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*Original Article*

# Brachial-ankle pulse wave velocity is associated with carotid intima-media thickness in middle-aged and elderly

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**Abstract:** Objectives: To determine the main factors affecting brachial-ankle pulse wave velocity (baPWV) and carotid intima-media thickness (CIMT), and to explore the correlation between baPWV and CIMT in the middle-aged and elderly population. Methods: Demographic and clinical data collected from 545 participants at Department of Physical Examination, the First Affiliated Hospital of Chongqing Medical University between July 2015 and May 2016. baPWV and CIMT were obtained with an automated device and carotid ultrasonography, respectively. Participants were divided into two groups according to baPWV, normal baPWV group (baPWV<1400 cm/s) and abnormal baPWV group (baPWV≥1400 cm/s), and into three groups according to CIMT, normal CIMT group (CIMT<1 mm), CIMT thickening group (1 mm≤CIMT<1.5 mm and CIMT plaque group (CIMT≥1.5 mm). Correlation between carotid artery CIMT and baPWV was analyzed with single factor linear regression. Results: Gender, age, waist, systolic pressure, and LDL influenced CIMT, and gender, weight, age, waist, systolic pressure, and diastolic pressure were contributing factors of altered baPWV. There was a positive correlation between baPWV and CIMT. Conclusion: A linear correlation between CIMT and baPWV exists. Early stage thickening of CIMT shows a baPWV value similar to that in plaque phase. Clinical intervention should begin during the early thickening phase as opposed to that in patients with plaques.

**Keywords:** Brachial-ankle pulse wave velocity, carotid intima-media thickness, atherosclerosis, influencing factor

## Introduction

Development of atherosclerosis, one of the leading cardiovascular diseases worldwide, is a complex and multi-factorial process. Development includes several stages such as arterial endothelial dysfunction, adhesion of inflammatory immune cells to the intima, abnormal lipid deposition, decrease in the vascular wall elasticity, and finally, plaque formation [1]. Thickness and stiffness of the arterial wall, which results from lipid deposition, are two important pathological changes in the pathogenesis of atherosclerosis [2]. While arterial stiffening decreases the capacity of an artery to dilate and constrict, arterial thickening narrows the lumen and thereby impairs blood flow. Hence, stiffness and thickness of the arterial wall are believed to be important indicators of the severity of cardiovascular disease [3], and, furthermore, are considered as independent assessors of cardiovascular morbidity and mortality [4-6]. Therefore, early detection of arterial stiffness and thickness is important for the prevention and effective treatment.

Pulse wave velocity (PWV) has been widely recognized as the gold standard for measurement of arterial stiffness [7, 8]. Various PWV values exist with aortic PWV reflecting the stiffening of the central arteries and represents an independent predictor of stroke, hypertension and coronary heart disease [9], while brachial-ankle artery PWV (baPWV) reflects the stiffening of both the aorta and peripheral arteries [10], and has been shown to have a predictive value for coronary atherosclerosis and peripheral artery diseases [11]. As both aortic PWV and baPWV may be used to evaluate the stiffness of central elastic arteries [12], a strong correlation between aortic PWV and baPWV has been reported [13]. However, compared with aortic PWV, measurement of baPWV is commonly clinically used due to the noninvasiveness nature and ease of convenience.

In addition to baPWV, the carotid artery intima-media thickness (CIMT) measured by carotid ultrasonography is also clinically employed to evaluate the severity of carotid atherosclerosis. In addition, CIMT has been shown as a predictor of acute myocardial infarction [14], and the risk of stroke increases with an increase in CIMT [15, 16]. However, to date, the correlation between baPWV and CIMT has not been extensively established. Therefore, the current study aimed to investigate the correlation between baPWV and CIMT and elucidate influencing factors.

## Methods

This retrospective study was conducted in the Department of Physical Examination, the First Affiliated Hospital of Chongqing Medical University, Chongqing, China between July 2015 and May 2016.

This study is a retrospective cross-sectional study. A total of 10,253 examinees were randomly selected from those who visited the hospital for routine physical exams, among whom 7192 with an age ≥45 years were finally registered in our study. Among these 7192, the patients who had one or more of the following were excluded from our study: insufficient data (6598), congenital artery disease (1), lower extremity arterial occlusion (2), severe renal insufficiency (6), severe arrhythmias (11), new malignancies and history of cancer (26), and pregnancy (3). Eventually, a total of 545 patients, with male 333 (61.1%), female 212 (38.9%), and aged 45-87 years, were finally included in this study.

Baseline characteristics and clinical data were collected, including age, gender, history of hypertension and diabetes. Blood pressure was measured according to the 2011 Chinese Hypertension Prevention Guide. Body weight, height and body mass index (BMI) were determined. Waist circumference was measured based on the midpoint between the front lower edge of the 12th rib and the iliac spine when the subject was standing, and the measurements were accurate to 1 cm. This study was approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University (Chongqing, China).

All participants fasted overnight (12 h), and venous blood was collected next morning. Serum was separated, and the total cholesterol (TC), fasting blood glucose (FBG), low-density lipoprotein (LDL), triglyceride (TG), and high-density lipoprotein (HDL) were determined using 7600 series (HITACHI, Japan).

baPWV was measured with VP-1000 (BP-203RPE-III, Omron). Briefly, after 5 min rest, the participant was laid in a supine position, with elbows and ankles fastened to the blood pressure cuff. An ECG electrode sheet and telepathy were placed on the wrists and chest, which automatically measured and analyzed baPWV from both left and right sides. The higher reading was incorporated into study. baPWV≥1400 cm/s was considered as the cutoff value of arterial stiffness based on "Cardiovascular Disease Prevention Guidelines and Consensus 2008".

CIMT was measured with GE Voluson730prov color ultrasound diagnostic apparatus with a probe frequency of 4-9 MHz. Participants were positioned in a supine position, and the intima-media thickness (IMT) in the distal wall (1~1.5 cm) of the proximal part at the bifurcation of bilateral carotid artery wall was measured with two-dimensional ultrasound technology. Referring to 2015 "Chinese Health People Carotid Ultrasonography Standard", thickening was defined as CIMT≥1.0 mm, and a plaque was defined as having all of the following: 1) CIMT≥1.5 mm, 2) CIMT was at least 0.5 mm or 50% larger than the normal CIMT of surrounding tissues, and 3) CIMT protruded into the lumen. The value of the thickest part of the plaque was taken as the CIMT value.

### *Statistical analysis*

All statistical analyses were performed with SPSS 22 (United States). Measurement data were presented as mean ± standard deviation (SD). Multivariate correlation was determined with linear regression analysis. Student's t test was used for statistically significant analysis between two groups, and ANOVA was used for multiple group comparison. $P<0.05$ was defined as statistically significant.

## Results

### *Determination of major factors affecting CIMT and baPWV*

Stepwise linear regression analysis was performed using CIMT or baPWV against the following factors, height, weight, BMI, age, waist

**Table 1.** Stepwise linear regression analysis of factors affecting CIMT

| | | B value | SE | t value | *P* value |
|---|---|---|---|---|---|
| Gender | M 333 F 212 | 0.616 | 0.076 | 8.121 | <0.0001 |
| Age | 56.57 ± 9.14 | 0.024 | 0.004 | 6.413 | <0.0001 |
| WC | 83.77 ± 8.74 | 0.149 | 0.004 | 3.735 | <0.0001 |
| SBP | 130.09 ± 19.03 | 0.007 | 0.02 | 3.599 | <0.0001 |
| LDL | 3.21 ± 0.84 | -0.01 | 0.04 | -2.318 | 0.021 |

M, male; F, female; WC, waist circumference; SB, systolic blood pressure; LDL, low-density lipoproteins.

**Table 2.** Stepwise linear regression analysis of factors affecting baPWV

| | | B value | SE | t value | *P* value |
|---|---|---|---|---|---|
| Gender | M 333 F 212 | 81.283 | 20.933 | 3.883 | <0.0001 |
| BW | 64.79 ± 10.3 | -6.945 | 1.558 | -4.459 | <0.0001 |
| Age | 56.57 ± 9.14 | 15.488 | 1.042 | 14.864 | <0.0001 |
| WC | 83.77 ± 8.74 | 3.945 | 1.637 | 2.41 | 0.016 |
| SBP | 130.09 ± 19.03 | 6.008 | 0.835 | 7.193 | <0.0001 |
| DBP | 78.9. ± 11.42 | 6.057 | 1.320 | 4.588 | <0.0001 |

M, male; F, female; BW, body weight; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure.

**Table 3.** Comparison of CIMT between normal and abnormal baPWV groups

| Group | n (%) | CIMT (mm) | t value | *P* value |
|---|---|---|---|---|
| Normal baPWV | 300 (55.04) | 1.23 ± 0.72 | 5.366 | <0.0001 |
| Abnormal baPWV | 245 (44.96) | 1.61 ± 0.89 | | |

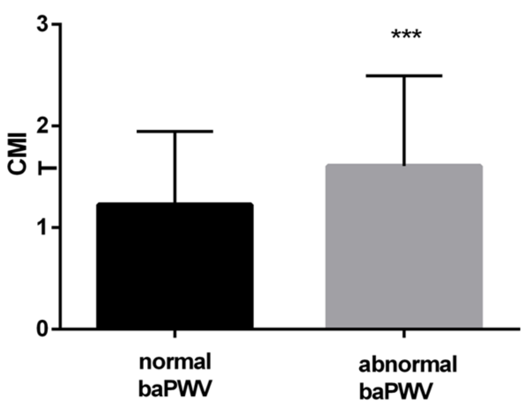


**Figure 1.** Comparison of CIMT between normal and abnormal baPWV groups.

circumference, systolic blood pressure, diastolic blood pressure, ABI, LDL, HDL, TC, TG, FBG, male gender (assigned as 1), and women (assigned as 0). As shown in **Table 1**, gender, age, waist circumference, systolic blood pressure, and LDL were major factors that affected CIMT, among which, LDL negatively correlated with CIMT. In addition, compared with women, men showed a higher CIMT value (0.616 more than women), indicating that middle-aged or elderly male populations were more predisposed to arterial thickness than age-matched females.

The main factors that affected baPWV were weight, gender, age, waist circumference, systolic blood pressure, and diastolic blood pressure, among which body weight negatively correlated with baPWV (**Table 2**). In addition, in line with CIMT comparison between males and females, males had higher baPWV values than females (81.283 more), suggesting that middle-aged and elderly males were predisposed to developing stiffness of central and peripheral arteries compared to females. Using regression coefficients, age was the most important factor affecting baPWV value, with an increase in baPWV by 15.488 for every year of age.

*Correlation between CIMT and baPWV*

To explore the correlation between CIMT and baPWV, participants were first divided into two groups based on the cutoff value of baPWV: normal baPWV group (baPWV<1400 cm/s) and abnormal baPWV group (baPWV≥1400 cm/s), and the CIMT values were compared between these two groups. As shown in **Table 3**; **Figure 1**, the abnormal baPWV group had a significantly higher CIMT than the normal baPWV group (P<0.001). Next, the participants were divided into three groups based on the cutoff values of CIMT: normal CIMT group (CIMT<1 mm), thickness group (1 mm≤CIMT<1.5 mm), and plaque group (CIMT≥ 1.5 mm), and baPWV was compared among these three groups. As shown in **Table 4**, the thickening and plaque CIMT groups had higher a baPWV value than the normal CIMT group (P<0.001), while there was no significant difference between the thickness and plaque CIMT groups (**Table 4**; **Figure 2**). Therefore, we concluded that baPWV positively correlated with CIMT.

**Table 4.** Comparison of baPWV between normal, thickening and plaque groups

| Group | n (%) | baPWV | *P* value |
|---|---|---|---|
| Normal | 237 (44.95) | 1392.01 ± 249.96 | <0.0001*,† |
| Thickening | 98 (17.03) | 1574.17 ± 306.28 | 0.72‡ |
| Plaque | 210 (38.02) | 1587.19 ± 338.40 | |

*: vs. thickening group; †: vs. plaque group; ‡: vs. plaque group.

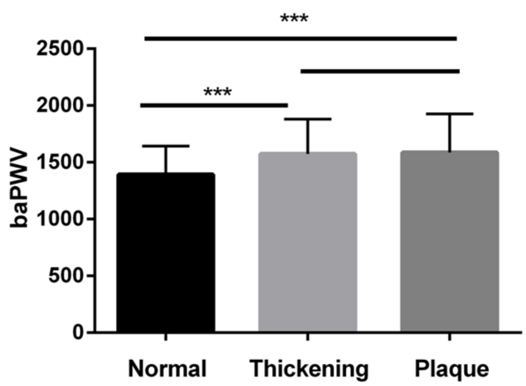


**Figure 2.** Comparison of baPWV between normal, thickening and plaque groups.

Next, we performed linear regression analysis to further explore the correlation between CIMT and baPWV. Taking CIMT as the dependent variable, and baPWV as the independent variable, a linear regression analysis was established and illustrated a linear relationship between CIMT and baPWV with a statistically significant difference (P<0.0001) (**Table 5**; **Figure 3**).

## Discussion

The major findings from the present study include: 1) middle-aged and elderly males have higher CIMT and baPWV values than age-matched females; 2) blood pressure and age are the two most critical factors for baPWV; 3) there is a significant correlation between baPWV and CIMT; 4) there is no significant difference in baPWV between early the thickening phase and the plaque phase of CIMT.

Previously, a number of studies have shown that gender, blood pressure and age were closely linked to the development of vascular stiffness [17]. Consistent with these reports, in the current investigation, we found that male gender, aging and blood pressure elevation affected CIMT and baPWV. Gender-linked changes in collagen isotypes and reduction in elastin were potentially responsible for this gender difference observed in arterial stiffness [18]. Aging causes degeneration of elastic fibers and deposition of collagen in the vascular wall [19], while high blood pressure may damage vascular wall and promote stiffness [20]. These degenerative changes in the vascular wall and changes in collagen content and amount lead to an elastic middle layer fracture and results in increased arterial stiffening. Among these three major factors, blood pressure is an easily modifiable risk factor. Therefore, based on our study, patients with hypertension are recommended to strictly control their blood pressure in order to reduce risk. Population with a normal blood pressure but baPWV≥1400 cm/s should modify life style risk factors, while we recommend the elderly should have routine monitoring of arterial stiffness.

It is well accepted that hyperlipidemia, in particular, LDL, leads to the formation of atherosclerotic plaques. Indeed, studies have shown that elevation in serum triglycerides promote the development atherosclerosis [21]. In line with previous observations, our findings also suggested that LDL correlated with CIMT. Consistent with other reports [22, 23], we found that there was no substantive link between LDL and baPWV. This may be accounted for by several explanations. In our study, subjects mainly originated from economically developed cities and usually had a higher socioeconomic status. Furthermore, nearby hospitals regularly monitor disease and have a high degree of health education and standardized treatment of cardiovascular diseases. This is demonstrated by the fact that of the 545 participants; 1) 117 had a history of hypertension and diabetes, among whom 109 received treatment, reaching a treatment rate of 93%; 2) among these 117, 51.3% (60) had normal LDL levels; 3) in 428 without a history of hypertension and/or diabetes, 185 (43.2%) had normal LDL levels. Hence, it was clear that participants with a history of hypertension and/or diabetes had improved control of blood lipid levels than those without a history of these conditions. We believe that treatments play a role in controlling blood lipid levels in the participants of our study, although we were unable to collect reliable therapeutic data in our study.

**Table 5.** Linear correlation between CIMT and baPWV

| | $R^2$ | F value | SE | B value | t value | *P* value |
|---|---|---|---|---|---|---|
| baPWV | 0.061 | 36.57 | 0.000 | 0.001 | 6.047 | <0.0001 |

NOTE: CIMT was taken as the dependent variable, and baPWV as the independent variable.

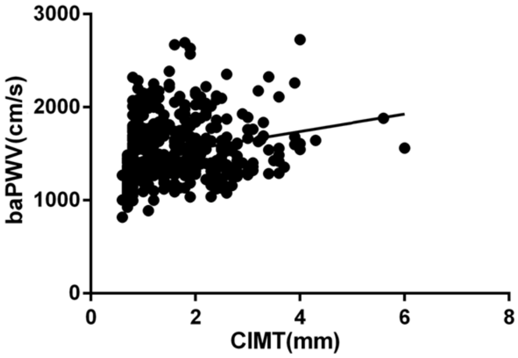


**Figure 3.** Linear regression analysis revealed a linear correlation between CIMT and baPWV. CIMT was taken as the dependent variable, and baPWV as the independent variable.

baPWV mainly reflects the stiffness of systemic peripheral arteries, however, some studies have also suggested that baPWV may also be used as an assessor of the stiffness of central elastic arteries [13]. Although CIMT may serve as an index of carotid atherosclerosis, whether local carotid atherosclerosis reflects systemic arteriosclerosis remains to be determined. We found that CIMT and baPWV had a strong linear correlation, demonstrating that an increase in CIMT thickening was accompanied by an increase in baPWV value and vice versa. We therefore concluded that CIMT indirectly reflect the status of systemic atherosclerosis. In addition, the normal CIMT group had a significantly lower baPWV than the thickening and plaque groups, while there was no significant difference in baPWV between the latter two groups. These findings collectively suggested that CIMT thickening at the early stage already indicates an increase in arterial stiffness. Hence, we recommended CIMT≥1.0 mm as a predictor of atherosclerosis, which requires medical intervention at the thickening stage, not only at the plaque stage.

The present study does, however, have some limitations. This was a retrospective study, and had disadvantages associated with the nature of retrospective design such as potential bias of sample selection. Also, this study was sponsored by a single center. In addition, some participants were not able to clearly specify the drugs they were currently prescribed. Hence, we were unable to analyze the effects of drugs, particularly antihypertensive and lipid-lowering medicines, on baPWV and CIMT.

In conclusion, in the current study, we demonstrated that age, gender and blood pressure are major determinants of CIMT and baPWV in the middle-aged and elderly population, and that CIMT and baPWV exhibit a linear correlation. Our study also suggests that CIMT≥1.0 mm (i.e. thickening stage) instead of CIMT≥1.5 mm (i.e. plaque stage) should be used as a cut-off value for medical intervention.

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## Disclosure of conflict of interest

None.

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