Characteristics of pulse wave velocity and its correlation with cardiovascular disease risk factors in healthy individuals

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Editorial

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ABSTRACT

Background: Cardiovascular disease (CVD) is a major cause of human mortality and has become the leading cause of death worldwide. Existing studies indicate that structural and functional damage to the main arteries represents a significant risk factor for early vascular lesions and many CVDs.

Aims: This study aimed to explore characteristics of carotid‐femoral pulse wave velocity (cfPWV) and its correlation with cardiovascular disease risk factors in healthy individuals.

Methods: Convenience sampling was used to collect demographics, risk factors, and laboratory examinations from 501 healthy individuals who underwent health checkups at our healthcare center from August 2020 to January 2021. Pearson correlation coefficients were used to examine the correlations between cfPWV and various parameters in both sexes. Multiple linear regression analysis was used to investigate the factors potentially influencing cfPWV.

Results: A statistically significant difference in cfPWV between sexes was observed only in the age group of subjects 38–47 years old. The results of the univariate analysis showed that in males, cfPWV was positively correlated with age, blood pressure, heart rate, and alcohol consumption and was negatively correlated with tehe resistive index. In females, cfPWV was positively correlated with age, blood pressure, heart rate, alanine aminotransferase, urea, creatine, uric acid, fasting blood glucose, triglycerides, total cholesterol, and heart rate. The results of multivariable analysis indicated that age, systolic blood pressure, heart rate, and alcohol consumption were influencing factors for cfPWV in males, while age, systolic blood pressure, heart rate, and creatinine were influencing factors for cfPWV in females (*P* <0.05 for all).

Conclusions: In healthy individuals, the distribution patterns of cfPWV values vary by sex and age. In the elderly population, especially elderly women, enhanced monitoring and regular follow‐ups are recommended to prevent the development and progression of CVDs in high‐risk individuals at an early stage.

Key words: cardiovascular disease, carotid‐femoral pulse wave velocity, health checkup, risk factor

INTRODUCTION

Cardiovascular diseases (CVDs) represent a major cause of mortality and a grave threat to human health. Every year, approximately 18.6 million of the global population die from CVDs, accounting for 32% of global deaths, making it the leading cause of death worldwide [1, 2]. In China, with the acceleration of population aging and urbanization, the incidence and prevalence of CVDs continue to rise [2, 3]. Currently, CVDs have affected as many as 290 million people in the country,

WHAT'S NEW?

This study investigated carotid-femoral pulse wave velocity (cfPWV) characteristics in the local healthy population and the relationship between cfPWV and cardiovascular disease risk factors through a large-sample arteriosclerosis screening at our hospital's healthcare center. We aimed to provide a basis for the early intervention and monitoring of atherosclerosis. The results of this study show that the distribution patterns of cfPWV values in healthy individuals vary with sex and age, and cfPWV values are associated with blood pressure and lipid levels. In clinical practice, it is important to enhance monitoring and regular follow-up for the elderly population, especially elderly women, which can help prevent the development and progression of cardiovascular disease in high-risk individuals at an early stage.

posing a significant public health challenge that urgently demands prevention and control [2, 3]. The known risk factors for CVDs primarily include hypertension, diabetes, and overweight/obesity [4]. As our understanding of CVDs deepens, early detection, prevention, and intervention have become a research hotspot. Existing literature indicates that structural and functional damage to the main arteries is a key risk factor for early vascular lesions and the development of CVDs [5]. Therefore, CVD prophylaxis should focus on the prevention and control of vascular lesions. In clinical practice, conventional techniques that enable the visualization of morphological changes, such as vascular ultrasound, arteriography, and magnetic resonance angiography, are frequently utilized to assess vascular lesions. Despite their respective advantages and irreplaceable roles in clinical practice, these techniques only visualize changes in vessels with evident organic lesions, which are irreversible. In this context, the existing methods exhibit limited utility in preventing CVDs. Pulse wave velocity (PWV), one of the important parameters used to study the real spreading of pulse waves in the human artery system [6], holds significant clinical value in researching and diagnosing arterial system diseases.

Based on which arterial segment is assessed, PWV can be classified as carotid‐femoral pulse wave velocity (cfPWV) and brachial‐ankle pulse wave velocity (baPWV). Specifically, cfPWV reflects the elasticity of aortic segments and is considered a gold standard for assessing arterial stiffness [7, 8]. In 2010, European scholars established reference/normal values for cfPWV based on data from 16 867 subjects, greatly facilitating the clinical application of cfPWV [9]. Over the past decade, baPWV has rapidly gained popularity due to its simple and convenient examination procedure, requiring no exposure of private body parts and offering advantages such as low risk, low costs, and repeatability [10]. In Asia, baPWV has been extensively employed to assess vascular health and screen for vascular lesions. In the United States and Europe, this parameter is gaining wider application in cohort studies [11]. Evidence has shown that baPWV is closely associated with cfPWV [12] and serves as an independent predictor for such clinical events as hypertension, coronary heart disease, stroke, and mortality [13]. Meta‐analyses have shown that for every standard deviation increase in baPWV, the risk of new‐onset CVDs increases by 19%, and the risk of all‐cause

mortality increases by 13% [14]. The Chinese guidelines for application on assessment system of vascular health recommend diagnosing arteriosclerosis with baPWV ≥1400 cm/s [15] — this criterion has already been used in high-quality clinical studies [16].

Despite the widespread use of cfPWV and baPWV in clinical practice and research, there remain gaps in understanding the distinct characteristics of these measures in healthy individuals, particularly in relation to sex and age. Previous studies have often focused on populations with existing health conditions or have not adequately addressed the variations in arterial stiffness parameters among different demographic groups [8, 9]. Additionally, the correlations between cfPWV and a comprehensive set of cardiovascular risk factors in a healthy population is not well-established. This study aimed to fill these gaps by investigating the characteristics of cfPWV and its correlations with cardiovascular disease risk factors in a local healthy population through a large-scale arteriosclerosis screening at our hospital's healthcare center. What makes our approach innovative is the provision of detailed analysis of cfPWV variations across both sexes and different age groups. In this way, our research offers new insights into early vascular health assessment and the potential for personalized prevention strategies. By identifying key influencing factors for cfPWV in healthy individuals, our study contributes to the development of more effective early intervention and monitoring protocols for atherosclerosis, ultimately aiding in the prevention and control of cardiovascular diseases.

MATERIAL AND METHODS

Study population

A total of 501 healthy individuals undergoing physical checkups at our healthcare center from August 2020 to January 2021 were recruited using convenience sampling (Figure 1). Convenience sampling means that participants were selected based on their availability and willingness to participate during their routine health checkups. Inclusion criteria were as follows: (1) \geq 18 years old; (2) undergoing cfPWV measurement; (3) good communication skills. Exclusion criteria included the presence of chronic diseases (including but not limited to hypertension, diabetes, cor-

Figure 1. Flow chart of patient selection Abbreviations: cfPWV, carotid‐femoral pulse wave velocity

onary heart disease, cerebral infarction, kidney and liver diseases, and malignant tumors) as determined by inquiry into medical histories. The study was approved by the local Institutional Review Board, and all participants provided informed consent.

Research methods

Measurements were conducted using a VINNO ultrasound system (compatible with the X4‐12L linear array transducer). The cfPWV measurement process was as follows. (1) After a 10‐minute rest, the subject assumed a supine position and was connected to electrocardiogram (ECG) leads. (2) After confirming the correct connection, the ECG system was set to the arterial spectrum mode. The subject turned his/her head 45° to the left, and the linear array transducer was placed at the point of maximum pulsation of the right carotid artery. The transducer was finely adjusted until the image was clear and stable, and then the blood vessel pulse wave (PW) was measured 1–2 cm before the bifurcation of the carotid artery. Fifteen cardiac cycles were collected, and dynamic spectrum images were stored. A mark was made on the skin to indicate the center of the transducer, i.e., the PW sampling point. (3) The right femoral artery was measured in the same manner as mentioned above, and a mark was made on the skin to indicate the central position of the transducer for sampling. (4) The distance between the two marked points was measured using a caliper (measurements were taken parallel to the skin to avoid errors due to differences in body shape). Measurements were taken three times and input into a program to average the results. (5) The stored carotid and femoral artery spectrum videos were sequentially retrieved for automatic measurement to obtain cfPWV values (Figure 2). All the above procedures were performed by one trained physician.

Individuals who smoked ≥1 cigarette/day for more than 1 year were considered to have a history of smoking; those who consumed ≥2 liang (approximately 50 grams) of alcohol/day for more than 5 years were considered to have a history of alcohol consumption (AC). Diabetes was diagnosed according to the criteria outlined in the Chinese Guidelines for Type‐2 Diabetes (2010 Edition) [17]. Hypertension was diagnosed using the criteria outlined in the 2010 Chinese Guidelines for the Management of Hypertension [18]. ECG was performed to determine the presence of myocardial ischemia. Fasting venous blood samples were collected and analyzed for biochemical parameters using the ABBOTT ARCHITECT C16000 Fully Automated Biochemical Analyzer and its corresponding reagents.

Data collection

Collection data included sex, age, body mass index, occupation, systolic blood pressure (SBP), diastolic blood pressure (DBP), cfPWV, smoking history, AC history, biochemical parameters, heart rate (HR), pulsatility index, and resistive index (RI).

Biochemical parameters included total protein, albumin, globulin, alanine aminotransferase, aspartate aminotransferase (AST), gamma‐glutamyl transferase, urea, creatinine (Cre), uric acid (UA), fasting blood glucose (FBG), triglycerides (TGs), total cholesterol (TC), high‐density lipoprotein (HDL), and low‐density lipoprotein.

Ethics

This study was approved by the ethics committee of the Affiliated Hospital of Yangzhou University, and all patients who participated in the study gave informed consent and volunteered to participate.

Figure 2. Automated carotid-femoral pulse wave velocity measurement

Statistical analysis

Statistical analysis was performed using statistical software SPSS 26.0. The normality of data was assessed using the Kolmogorov–Smirnov test. Normally distributed measurement data were expressed as means (standard deviations), and independent sample t‐tests were used for intergroup comparisons. Non‐normally distributed data were represented by medians (interquartile ranges), and the Mann–Whitney U test was used for intergroup comparisons. Enumeration data were denoted as frequencies (n) or percentages (%), and the χ^2 test was used for conditions that met the assumptions, while Fisher's exact probability test was used for conditions that did not meet the assumptions. Pearson correlation coefficient (r) was used for correlation analysis, and multiple regression analysis was conducted for multivariable analysis. A bilateral *P*-value of less than 0.05 was considered statistically significant.

To examine the relationships between cfPWV and various cardiovascular risk factors, a univariate correlation analysis was performed separately for males and females. The statistical significance of these correlations was assessed with a significance level set at *P* <0.05.

To further investigate the influencing factors for cfPWV, a stepwise multivariable regression analysis was conducted. The dependent variable was cfPWV, and the independent variables included those with statistically significant correlations identified in the univariate analysis. The stepwise regression method was used to include and exclude independent variables with α entry set at 0.05 and α removal set at 0.1.

The variables were entered into the model as follows: for categorical variables such as AC, the assigned values were yes $= 1$ and no $= 0$, while continuous variables were included as they were. The final regression models were evaluated for goodness of fit using the $R²$ statistic, and the significance of the model was determined using the F-statistic and its associated *P*-value. Multicollinearity among the independent variables was assessed using variance inflation factors (VIFs), with values below 10 indicating no significant multicollinearity.

RESULTS

Comparison of relevant parameters between different sexes

The results showed significant differences between male and female subjects in cfPWV, body mass index, SBP, DBP, albumin, globulin, alanine aminotransferase, AST, gamma-glutamyl transferase, urea, Cre, UA, TGs, HDL, pulsatility index, RI, smoking prevalence, and AC prevalence. In contrast, no statistical significance was found in other aspects (Table 1).

Comparison of cfPWV between different sexes and age groups

The results showed a statistically significant difference in cfPWV between male and female subjects in the age group of 38–47 years old. In other age groups, there was no statistically significant difference in cfPWV between sexes (Table 2).

Table 1. Comparison of relevant parameters between different sexes

Values are expressed as mean (standard deviation) or counts (percentages) or median (interquartile range)

Abbreviations: AC, alcohol consumption; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; cfPWV, carotid‐femoral pulse wave velocity; Cre, creatinine; DBP, diastolic blood pressure; FBG, fasting blood glucose; GGT, gamma‐glutamyl transferase; Glb, globulin; HDL, high‐density lipoprotein; HR, heart rate; LDL, low‐density lipoprotein; PI, pulsatility index; RI, resistive index; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; TP, total protein; UA, uric acid

Table 2. Comparison of cfPWV between different genders and age groups

Values are expressed as mean (standard deviation)

Correlations of cfPWV with various parameters in different sexes

The results demonstrated that in males, cfPWV was positively correlated with age, SBP, DBP, and HR while it was negatively correlated with RI. In females, cfPWV was positively correlated with age, SBP, DBP, AST, urea, Cre, UA, FBG, TGs, TC, and HR (Table 3).

Multivariable analysis of influencing factors for cfPWV

The results showed that in males, no variables were excluded during the inclusion/exclusion process, yielding a regression model with an R^2 of 0.443, indicating that all included variables can explain 44.3% of the variance in cfPWV values. The F-statistic was 22.304 with a significance level of *P* <0.001, indicating that the model is statistically

significant. The Durbin-Watson statistic was 1.995, indicating no autocorrelation among the residuals. Several independent variables, including age, SBP, HR, and alcohol consumption, were statistically significant and were retained in the model. The VIFs for these variables were 1.207, 1.248, 1.036, and 1.042, respectively, indicating no multicollinearity. The standardized regression coefficients indicate the relative impact of each independent variable on cfPWV values: for males, age has the greatest impact, followed by SBP and HR (Table 4).

As to females, no variables were excluded during the inclusion/exclusion process, resulting in a regression model with an $R²$ of 0.627, an F-statistic of 45.761, and a significance level of *P <*0.001. The VIF values for the independent variables were all well below 10, indicating no multicollinearity among them. Based on the standardized regression

Table 3. Correlation of cfPWV with various parameters in different genders

Abbreviations: see Table 1

Table 4. Multivariable linear regression analysis of cfPWV values in different genders

Abbreviations: CI, confidence interval; other — see Table 1

coefficients, the respective impact of each independent variable on cfPWV values can be determined as follows: age > SBP *>* HR > Cre (Table 4).

DISCUSSION

This study demonstrates that in healthy individuals, cfPWV varies significantly with sex and age and is correlated with multiple cardiovascular risk factors. Specifically, cfPWV in males is positively correlated with age, SBP, DBP, and HR and negatively correlated with RI. In females, cfPWV is positively correlated with age, SBP, DBP, AST, urea, creatinine, UA, FBG, TGs, TC, and HR. These findings emphasize the importance of early detection and focused monitoring of arterial stiffness to prevent and delay the onset and progression of cardiovascular and cerebrovascular diseases. Given that cfPWV measurement is a non-invasive and reliable method for assessing arterial stiffness, it holds significant clinical value for routine health examinations and screenings. Enhanced monitoring, particularly for high-risk groups such as elderly individuals and postmenopausal women, can facilitate early intervention strategies aimed at reducing cardiovascular risk.

Age is a determinant factor for PWV, with PWV values showing a significant positive correlation with age [19]. In the early stages of vascular pathology, endothelial dysfunction leads to decreased release of vasodilators and increased release of vasoconstrictors, resulting in vascular remodeling. On the other hand, with aging, degenerative changes occur in the vascular wall's middle layer, namely the tunica media, leading to an increase in tunica media substances and collagen content. This causes the elastic layer to fracture with age, accompanied by fibrosis and calcification of the tunica media [20]. The study by Shen YH et al. [21] on 980 hypertensive individuals versus 212 controls indicated that cfPWV increased with age. Similarly, Meani et al. [22], in a 3.7‐year follow‐up study of 333 hypertensive patients, reached the same conclusion. In this study, both male and female subjects exhibited a clear positive correlation between age and cfPWV, consistent with the aforementioned findings.

Blood pressure is another important determinant of PWV [19], and hypertension often occurs concurrently with tachycardia, making HR one of the influencing factors for PWV. Studies have shown that arterial stiffness increases before the onset of hypertension, and individuals with higher arterial stiffness measurements but normal blood pressure are more likely to develop hypertension [23]. Franklin et al. [24] found that increasing mean arterial pressure leads to an increase in PWV. For instance, at a pressure of 40 mm Hg, PWV is approximately 3.7 m/s, while it increases to 6.0 m/s when the pressure rises to 100 mm Hg. Moreover, as arterial pressure continues to rise, the spreading velocity of the pulse wave increases even faster. Harada et al. [25] observed that PWV is proportional to pulse pressure in hypertensive patients, meaning that when SBP is constant, PWV increases as DBP decreases; when DBP is constant, PWV increases as SBP increases. The results of this study showed positive correlations between SBP, DBP, HR, and cfPWV values, consistent with the aforementioned studies. Cebrowska et al. [26] demonstrated that arterial stiffness can acutely increase in response to an isometric handgrip in healthy individuals, underscoring the dynamic nature of arterial stiffness in response to physical stress. This finding aligns with our observation of cfPWV variations with different physiological and demographic factors, highlighting the importance of considering both chronic and acute influences on arterial health. Stopa et al. [27] compared unattended automatic blood pressure measurements with conventional office readings, highlighting the importance of accurate blood pressure assessment in predicting hypertension-mediated organ damage. This reinforces the significance of our findings regarding the correlations between blood pressure parameters and cfPWV, as accurate blood pressure measurement is crucial for reliable assessment of arterial stiffness and cardiovascular risk.

Atherosclerosis is a systemic pathological change, and dyslipidemia is a significant influencing factor in the formation of atherosclerosis. Studies have shown that children with heterozygous familial hypercholesterolemia have reduced aortic elasticity [28]. A recent study by Riggio et al. [29] has demonstrated that both local and systemic arterial stiffness increase in children with hyperlipidemia who have normal blood pressure and no symptoms. Compared to the control group, children with hyperlipidemia showed higher levels of β‐index, PWV, and augmentation index

of arterial stiffness. Their multivariable regression analysis also indicates that arterial stiffness is independently correlated with cholesterol levels [29]. Likewise, the results of our study demonstrated a positive correlation between related lipid levels and cfPWV values, consistent with the aforementioned findings. However, our study did not find any correlation between HDL, low-density lipoprotein, and cfPWV, which might be explained by the small sample size.

Research indicates that sex is a risk factor for PWV [30]. Our study also confirms this finding although the *P*‐value is close to 0.05. Therefore, future research in the region should focus on comprehensive analyses of similar studies with larger‐scale and more datasets.

Smoking is widely recognized as a significant cardiovascular risk factor, primarily due to its detrimental effects on vascular health. It can impair the bioactivity of nitric oxide in blood vessels through oxidative stress damage and inhibit the expression of endothelial nitric oxide synthase in endothelial cells, thereby adversely affecting endothelial function [31]. Moreover, smoking has been associated with promoting collagen fiber synthesis and smooth muscle cell proliferation, leading to alterations in vascular structure and function [32]. Additionally, several studies have highlighted the interaction between smoking and other cardiovascular risk factors such as alcohol consumption, hyperlipidemia, hypertension, obesity, and diabetes, resulting in increased arterial stiffness and heightened risk of cardiovascular events [5, 33]. However, it is noteworthy that our study did not find a significant association between smoking and cfPWV. One plausible explanation for this observation could be the characteristics of the study population, consisting primarily of individuals undergoing routine health checkups. It is conceivable that individuals who regularly engage in health screenings exhibit heightened awareness and proactive management of their health status, which may include lifestyle modifications such as smoking cessation among those at high risk of cardiovascular diseases. Therefore, within this particular cohort, the impact of smoking on arterial stiffness may not have been as pronounced, reflecting the beneficial effects of health-conscious behavior on mitigating cardiovascular risk factors.

It should be noted that this study has some limitations. First, as the included subjects all came from one hospital, there are restrictions related to the region and personnel. Second, the scope and population of this study are limited. Additionally, the sampling method used in this study, i.e., convenience sampling, limits the representativeness and generalizability of its conclusions. Future studies may expand this research area and use random or stratified sampling to conduct research in different provinces and cities nationwide, thereby increasing the generalizability of results. Lastly, this study is a cross‐sectional survey. Longitudinal studies are recommended to enhance the reliability of study conclusions.

CONCLUSION

In conclusion, our study highlights sex and age variations in cfPWV values among individuals undergoing health checkups, emphasizing the importance of tailored risk assessment. Enhanced monitoring, especially in elderly women, is crucial for early detection and prevention of cardiovascular diseases. Moving forward, integrating cfPWV measurements into routine health screenings may aid in proactive cardiovascular risk management.

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