Clinical Research

Brachial-ankle pulse wave velocity is an independent predictor of carotid artery atherosclerosis in the elderly

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Objective  Brachial-ankle pulse wave velocity (baPWV) is widely used as a simple noninvasive measure of arterial stiffness. The aim of this study was to evaluate the usefulness of baPWV as a predictor of the carotid artery atherosclerosis in the elderly. Methods  A total of 721 elderly participants (mean ± SD age, 70.3 ± 5.6 years) were enrolled in the current study. All participant underwent both baPWV measurement and B-mode ultrasound for the intima-media thickness. Carotid atherosclerosis (CAS) was defined as the present of carotid plaque or and/or intima media thickness for at least 1.1 mm. Results  A multivariate logistic regression analysis reveals that age, sex, brachial-ankle pulse wave velocity, smoking and LDL-C level showed a significant correlation with the presence of CAS. The odds ratios of CAS associated with a 500 cm/s increase of brachial-ankle pulse wave velocity were 2.378 [95% confidence interval, 1.36 to 4.00, P<0.05], 3.733 [95% confidence interval, 1.729 to 8.058, P<0.01], 4.438 [95% confidence interval, 1.659 to 11.803, P<0.01]. The baPWV significantly correlated with IMT by bivariate correlation analysis (r=0.39; p=0.001). After adjusting for factors influencing, baPWV all the same correlated with IMT (r=0.35; p=0.001). Conclusion  These results indicate that brachial-ankle PWV is an independent predictor of CAS in the elderly. It also means that the direct measurement of arterial stiffness by this simple method may be of great help for the evaluation of carotid arteriosclerosis, at least in the elderly (J Geriatr Cardiol 2010; 7:157-160).

Key words  Aortic stiffness; carotid arteriosclerosis; pulse wave velocity

Introduction

Arteriosclerosis is a major contributor to cardiovascular disease, accounting for a high percentage of mortality and morbidity. The diagnosis of carotid atherosclerosis by high-resolution B-mode ultrasonography has been reported to be an independent predictor of coronary heart disease. The relationship between carotid and coronary atherosclerosis has been demonstrated using carotid ultrason. Previous studies have focused on either morphological changes such as carotid artery plaque burden or functional changes such as carotid arterial stiffness. There are various noninvasive methods for measuring arterial functional changes, such as ultrasound and MRI. These technologies detect changes in the diameter (or area) of an artery in response to distending pressure, and pulse wave velocity (PWV). Among these measurements, pulse wave velocity (PWV) is a simple index derived from pressure-sensitive transducers, doppler ultrasound, or applanation tonometry. Thus, it is widely used in clinical settings. PWV is a reproducible and non-invasive measurement which can be used as a valuable index of arterial stiffness.

However, there have been few direct analyses of the association between brachial-ankle PWV and carotid artery atherosclerosis and intima-media thickness (IMT), especially in the elderly. The aim of this study was to evaluate the usefulness of baPWV as a predictor of the carotid artery atherosclerosis in the elderly.

Methods

Study Population

The study populations were randomly selected from 8202 retired military officers and their spouses who aged 60 or over. Subjects were excluded if the had impaired renal function (serum creatinine concentration >1.5 mg/dl; n=13), chronic atrial fibrillation (n=31), valvular heart disease (moderate or severe; n=20), decreased left ventricular function (ejection fraction <50%; n=17), peripheral arterial disease defined as ankle brachial index (ABI) <0.9 (n=18). Finally a total of 721 subjects (365 male and 256 female, mean age 70.4 years) were included.

All participants were administered a standardized questionnaire that provided information about demographic background, occupation, medical history, drug use, and...
personal habits such as cigarette consumption. The body mass index (BMI) was computed as weight, (in kilograms) divided by height, (in meters) squared. Supine blood pressure was measured before the B-mode ultrasound examination in the right arm with the use of a manual sphygmomanometer. After a 10-minute rest period, systolic and diastolic blood pressures were measured 3 times with a 5-minute interval, and the average of the last 2 measurements was used in the statistical analyses. The study was conducted in accordance with guidelines approved by the institutional ethics committee.

Blood samples were collected in the morning after 12 h of fasting. Total cholesterol (TC), triglyceride (TG), low-density lipoprotein-cholesterol (LDL-C), and high density lipoprotein-cholesterol (HDL-C) were measured. Patients were examined for arteriosclerosis risk factors including age, smoking, hypertension, hyperuricemia, diabetes mellitus, hypercholesterolemia, high LDL-C, hypertriglyceridemia, low HDL-C, obesity and a history of CAD.

Smoking was recorded as positive in the case of current or a past history of cigarette smoking. Hypertension was defined as a history of hypertension (systolic pressure \( \geq 140 \text{mmHg} \) or diastolic pressure \( \geq 90 \text{mmHg} \)). Hyperlipidemia was defined as a history of high TC (\( \geq 220 \text{mg/dl} \)), high LDL-C (\( \geq 140 \text{mg/dl} \)) and/or high TG (\( \geq 150 \text{mg/dl} \)).

A history of CAD was defined as documentation of medication and history of myocardial infarction, angina pectoris, and/or previous coronary intervention confirmed by reviewing the medical records.

**Measurement of brachial-ankle pulse wave velocity**

Brachial-ankle pulse wave velocity was measured using an automated waveform analyzer (Colin VP-1000, Colin Medical Instruments Corp., Komaki, Japan). 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.

**Carotid Ultrasound**

After the subject had rested in the supine position, the neck was slightly hyperextended and optimal bilateral visualization of the carotid arteries was performed. Carotid scans were acquired using high-resolution ultrasound (SSA-700A Apio; Toshiba Medical System) with a 7.5-MHz or 12-MHz linear array transducer. Carotid atherosclerosis (CAS) was defined as any focal structure that protruded in the lumen. The intima-media thickness (IMT) was measured as the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line. Three measurements of the IMT were made: at the thickest point by visual examination and at 2 other points (1 cm proximal and 1 cm distal to the thickest site). The average of these 3 measurements was calculated. All the subjects were divided into 2 groups: \( e \) carotid atherosclerosis (CAS) and normal (non-CAS).

**Statistical analysis**

Standard procedures from the Statistical Analysis System (SAS) were used for statistical analyses. Values are expressed as the mean \pm standard deviation. Continuous variables were compared using the unpaired t-test, and differences in frequencies among the groups were tested by \( \chi^2 \) analysis. Multiple logistic regression models were used for multivariate analysis. Potential confounding cardiovascular risk factors considered in the analyses were age, brachial-ankle pulse wave velocity, sex, hypertension, systolic blood pressure, diastolic blood pressure, smoking, TC, and LDL-C. Pearson product-moment correlation was used to assess the correlations between baPWV and IMT. Values of \( p<0.05 \) were considered to indicate statistical significance.

**Result**

**Baseline characteristics of study population**

Table 1 shows the baseline clinical characteristics of subjects divided according to the presence or absence of CAS. As expected, subjects without CAS had lower means of age, systolic blood pressure, diastolic blood pressure, total and LDL cholesterol. They also had higher proportions of women and never-smokers and lower proportions of hypertensive individuals. The other cardiovascular risk factors were not statistically different between subjects with CAS and without CAS. Brachial-ankle pulse wave velocity was positively associated with CAS (Table 1). Subjects with CAS had a higher mean brachial-ankle pulse wave velocity compared with those without CAS (\( P<0.001 \)).

**Relationship of brachial-ankle pulse wave velocity and CAS**

We performed a multivariate logistic regression analysis of age, brachial-ankle pulse wave velocity, sex, hypertension, systolic blood pressure, diastolic blood pressure, smoking, TC, and LDL-C. As a result, age, sex, brachial-ankle pulse wave velocity, smoking and LDL-C level showed a significant correlation with the presence of CAS, although systolic blood pressure, diastolic blood pressure, and hypertension did not exhibit a correlation. The odds ratios of CAS associated with a 500 cm/s increase of brachial-ankle pulse wave velocity were 2.378 [95% confidence interval, 1.36 to 4.00, \( P<0.05 \)], 3.733 [95% confidence interval, 1.729 to 8.058, \( P<0.01 \)], 4.438 [95% confidence interval, 1.659 to 11.803, \( P<0.01 \)].

**Correlation between brachial-ankle pulse wave velocity and intima-media thickness**

Among the entire study population, the baPWV significantly correlated with IMT by bivariate correlation analysis.
(r=0.39; p=0.001). After adjusting for factors influencing, including age, sex, BMI, hypertension, systolic blood pressure, diastolic blood pressure, heart rate, smoking, diabetes, TC, and LDL-C, baPWV all the same correlated with IMT (r=0.35; p=0.001).

**Discussion**

The present study provides evidence that baPWV is significantly associated with the presence of carotid atherosclerosis and IMT in the elderly.

In the present study, we used brachial-ankle PWV as a marker of aortic stiffness. There have been several previous cross-sectional studies focusing on brachial-ankle PWV. Nakamura et al. reported that brachial-ankle PWV is useful for estimating aortic damage. Yamashita et al. reported that brachial-ankle PWV may be a useful measure for arterial stiffness. Furthermore, Yamashita et al. also reported that brachial-ankle PWV can be considered an acceptable marker with an efficacy comparable to that of carotid-femoral PWV. Cortez-Cooper et al. reported the accuracy and the variability of this automatic device for measuring arterial stiffness and the ankle-brachial index. The method that we used to measure brachial-ankle PWV does not require any specialized technique, but rather measures brachial-ankle PWV automatically. Increase in arterial stiffness measured as increased PWV, has been reported to be associated with atherosclerosis. Previous studies using aortic pulse wave velocity (baPWV) reported increases in odds ratio by 1.34 for cerebrovascular accident, 1.38 for CAD, and 1.23 for cardiovascular mortality, for each increase of baPWV by 340 cm/s. However, the study of the relationship between PWV and carotid atherosclerosis has not reported in the elderly.

We assessed the carotid artery as an index of atherosclerotic (structural) changes and PWV of the aorta as an index of sclerotic (functional) changes in the present study. Hemodynamic data and atherosclerosis risk factors such as age, sex, brachial-ankle pulse wave velocity, smoking and LDL-C level were significantly related to the presence of CAS in the elderly. However, those factors such as systolic blood pressure, diastolic blood pressure, TC, and hypertension lost their significance in multivariate logistic regression analysis. This may be explained by the fact that some of the patients with risk factors had been previously treated. In terms of a 500 cm/s increase of brachial-ankle pulse wave velocity, the subjects was recorded at the time of examination and was graded from 1 to 4. Multivariate logistic regression analysis show odds ratios of CAS increase from 1 to 4 independent of other risk factors.

IMT of carotid artery can be assessed by B-mode ultrasound in a relatively simple way and represents a safe, inexpensive, precise and reproducible measure. Recent studies have suggested increased IMT of the carotid artery has been shown to indicate the presence of atherosclerosis and predict cardiovascular morbidity and mortality. Since carotid IMT is a marker of early arterial wall change, including atherosclerosis and/or vascular hypertrophy, its detection by B-mode ultrasonography might participate in the diagnosis of high cardiovascular risk and in the decision to treat aggressively those patients at risk with drug treatments. In the present study, the baPWV significantly correlated with IMT by bivariate correlation analysis. After adjusting for factors
influencing. baPWV all the same correlated with IMT. These results indicate that brachial-ankle PWV is an independent predictor of CAS in the elderly. It also means that the direct measurement of arterial stiffness by this simple method may be of great help for the evaluation of arteriosclerosis, at least in the elderly.

There are several mechanisms that might explain the association between increased PWV and artery arteriosclerosis. Arterial stiffness causes premature return of the reflected pulse wave in late systole, leading to an increase in central pulse pressure and, consequently, to increased load on the ventricle. This results in decreased ejection fraction and increased myocardial oxygen demand. In addition, the decreased absorption capacity of the arterial wall leads to wall injury, which accelerates the progression of arteriosclerosis.

**Study Limitations**

Several limitations of this study must be addressed. First, BaPWV cannot be accurately measured if the ABI <0.90. Accordingly, patients with ABI <0.90 were excluded in the present study. In addition, patients with systolic dysfunction, atrial fibrillation/flutter, aortic disease and/or valvular heart disease were also excluded because these conditions can affect arterial stiffness. Brachial-ankle pulse wave velocity (baPWV) is the most widely used PWV index because of its convenience. Second, as mentioned previously, the current study population were retired military officers and their spouses, who had good living conditions, medical insurance and periodic physical examination, therefore extrapolating the findings of our study to the general population is difficult, and further studies of various study populations are needed.

**References**


