

Brachial-ankle pulse wave velocity as a measurement for increased carotid intima-media thickness: A comparison with carotid-femoral pulse wave velocity in a Chinese community-based cohort

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Abstract

Carotid-femoral pulse wave velocity (cfPWV) and brachial-ankle pulse wave velocity (baPWV) act as two most frequently applied indicators to evaluate arterial stiffness. Limited studies have systematically compared the relationships between cfPWV/baPWV and increased carotid intima-media thickness (cIMT). This study aimed to investigate the associations of the two PWV indices with cIMT in a Chinese community-based population. A total of 6026 Chinese participants from an atherosclerosis cohort were included in our analysis. Increased cIMT was defined as the maximum of cIMT > 0.9 mm in end-systolic period of carotid artery. Mean (SD) cfPWV and baPWV were 8.55 ± 1.83 and 16.79 ± 3.35 m/s, respectively. The prevalence of increased cIMT was 59.58%. In multivariable logistic regression, both PWVs were independently associated with increased cIMT after adjustment for various confounders (for 1 m/s increase of cfPWV: OR = 1.07, 95% CI: 1.02-1.11; for 1 m/s increase of baPWV: OR = 1.03, 95% CI: 1.00-1.05). The highest cfPWV and baPWV quartile groups had higher prevalence of increased cIMT when compared with the lowest quartile groups (for cfPWV: OR = 1.28, 95% CI: 1.06-1.55; for baPWV: OR = 1.23, 95% CI: 1.00-1.50). However, when both PWVs were added into multivariable model simultaneously, only cfPWV was associated with odds of increased cIMT. Subgroup analyses further showed cfPWV was more strongly associated with increased cIMT than baPWV in males, participants aged ≥ 65 years, and those with other cardiovascular risk factors. In conclusion, both cfPWV and baPWV are associated with increased cIMT in

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a Chinese community-based population. Furthermore, cfPWV is more strongly correlated with increased cIMT compared to baPWV.

KEYWORDS

arterial stiffness, brachial-ankle pulse wave velocity, cardiovascular disease risk factors, carotid intima-media thickness, carotid-femoral pulse wave velocity

1 | INTRODUCTION

Cardiovascular disease is the leading cause of global morbidity and mortality with increasing quantity of patients.^{1,2} The structure and function of arterial wall changes are the early signs of cardiovascular disease. Carotid intima-media thickness (cIMT), noninvasively measured by high-resolution ultrasound, has been widely used as a surrogate of atherosclerosis. Increased cIMT has been confirmed by many previous large studies and recommended by international guidelines as an intermediate surrogate endpoint and a predictor for the risk of cardiovascular events,³⁻⁸ which is also a critical indicator of early target organ damage in hypertension and can be regarded as a marker of arterial injury or remodeling as well.^{9,10}

Pulse wave velocity (PWV) is the measurement of arterial stiffness, of which carotid-femoral pulse wave velocity (cfPWV) and brachial-ankle pulse wave velocity (baPWV) are commonly used in clinical and research fields. CfPWV is proven to be a predictor of cardiovascular events in a variety of patients, such as the general population and those with end-stage renal disease, diabetes, and hypertension, independent of traditional risk factors,¹¹⁻¹⁴ and be widely used in Western countries with recommendations for cardiovascular risk stratification in hypertensive patients by many guidelines. In the meanwhile, baPWV is mainly used in East Asia and the predictive value of it has been indicated in the general population^{15,16} and in high-risk population.^{17,18} CfPWV has been considered as the gold standard for measuring arterial stiffness,¹⁹ however, it requires a higher technical skill, and has a poor privacy. Compared to cfPWV, the measurement of baPWV is simpler, easier, less time-consuming, and less stressful for participants.

Advanced assessment of PWV before development of increased cIMT may facilitate improvement in early prevention of arterial remodeling, atherosclerosis, target organ damage in hypertension, and cardiovascular disease. However, previous studies have demonstrated controversial relationships between cIMT and cfPWV/baPWV. cIMT is significantly associated with cfPWV in general population, and patients with hypertension or type 2 diabetes,²⁰⁻²² as well as significantly associated with baPWV in general population, and patients with hypertension or end-stage renal disease.²³⁻²⁵ Whereas other studies have failed to find a correlation between PWV and increased cIMT.^{26,27} Moreover, evidence is very limited for the comparison of the associations of increased cIMT with cfPWV and baPWV. Up to now, only Lu and associates indicated that cfPWV, but not baPWV showed significant association with cIMT and increased cIMT when cfPWV and baPWV were both put into the stepwise linear or logistic regression model in aged over 65 years community-based population.²⁰ So, it is uncertain which

PWV is more relevant to increased cIMT, and whether there is the particularity of population.

Furthermore, there are few large-scale studies comparing the two PWV indices in Chinese population. Therefore, the present study aimed to investigate and compare the associations of increased cIMT with cfPWV and baPWV in a Chinese community-based cohort.

2 | METHODS

2.1 | Study population

Participants included in this study were from an atherosclerosis cohort established in the Pingguoyuan and Gucheng communities of Shijingshan district in Beijing, China.²⁸ A total of 6568 participants were followed up between September to December 2018. In this study, participants without carotid ultrasonography and cfPWV or baPWV measurement data were excluded. We also excluded those who did not have standard baPWV measurement at baseline because of ankle brachial index were ≤ 0.9 , and who already had peripheral arterial disease at baseline. Ultimately, 6026 participants were eligible for the final analysis. This study was approved by the Ethics Committee of Peking University First Hospital. Each participant signed written informed consent.

2.2 | Data collection

As described in our previous report,²⁸ baseline data were collected by trained researchers according to standard procedures. All participants were interviewed face to face using a standardized questionnaire to obtain basic information on sociodemographic characteristics, diet, lifestyle, health behavior, and the personal and medical history.

Current smoking was defined as smoking one or more cigarettes per day for at least six months. Current drinking was defined as drinking once per week for at least six months. Hypertension was defined as any self-reported history of hypertension or systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg or use of antihypertensive medication. Diabetes mellitus was defined as any self-reported history of diabetes, or fasting plasma glucose ≥ 7.0 mmol/L, or 2-hour oral glucose tolerance test ≥ 11.1 mmol/L, or use of hypoglycemic medication. Dyslipidemia was defined as any self-reported history of dyslipidemia, or triglyceride (TG) ≥ 1.7 mmol/L (150 mg/dL), or total cholesterol

(TC) ≥ 5.18 mmol/L (200 mg/dL), or low-density lipoprotein cholesterol (LDL-C) ≥ 3.37 mmol/L (130 mg/dL), or high-density lipoprotein cholesterol (HDL-C) < 1.04 mmol/L (40 mg/dL), or use of lipid-lowering medication. History of cardiovascular disease was defined as any self-reported history of coronary heart disease, stroke, or transient ischemic attack.

2.3 | Physical examination

Anthropometric measurements were taken according to a standard operating procedure. Body mass index (BMI) was calculated as weight in kilograms divided by square of height in meters. Seated right brachial blood pressure was measured by well-trained researchers using an Omron HEM-7130 electronic sphygmomanometer with the standard calibration protocol and appropriately sized cuffs after a 5-minute rest. All participants were forbidden to smoke, exercise intensely or drink coffee before the measurement. Triplicate measurements were taken at intervals of at least 1 minute. The mean of the three consecutive measurements of each participant's SBP and DBP were taken for analysis.

2.4 | Laboratory measurements

After overnight fasting for at least 12 hours, a 3.5 mL venous blood sample was obtained from the median cubital of each participant, which was used for measurement of TC, TG, LDL-C, HDL-C, fasting blood glucose, the standard 75 g oral glucose tolerance test, and serum creatinine (Scr) concentrations. All laboratory samples were measured by enzymatic techniques using the HITACHI 7100 Automatic Analyzer. Additionally, the estimated glomerular filtration rate (eGFR) was calculated using the following equation derived from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI, 2009)²⁹: $eGFR = 141 \times \min(Scr/\kappa, 1)^\alpha \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ (if female), of which Scr is serum creatinine (mg/dL); κ , 0.7 for females and 0.9 for males; α , -0.329 for females and -0.411 for males; min, the minimum of Scr/ κ or 1; and max, the maximum of Scr/ κ or 1.

2.5 | Pulse wave velocity measurements

BaPWV was measured by well trained technicians using the Omron Colin BP-203RPEIII device (Omron Healthcare, Kyoto, Japan) based on a standard protocol. The details of the oscillometric method have been described and validated previously.³⁰ Briefly, baPWV for each participant was measured in the supine position after a 5-minute rest. Pulse waves of brachial and posterior tibial arteries at the pressure cuffs were recorded by the device, respectively, and the distance between the upper arm and ankle is calculated using a linear regression of body height. BaPWV on both sides was obtained using the distance divided

by the time difference via the device automatically. The higher baPWV was used for further analysis.

The measurement of cFPWV was performed by professional technicians using the PulsePen device (DiaTecne, Italy) in accordance with standard operating procedures. After resting in the supine position for at least 5 minutes, pulse waveforms of the strongest beating points of each participant's right carotid and femoral were collected. The distances from carotid to femoral, carotid to sternal angle, and sternal angle to femoral were measured simultaneously and the pass time was calculated by the "foot-to-foot" method, which were taken into the device for automatic calculation of cFPWV. The mean of at least two measurements of cFPWV was obtained from each participant.

2.6 | Carotid ultrasonography

All participants underwent carotid ultrasonography using the Terason Echo ultrasound system (Terason, USA) with an 8-MHz linear array vascular probe according to standard protocol by a trained and certified sonographer. Briefly, the figures of bilateral common carotid arteries IMT were clearly retained in segments free of plaques and about 10 mm in length near the bulb. Finally, cIMT was measured by certified sonographers using the Vascular research tools 6 (MIA-Carotid Analyzer 6.0) software by a semiautomatic method. Increased cIMT was defined as either of the two cIMT of both sides in the far wall of common carotid arteries > 0.9 mm in systole.^{9,31}

2.7 | Statistical analysis

Normally distributed continuous variables were expressed as mean \pm standard deviation (SD), and were compared using one-way ANOVA between multiple groups. Skewed distributed continuous variables were expressed as median (interquartile range), and were compared by Kruskal-Wallis test. Dichotomous variables were expressed as numbers (percentages, %), and were compared by chi-squared test. Logistic regression models were used to investigate the relationships between PWV indices and increased cIMT in both univariable and multivariable analyses adjusting age, sex, BMI, SBP, DBP, eGFR, TG, LDL-C, HDL-C, fast blood glucose, current smoking, current drinking, antihypertensive drugs, hypoglycemic drugs, lipid-lowering drugs, and history of cardiovascular disease, which were selected based on previous studies showing a relation to PWV or cIMT. To compare the association between different PWV indices and increased cIMT, cFPWV, and baPWV were first individually and then simultaneously put into the multivariable regression models. The odds ratios (OR) of increased cIMT associated with PWV indices were reported according to 1 m/s increase and quartiles of cFPWV and baPWV.

Subgroup and interaction analyses were developed to examine the relationships between PWV indices and increased cIMT in terms of specific covariates. Tests for interaction in the logistic-regression models were used to compare ORs between the analyzed subgroups.

All analyses were performed using Empower (R) (www.empowerstats.com, X&Y solutions, Inc, Boston, MA, USA) and R-3.5.1 (<http://www.R-project.org>). A *P* value of < .05 was considered to be statistically significant for all tests.

3 | RESULTS

3.1 | Baseline characteristics of participants

Baseline characteristics of all participants are presented overall and according to quartiles of cfPWV (Table 1) and baPWV (Table S1). Participants were 62.32 ± 7.63 years old, and 34.14% ($n = 2057$) were males. Mean (SD) BMI was 25.21 ± 3.31 kg/m², and mean (SD) baseline eGFR was 93.29 ± 11.44 mL/min/1.73 m². Mean (SD) cfPWV and baPWV were 8.55 ± 1.83 and 16.79 ± 3.35 m/s, respectively. The prevalence of hypertension, diabetes mellitus, dyslipidemia, and cardiovascular disease were 54.40% ($n = 3278$), 28.69% ($n = 1729$), 80.53% ($n = 4853$), and 16.32% ($n = 983$), respectively. Mean (SD) cIMT was 0.90 ± 0.15 mm, and the prevalence of increased cIMT was 59.58% ($n = 3590$). All variables were significantly different according to the quartiles of cPWV.

3.2 | Associations of cfPWV and baPWV with increased cIMT when considered individually

As shown in Figure S1, there was a positive correlation between the odds of increased cIMT and either of different PWV indices after adjusting for age and sex, while the growth rate of the smoothing curve tended to slow down with baPWV more than 14 m/s.

Table 2 shows the results of logistic regressions for the effects of cfPWV and baPWV on the odds of increased cIMT. Whether PWVs were treated as continuous or categorical variables, increased cIMT was associated with both cfPWV and baPWV in crude models. Both relationships remained statistically significant after adjusting for various baseline parameters with OR (95% confidence interval [CI]) of 1.07 (1.02-1.11) for 1 m/s increase of cfPWV, as well 1.03 (1.00-1.05) for 1 m/s increase of baPWV. However, after adjusting for various confounders, the relationship was not in a clear dose-dependent manner. Only for the top quartile (cfPWV ≥ 9.43 m/s and baPWV ≥ 18.62 m/s), cfPWV and baPWV were associated with increased cIMT with an OR (95% CI) of 1.28 (1.06-1.55) and 1.23 (1.00-1.50), respectively, when comparing with the bottom quartile.

3.3 | Associations of cfPWV and baPWV with increased cIMT when considered simultaneously

As shown in Table 3, when cfPWV and baPWV were added into the model simultaneously, only cfPWV was independently associated with increased cIMT whether PWVs as continuous or categorical variables. The significant relationship between baPWV and increased cIMT dis-

appeared. Among the categorical variable sets, only the highest quartile of cfPWV was related to increased cIMT with an OR (95% CI) of 1.23 (1.00-1.51). And the relationship between continuous variable and increased cIMT was significant with an OR (95% CI) of 1.05 (1.01-1.10) for 1 m/s increase of cfPWV.

Subgroup analyses are presented in Table 4 when cfPWV and baPWV simultaneously entered into the multivariate regression stratified by the specified variables. The results showed that cfPWV was more strongly associated with increased cIMT than baPWV in male, participants aged 65 years or more, those with BMI ≥ 24 kg/m², hypertension, diabetes mellitus, or dyslipidemia.

4 | DISCUSSION

The relationship between PWV and increased cIMT was observed in the present study. There were two main findings of this study as follows: (1) both cfPWV and baPWV were significantly associated with increased cIMT, independent of common risk factors of cardiovascular disease; (2) compared with baPWV, the association between cfPWV and increased cIMT was stronger in a Chinese community-based population, especially in men, participants aged ≥ 65 years, and those with obesity, hypertension, diabetes mellitus, or dyslipidemia.

Early detection of arterial injury, remodeling, or atherosclerosis is crucial for reducing cardiovascular risk. Throughout the 20th century, vascular disease has been considered synonymous with atherosclerosis. The role of arterial stiffness in the risk assessment of cardiovascular disease was not taken seriously, until epidemiological studies revealed the predictive effect of it independent of traditional factors on cardiovascular disease.^{11,32} There is a close interaction between arterial stiffness and atherosclerosis. Although cIMT is not synonymous with atherosclerosis, the potential value of increased cIMT as a surrogate marker for arterial injury and atherosclerosis has been evaluated.^{33,34} PWV, the most widely used measurement of arterial stiffness, has emerged as a useful tool for the diagnosis and risk stratification of cardiovascular disease. The two most commonly used PWV indices in clinical practice are cfPWV and baPWV, both of which have been separately analyzed for their association with cIMT.

Most previous cross-sectional studies have indicated that cfPWV was associated with cIMT in different populations. Zureik and associates²⁶ and Taniwaki and associates²² demonstrated that cfPWV was positively associated with cIMT in general population ($r = 0.39$, $P < .001$) and type 2 diabetes patients ($r = 0.482$, $P < .0001$), respectively. Similarly, Sumbul and associates²¹ discovered that 0.1 mm increase of cIMT was associated with increased cfPWV by 50% in hypertensive. Furthermore, Kubozono and associates first reported that high baPWV was a strong predictor of increased cIMT (≥ 1.0 mm) among 1583 Japanese male undergoing routine health examination.²³ Baseline cfPWV was also found to be independently associated with increased cIMT during a four-year period in a hypertensive old-aged cohort.³⁵

However, there have been some studies to the contrary. The study of Bai and associates suggested that cfPWV was only significantly

TABLE 1 Baseline characteristics of all eligible participants, overall and according to the quartile of cfPWV

| Variables | Overall | cfPWV, m/s | | | | P |
|---------------------------------|--------------------|--------------------|--------------------|--------------------|--------------------|-------|
| | | Q1 (≤ 7.31) | Q2 (7.32-8.19) | Q3 (8.20-9.42) | Q4 (≥ 9.43) | |
| N | 6026 | 1504 | 1503 | 1509 | 1510 | |
| Age, y | 62.32 \pm 7.63 | 58.64 \pm 6.56 | 60.56 \pm 6.15 | 62.82 \pm 6.82 | 67.23 \pm 8.03 | <.001 |
| Male, n (%) | 2057 (34.14%) | 333 (22.14%) | 463 (30.81%) | 567 (37.57%) | 694 (45.96%) | <.001 |
| BMI, kg/m ² | 25.21 \pm 3.31 | 24.81 \pm 3.23 | 25.19 \pm 3.19 | 25.53 \pm 3.48 | 25.31 \pm 3.28 | <.001 |
| SBP, mmHg | 132.93 \pm 16.63 | 122.74 \pm 13.92 | 130.04 \pm 14.43 | 135.92 \pm 14.84 | 142.98 \pm 16.19 | <.001 |
| DBP, mmHg | 78.98 \pm 9.51 | 76.20 \pm 8.55 | 79.01 \pm 9.09 | 80.40 \pm 9.51 | 80.28 \pm 10.20 | <.001 |
| eGFR, mL/min/1.73m ² | 93.29 \pm 11.44 | 96.66 \pm 9.85 | 95.07 \pm 10.39 | 93.12 \pm 10.72 | 88.36 \pm 12.84 | <.001 |
| Fasting glucose, mmol/L | 6.15 \pm 1.85 | 5.62 \pm 1.09 | 5.96 \pm 1.65 | 6.21 \pm 1.76 | 6.81 \pm 2.44 | <.001 |
| TC, mmol/L | 5.33 \pm 1.03 | 5.39 \pm 1.01 | 5.39 \pm 1.00 | 5.31 \pm 1.04 | 5.24 \pm 1.06 | <.001 |
| TG*, mmol/L | 1.37 (0.98-1.93) | 1.29 (0.92-1.75) | 1.40 (0.99-1.95) | 1.39 (1.00-2.01) | 1.41 (1.00-2.00) | <.001 |
| LDL-C, mmol/L | 3.42 \pm 0.97 | 3.46 \pm 0.93 | 3.47 \pm 0.96 | 3.41 \pm 0.99 | 3.36 \pm 1.00 | .010 |
| HDL-C, mmol/l | 1.50 \pm 0.35 | 1.56 \pm 0.37 | 1.50 \pm 0.35 | 1.48 \pm 0.35 | 1.45 \pm 0.33 | <.001 |
| cfPWV, m/s | 8.55 \pm 1.83 | 6.68 \pm 0.47 | 7.76 \pm 0.25 | 8.75 \pm 0.35 | 11.00 \pm 1.69 | <.001 |
| baPWV, m/s | 16.79 \pm 3.35 | 14.32 \pm 2.05 | 15.71 \pm 2.27 | 17.29 \pm 2.61 | 19.83 \pm 3.47 | <.001 |
| Current smoking, n (%) | 831 (13.93%) | 162 (10.87%) | 221 (14.82%) | 226 (15.17%) | 222 (14.84%) | .001 |
| Current drinking, n (%) | 625 (10.44%) | 106 (7.08%) | 129 (8.65%) | 176 (11.74%) | 214 (14.28%) | <.001 |
| Prevalence of disease, n (%) | | | | | | |
| Hypertension | 3278 (54.40%) | 437 (29.06%) | 708 (47.11%) | 939 (62.23%) | 1194 (79.07%) | <.001 |
| Dyslipidemia | 4853 (80.53%) | 1171 (77.86%) | 1248 (83.03%) | 1223 (81.05%) | 1211 (80.20%) | .004 |
| Diabetes mellitus | 1729 (28.69%) | 238 (15.82%) | 354 (23.55%) | 471 (31.21%) | 666 (44.11%) | <.001 |
| Coronary heart disease | 718 (11.92%) | 117 (7.79%) | 137 (9.12%) | 181 (11.99%) | 283 (18.74%) | <.001 |
| Stroke / TIA | 265 (4.40%) | 36 (2.39%) | 48 (3.19%) | 72 (4.77%) | 109 (7.22%) | <.001 |
| Medication, n (%) | | | | | | |
| Antihypertensive drugs | 2159 (35.86%) | 303 (20.16%) | 454 (30.25%) | 609 (40.38%) | 793 (52.59%) | <.001 |
| Hypoglycemic drugs | 975 (16.19%) | 133 (8.85%) | 180 (11.98%) | 254 (16.84%) | 408 (27.04%) | <.001 |
| Lipid-lowering drugs | 1200 (19.95%) | 254 (16.92%) | 283 (18.85%) | 323 (21.45%) | 340 (22.56%) | <.001 |

Data are presented as mean \pm standard deviation (SD) or median (interquartile range) for continuous variables and percentage (%) for categorical variables. Abbreviations: baPWV, brachial-ankle pulse wave velocity; BMI, body mass index; cfPWV, carotid-femoral pulse wave velocity; cIMT, carotid intima-media thickness; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, Triglycerides; TIA, transient ischemic attack.

*Median (interquartile range).

associated with cIMT as a continuous variable, but not with increased cIMT as a dichotomous one (OR = 1.25, 95% CI: 0.97-1.60, per SD).³¹ A cross-sectional study performed in 155 individuals aged over 75 years also showed baPWV was not associated with cIMT, which might be related to the older participants.²⁷ Joo and associates demonstrated that participants with higher baPWV had a significantly higher prevalence of composite coronary and carotid atherosclerosis but increased cIMT was not significantly associated with higher baPWV.³⁶ Besides, another study involving patients with acute ischemic stroke

also revealed increased baPWV was associated with the presence of atherosclerosis in the intracranial cerebral artery, but not with atherosclerosis in the extracranial cerebral artery.³⁷

Noticeably, to the best of our knowledge, only one cross-sectional study has compared the correlations of cfPWV/baPWV separately or simultaneously with increased cIMT. This community-based Chinese cross-sectional study, including 1599 elderly participants aged over 65 years, revealed that only cfPWV, but not baPWV, was significantly associated with increased cIMT (OR = 1.34, 95% CI: 1.02-1.76), when

TABLE 2 Logistic regressions for the effects of cfPWV and baPWV on the odds of increased cIMT

| Variables | n (%) | Crude | | Model I | | Model II | |
|-------------------------------|---------------|------------------|-------|------------------|-------|------------------|------|
| | | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P |
| cfPWV (continuous), per 1 m/s | | 1.29 (1.25-1.34) | <.001 | 1.13 (1.09-1.17) | <.001 | 1.07 (1.02-1.11) | .003 |
| cfPWV Quartiles, m/s | | | | | | | |
| Q1: (≤ 7.31) | 709 (47.14%) | 1.0 (Reference) | | 1.0 (Reference) | | 1.0 (Reference) | |
| Q2: (7.32-8.19) | 845 (56.22%) | 1.44 (1.25-1.66) | <.001 | 1.25 (1.08-1.45) | .003 | 1.14 (0.98-1.33) | .097 |
| Q3: (8.20-9.42) | 936 (62.03%) | 1.83 (1.58-2.12) | <.001 | 1.35 (1.16-1.57) | <.001 | 1.13 (0.96-1.33) | .158 |
| Q4: (≥ 9.43) | 1100 (72.85%) | 3.01 (2.58-3.50) | <.001 | 1.65 (1.40-1.95) | <.001 | 1.28 (1.06-1.55) | .011 |
| P for trend | | <.001 | | <.001 | | .021 | |
| baPWV (continuous), per 1 m/s | | 1.14 (1.12-1.16) | <.001 | 1.06 (1.04-1.08) | <.001 | 1.03 (1.01-1.05) | .029 |
| baPWV Quartiles, m/s | | | | | | | |
| Q1: (≤ 14.44) | 693 (45.99%) | 1.00 (Reference) | | 1.00 (Reference) | | 1.00 (Reference) | |
| Q2: (14.45-16.26) | 848 (56.50%) | 1.53 (1.32-1.76) | <.001 | 1.26 (1.08-1.46) | .003 | 1.08 (0.92-1.26) | .353 |
| Q3: (16.27-18.61) | 950 (63.04%) | 2.00 (1.73-2.32) | <.001 | 1.38 (1.18-1.61) | <.001 | 1.05 (0.89-1.25) | .547 |
| Q4: (≥ 18.62) | 1099 (72.73%) | 3.13 (2.69-3.65) | <.001 | 1.70 (1.44-2.01) | <.001 | 1.23 (1.00-1.50) | .046 |
| P for trend | | <.001 | | <.001 | | .081 | |

Model I: adjusted for age and sex. Model II: adjusted for age, sex, body mass index, smoking and drinking status, systolic and diastolic blood pressure, eGFR, fasting glucose, high/low-density lipoprotein cholesterol, triglycerides, cardiovascular disease, antihypertensive drugs, lipid-lowering drugs, and hypoglycemic drugs.

Abbreviations: baPWV, brachial-ankle pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; CI, confidence interval; cIMT, carotid intima-medium thickness; OR, odds ratio.

TABLE 3 Multivariable logistic regressions for the effects of cfPWV and baPWV on the odds of increased cIMT when considered simultaneously

| PWV, m/s | Increased cIMT | |
|-------------------------------|------------------|------|
| | OR (95% CI) | P |
| cfPWV (Continuous, per 1 m/s) | 1.05 (1.01-1.10) | .024 |
| cfPWV Quartiles, m/s | | |
| Q1: (≤ 7.31) | 1.0 (Reference) | |
| Q2: (7.32-8.19) | 1.13 (0.97-1.33) | .118 |
| Q3: (8.20-9.42) | 1.11 (0.93-1.32) | .246 |
| Q4: (≥ 9.43) | 1.23 (1.00-1.51) | .049 |
| baPWV (Continuous, per 1 m/s) | 1.01 (0.99-1.04) | .309 |
| baPWV Quartiles, m/s | | |
| Q1: (≤ 14.44) | 1.0 (Reference) | |
| Q2: (14.45-16.26) | 1.06 (0.90-1.24) | .511 |
| Q3: (16.27-18.61) | 1.01 (0.84-1.21) | .940 |
| Q4: (≥ 18.62) | 1.14 (0.92-1.42) | .236 |

cfPWV and baPWV were entered into the model simultaneously. The models were adjusted for age, sex, body mass index, smoking and drinking status, systolic and diastolic blood pressure, eGFR, fasting glucose, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, coronary heart disease, stroke, antihypertensive drugs, lipid-lowering drugs, and hypoglycemic drugs.

Abbreviations: baPWV, brachial-ankle pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; CI, confidence interval; cIMT, carotid intima-medium thickness; OR, odds ratio.

both PWV indices were simultaneously put into the stepwise logistic regression model.²⁰ Similarly, cfPWV has shown a better link with increased cIMT than baPWV in participants aged 65 years or more in our study. Meanwhile, we also found similar results among those with obesity, hypertension, diabetes mellitus, or dyslipidemia, which may indicate cfPWV should be more recommended than baPWV for the marker of increased cIMT in populations with already existed cardiovascular risk factors.

The stronger relationship of cfPWV than baPWV with increased cIMT in our study was not surprising. The arterial system is composed of elastic arteries, muscular arteries, and arterioles, among which the carotid artery belongs to elastic arteries. By contrast, cfPWV includes only elastic arteries, while baPWV includes large portion of peripheral muscular artery.³⁸ Therefore, cfPWV may be more sensitive to stiffness of elastic arteries than baPWV.

Increased cIMT could be used to determine atherosclerosis in early stage noninvasively.³³ Endothelial dysfunction is initial mechanism of atherosclerotic process. Meanwhile, previous study has summarized the multiple causes and locations of arterial stiffness, including endothelial cells dysfunction, as well as the deposition of cellular elements such as collagen in intima and media of the vessel wall.³⁹ On gross pathologic vascular specimens, these molecular changes manifest as a doubling to tripling of intima-media thickness between ages 20 and 90.⁴⁰ Thus, increased cIMT is not only associated with atherosclerosis, but also with arterial stiffness. Besides, increased PWV shares the common risk factors with increased cIMT, such as diabetes mellitus, hypertension, and dyslipidemia, which might be another crucial mechanism of the correlation between PWV and cIMT.^{41,42}

TABLE 4 Subgroup analyses for the effects of cfPWV and baPWV when considered simultaneously on the odds of increased cIMT stratified by the specified variables

| Subgroups | n (%) | cfPWV | | baPWV | |
|------------------------------|---------------|-------------------|------|-------------------|------|
| | | OR (95% CI) | P | OR (95% CI) | P |
| Age, years | | | | | |
| <65 | 2104 (52.12%) | 1.03 (0.97-1.09) | .386 | 1.03 (0.99, 1.06) | .101 |
| ≥65 | 1486 (74.71%) | 1.10 (1.03, 1.18) | .008 | 0.99 (0.95, 1.03) | .707 |
| Sex | | | | | |
| Male | 1394 (67.77%) | 1.14 (1.05, 1.23) | .002 | 1.01 (0.97, 1.06) | .600 |
| Female | 2196 (55.33%) | 1.02 (0.96, 1.08) | .599 | 1.01 (0.98, 1.05) | .403 |
| BMI, kg/m² | | | | | |
| <24 | 1176 (52.81%) | 0.99 (0.92, 1.06) | .760 | 1.03 (0.99, 1.08) | .135 |
| ≥24 | 2414 (63.54%) | 1.11 (1.04, 1.18) | .001 | 1.00 (0.97, 1.03) | .937 |
| Hypertension | | | | | |
| No | 1400 (50.95%) | 1.01 (0.94, 1.10) | .710 | 1.01 (0.97, 1.06) | .598 |
| Yes | 2190 (66.81%) | 1.07 (1.01, 1.14) | .015 | 1.01 (0.98, 1.05) | .449 |
| Diabetes mellitus | | | | | |
| No | 2434 (56.64%) | 1.04 (0.98, 1.10) | .189 | 1.02 (0.99, 1.05) | .231 |
| Yes | 1156 (66.86%) | 1.09 (1.01, 1.18) | .033 | 1.00 (0.96, 1.05) | .940 |
| Dyslipidemia | | | | | |
| No | 666 (56.78%) | 1.01 (0.92, 1.12) | .805 | 1.04 (0.99, 1.10) | .147 |
| Yes | 2924 (60.25%) | 1.06 (1.01, 1.12) | .022 | 1.01 (0.98, 1.04) | .586 |

cfPWV and baPWV were entered into the model simultaneously. The model adjusted for age, sex, body mass index, smoking and drinking status, systolic and diastolic blood pressure, eGFR, fast glucose, high/low-density lipoprotein cholesterol, triglycerides, coronary heart disease, stroke, antihypertensive drugs, lipid-lowering drugs, and hypoglycemic drugs.

Abbreviations: baPWV, brachial-ankle pulse wave velocity; BMI, body mass index; cfPWV, carotid-femoral pulse wave velocity; cIMT, carotid intima-medium thickness, CI, confidence interval; OR, odds ratio.

Our study has several potential limitations. First, all participants were from a Chinese community-based population. The generalizability of our results to other populations is remained to be determined. Second, the present study is a cross-sectional study, a longitudinal approach is needed to confirm the associations between PWV measurements and the risk of increased cIMT. Thus, it should be studied further whether cfPWV and baPWV should be treated differently when serves as predictors of the progression of carotid wall thickening. Third, a recent study found that increased baPWV, not increased cIMT, was significantly associated with total cerebral small vessel disease burden in a Chinese rural community-based population.⁴³ Therefore, even if cfPWV was more strongly associated with increased cIMT than baPWV in our study, we cannot infer that cfPWV is better associated with overall cardiovascular disease or other hypertensive target organ damage.

5 | CONCLUSIONS

Our findings show that both cfPWV and baPWV are independently associated with increased cIMT in a Chinese community-based population without peripheral arterial disease. CFPWV is more strongly

correlated with increased cIMT than baPWV, especially in males, the elder, and people with obesity, hypertension, diabetes mellitus, or dyslipidemia. In view of the lack of current data for comparing the association between different PWV indices and increased cIMT, the results of the present study may provide some guiding significance in this field. Future research should focus on investigating the longitudinal relationships between different PWV indices and the early indicators of atherosclerosis.

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CONFLICTS OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Danmei He, Fangfang Fan, Yan Zhang, Jianping Li, and Yong Huo designed the study; Fangfang Fan, Jia Jia, Lan Gao, Ying Yang, Yimeng Jiang, Danmei He, Pengfei Sun, and Bo Liu collected and re-checked the data; Fangfang Fan, Jia Jia, and Danmei He analyzed and interpreted the data; Danmei He wrote the paper; Fangfang Fan and Yan Zhang revised the manuscript. All authors have read and approved the submitted manuscript.

Yan Zhang and Fangfang Fan agree to be responsible for all aspects of the work to ensure that issues relating to accuracy or completeness of any part of the work are properly investigated and resolved.

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