2.634–4.977	<0.001
T2DM	2.854	1.841–4.422	<0.001
CHD	1.246	0.898–1.677	0.198
Stroke	1.236	0.865–1.820	0.232

PWV, pulse wave velocity; OR, odds ratio; CI, confidence interval; BMI, body mass index; HP, hypertension; T2DM, type 2 diabetes mellitus; CHD, coronary heart disease.

45.1%; OR: 1.246), stroke (26.6% *vs*. 19.2%; OR: 1.236) and higher BMI (25.31±3.02 *vs*. 24.99±3.09; OR: 1.001). The comparison of ORs between the arteriosclerosis and non-arteriosclerosis groups demonstrated that these conditions were inversely related to PWV.

As shown in Table 3, CHD was present in 56.1% of patients with arteriosclerosis and 45.1% of patients without it (p=0.002); for stroke, these values were 26.6% *vs*. 19.2% (p=0.015); for T2DM, 24.8% *vs*. 11.1% (p<0.001); and for HP, 63.3% *vs*. 34.0% (p<0.001). After multiple logistic regression analysis, female sex, older age, HP and T2DM were risk factors for large artery arteriosclerosis. However, the OR values for CHD and stroke were not significant different (p>0.05).

Discussion

This is the first large-scale study of Chinese patients with arteriosclerosis and its comorbidities. We demonstrated that a higher PWV was associated with age, female sex, BMI, HP, T2DM, CHD and stroke. Our data suggested that measurements of PWV might be useful indicators of systemic atherosclerosis in Chinese patients with cardiovascular risk factors. Previous studies (*6–12*) reported that PWV could be used to predict the mortality from HP, T2DM, CHD and stroke, all of which were associated with cardiovascular events and risk factors. The results of this study are consistent with these observations.

Our study was based on relatively old outpatients; hence the results cannot be fully generalized to a large population. Nonetheless, our results clearly showed a substantial prevalence of arteriosclerosis in patients at high risk for cardiovascular disease. In this study, large artery arteriosclerosis was more prevalent in females (76.1%) than in males (64.3%), which was consistent with other studies. The reason for this sex difference is that the patients in our study were relatively old (mean age, 73.67 years old), so menopause probably contributed to atherosclerosis in females (*13–16*).

In our study, HP and T2DM increased the risk of large artery arteriosclerosis. Several studies have shown that the structure of a vessel changes when an increase in blood pressure augments vascular tension (*6*, *17–20*). That is to say, with vascular smooth muscle cell hyperplasia and vessel wall thickening, diffuse fibrosclerosis and local atherosclerosis will occur in the vessel wall over the long term. Moreover, long-lived proteins (*e.g.*, vascular collagen) undergo continual cross-linking because diabetes increases the formation of

advanced glycation end products (AGEs). In the cardiovascular system, the presence of AGE cross-links within the vascular wall increases vascular stiffness (*21–23*). These effects, in turn, lead to increased arterial stiffness, a quickening of PWV and the prevalence of large artery atherosclerosis.

Univariate regression analysis showed that CHD and stroke were associated with large artery atherosclerosis, but logistic regression analysis showed that they were not risk factors for atherosclerosis. On the other hand, studies have reported that PWV is an independent predictor of CHD and stroke in hypertensive patients (*7–10*, *24*). The discrepancy can be partly explained by the effects of hypertension on PWV. The relationships between PWV and both CHD and stroke need to be further studied. There were certain limitations to our study. Because this was the cross-sectional part of our investigation, we could not determine whether PWV could predict cardiovascular events. Further longitudinal studies will reveal the clinical significance of PWV.

Our study suggests that PWV might be a marker of arteriosclerosis and its comorbidities. Furthermore, non-invasive measurements such as PWV can accurately reveal cardiovascular abnormalities and might be used to screen for arteriosclerotic diseases in Chinese patients with risk factors. The prevalence of cardiovascular disease has been increasing in China due to recent changes in diet and lifestyle. Therefore, the screening for arteriosclerosis described in the present report may be particularly useful in the future. PWV measurement can be used as a routine clinical evaluation of high-risk patients. Arteriosclerotic risk factors such as HP, T2DM, CHD and stroke should be treated adequately.

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