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The association between arterial stiffness and risk of coronary artery disease in a community-based population

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Abstract: To investigate the association between caPWV and risk of coronary artery disease (CAD). A community-based cross-sectional study was conducted for subjects living in Beijing, China. We collected 213 subjects with coronary artery disease and 1266 subjects without CAD between September 2007 and January 2009 in a community center of Beijing. A multivariate logistic regression analysis was carried out to assess the odds ratios of factors related to CAD. We found CAD subjects were more likely to have a higher BMI, fasting glucose, uric acid, LDL cholesterol, hs-CRP, cfPWV and caPWV ($P<0.05$), and CAD subjects had a significantly lower HDL cholesterol levels ($P<0.05$). The multiple logistic regression analysis showed that hypertension, higher uric acid, hs-CRP, cfPWV and caPWV levels significantly increased the risk of CAD, with ORs (CI) of 1.47, 1.17, 1.35, 1.15 and 1.07, respectively. Higher HDL cholesterol was significantly associated with reduced risk of CAD, with ORs (CI) of 0.58. The cfPWV and caPWV is independently associated with significant CAD, and cfPWV has significant correlation with age and hypertension. CfPWV and caPWV may be used as a practical tool for predicting the risk of CAD.
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1. Introduction

Arterial stiffness is well known as an important risk factor for coronary artery disease (CAD). Increased arterial stiffness is associated with hypertension, end-stage renal disease, and atherosclerosis 1-3. Pulse wave velocity (PWV) is a non-invasive method used for assessing arterial stiffness, and previous studies reported a significant association between PWV and development of atherosclerotic disease 4-6. PWV can be measured at different sites of the arterial tree, such as carotid-femoral pulse wave velocity (cfPWV) and carotid-ankle pulse wave velocity (caPWV) 7. Recent studies have indicated that PWV is both predictive and prognostic factor for CVD 6,8-10

Among the several ways which assessing the PWV of arterial stiffness, carotid-femoral PWV (cfPWV) is a value for measuring stiffness of the thoracic and abdominal aorta. Previous studies have indicated that increased caPWV is correlated with type 2 diabetes, cardiovascular disease, stroke and renal disease11-14. CaPWV is associated with stiffness in both central and periopheral arteries7. Previous studies have indicated that cfPWV could be used for measuring arterial stiffness, and is correlated with risk of CAD15-18. However, few studies investigate the association between caPWV and risk of CAD in Chinese population and its association with other potential risk factors of CAD, such as smoking, hypertension and diabetes. Therefore, we aimed to investigate the association between cfPWV and caPWV levels and risk of CAD, and the interaction between cfPWV and caPWV levels and other potential risk factors of CAD.

2. Material and Methods

2.1 Study population

A community-based cross-sectional study was conducted for subjects living in the Pingguoyuan area of Shijingshan district, a metropolitan area in Beijing, China. All subjects were recruited from population who came for routine health check-up from September 2007 and January 2009, which were described in a previous study19. Subjects with bedridden status, mental illness, malignant tumors and severe systemic diseases were excluded from the analysis. Initially, 1,859 participants were included. Among them, 1479 subjects provided

blood samples for the testing of cardiac biomarkers, with a participation rate of 92.38%.

A face to face interview was conducted to collect information about drinking and smoking status, hypertension and CAD were gained by self-reporting, standardized questionnaires. The diagnosis criteria of CAD were more than 50% stenosis in at least one one major coronary artery, as identified by coronary angiography, coronary artery bypass graft, percutaneous coronary intervention, and/or myocardial infarction. The investigation was conducted by trained physicians from the Department of Geriatric Cardiology of People's Liberation Army General Hospital. Height, weight, and circumferences of the waist and hip were measured to calculate the body mass index (BMI) and waist-to-hip ratio (WHR). The measurement of blood pressure was done using a calibrated desktop sphygmomanometer (Yuyue, Armamentarium Limited Company, Jiangsu, China) after participants had been in the supine position for ≥5 min 17.

Hypertension was defined as a mean of three independent measures of blood pressure ⩾ 140/90 mmHg or current use of antihypertensive drugs. Diabetes was diagnosed when the subject had a fasting glucose ⩾7.8 mmol/L, glucose ⩾11.1 mmol/L at two hours after an oral 75 g glucose challenge, or both, or current use of anti-diabetic agents.

2.2 Measurement of other risk factors of CAD

Concentrations of fasting glucose, uric acid, total cholesterol, triglyceride, high-density lipoprotein (HDL)-cholesterol and low-density lipoprotein (LDL)-cholesterol were determined by the enzymatic assays (Roche Diagnostics GmbH, Mannheim, Germany) on an autoanalyzer (Roche Diagnostics, Indianapolis, IN, USA). Concentrations of high-sensitivity C-reactive protein (hs-CRP) were measured by an immunoturbidimetric assay (Siemens Healthcare Diagnostics, Los Angeles, CA, USA) and a Dimension RxL Max analyzer (Siemens Healthcare Diagnostics).

2.3 Measurement of cfPWV and caPWV

Regional arterial stiffness was assessed by measuring the carotid–femoral and carotid-ankle PWV in the morning, in a quiet environment, at stable temperature. Arterial stiffness was assessed by automatic carotid–femoral measurements using the Complior Colson device (Createch Industrie, France). the technical characteristics of this device have been described previously18.

PWV along the artery was measured by using two strain-gauge transducers fixed transcutaneously over the course of a pair of arteries separated by a known distance; the carotid, femoral, and ankle arteries (all on the right side) were used. Measurements were repeated over 10 different cardiac cycles, and the mean value was used for the final analysis. PWV was calculated from the measurement of the pulse transit time and the distance traveled by the pulse between the two recording sites (measured on the surface of the body in meters), according to the following formula: PWV (m/s) = distance (m)/transit time (s). All measurements were conducted by a single examiner who was blinded to the clinical data.

2.4 Statistical analysis

Statistical analysis was conducted using SPSS® version 11.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Continuous and categorical variables were expressed as mean ± SD and n of subjects (%). Comparisons between cases and controls were made using the student's t and $\chi 2$ tests. A multivariate logistic regression analysis was carried out to assess the odds ratios of factors related to CAD, with results expressed as odds ratios (OR) and corresponding 95% confidence intervals (CI). Pearson correlation was conducted to analyze the relationship between caPWV and other potential risk factors of CAD. A P value <0.05 was considered statistically significant, and all tests were two-sided.

3. Results

The clinical and laboratory characteristics of the subjects are summarized in Table 1. The age of the enrolled CAD subjects ranged from 20 to 95 years (female, 118; male, 95) with a mean age of 68.26± 0.71 years, and the mean age of non-CAD subjects was 59.64 ± 0.40 years (female, 742; male, 524). CAD subjects were more likely to be older and have a higher BMI, fasting glucose, uric acid, LDL cholesterol, Hs-CRP, cfPWV and caPWV (P<0.001), and lower HDL cholesterol levels (P<0.001). Moreover, the proportion of hypertension and diabetes in CAD subjects was significantly higher than non-CAD subjects.

The association between the clinical and demographic factors and risk of CAD was shown in Table 2. The multiple logistic regression analysis showed that hypertension, higher levels of uric acid, hs-CRP, cfPWV and caPWV were significantly increased the risk of CAD, with ORs (CI) of 1.47(1.25-1.74), 1.17(1.01-1.26), 1.35(1.10-1.67), 1.15(1.09-1.19) and 1.07(1.01-1.15), respectively. Reversely, higher HDL cholesterol was significantly associated with reduced risk of CAD, with ORs (CI) of 0.58 (0.40-0.83). However, BMI, waist-hip ratio, smoking status, drinking status, levels of fasting glucose, total cholesterol, and LDL cholesterol were not significantly associated with CAD (P>0.05).

Further analysis was conducted to assess the association of cfPWV with other risk factors of CAD (Table 3). We found that cfPWV had significant

correlation with age, hypertension and LDL cholesterol respectively. Other clinical variables, such as BMI, waist-hip ratio, smoking status, drinking status, fasting glucose, total cholesterol, triglyceride and HDL cholesterol, were not significantly correlation with cfPWV (P>0.05). For caPWV, we did not find significant interaction with the potential risk factors of CAD.

4. Discussions

In this present study, we demonstrated that cfPWV and caPWV was independently and positively associated with risk of CAD, and higher hypertension, uric acid, Hs-CRP and cfPWV were significantly increased the risk of CAD, whereas HDL cholesterol level was negatively associated with risk of CAD. Moreover, we found that cfPWV had significant correlation with age, hypertension, LDL cholesterol. These results indicate that cfPWV and caPWV may play an important role in the development of CAD. Our data are in agreement with previous studies, which also showed that cfPWV was associated with increased arterial stiffness of central artery15,16.

Previous clinical studies reported a significantly positive association between cfPWV level and risk of CAD and other cardiovascular events15,16 19-21 .A study conducted in Chinese population reported that cfPWV was an independent predictor of significant CAD, and there was a positive correlation between PWV and CAD risk 15. Another study conducted in Poland showed that higher cfPWV was a predictive marker for cardiovascular events, and strongly associated with coronary artery stenosis16. A study conducted in American population indicated that caPWV was correlated with CAD risk, and cfPWV had significantly correlation with age, gender, systolic blood pressure, HDL-C and LDL-C22. There are several mechanisms that may explain the association between cfPWV and CAD. Arterial stiffness causes premature return of the reflected pulse wave in later systole, leading to enhance central pulse pressure and load on the left ventricle, and thus reduce ejection fraction and enhance myocardial oxygen demand 23. The reduced absorption capacity of the arterial wall could induce wall injury, and promote the progression of atherosclerosis24 .The results of present study reports that cfPWV has a close association with CAD, which is an index of central arterial stiffness. However, no previous studies reported an association between caPWV and risk of CAD. Only one study reported the association between caPWV and type 2 diabetes8. Zhang et al. reported that patients with type 2 diabetes had no correlation with elevated level of caPWV 11 .In our study, we found an association between caPWV and risk of CAD.

Our study reports an association between cfPWV and age, hypertension and caPWV, which is in concordance with an earlier study showing an significant association between caPWV and blood pressure22, which suggests that blood pressure predicts arterial stiffness measured as cfPWV. Another study showed that blood pressure was associated with cfPWV in young adults 24. Zhu et al. reported that caPWV was significantly associated with age, BMI, TC, TG, HDL-C and LDL-C 25. However, we did not find the correlation between caPWV and potential risk factors of CAD. Therefore, further studies are greatly needed to verify the interaction between caPWV and other risk factors of CAD.

Our study has two strengthens. Firstly, this study is of relatively large scale sample compared to others. Secondly, it is based on general subjects who come for routine health check-up, and these subjects could better represent the general population. These points could enable our results to be clinically applicable. However, two limitations should be considered in our study. First, the present study is a community-based cross-sectional study, and the participants who came for routine health check-up, may pay more attention to their health no matter with or without CAD. Therefore, there was still a certain risk of selection bias since they were not a random sample of the general population. Second, only 213 subjects were diagnosed with CAD, and the number is relatively small comparing with the subjects without CAD. The unmatched sample size may reduce the statistical power.

In conclusion, this study demonstrates that the cfPWV and caPWV is independently associated with CAD, and cfPWV has significant correlation with age and hypertension. Therefore, higher cfPWV and caPWV levels may have a predictive value in assessing risk of CAD.

Table 1. The clinical characteristics of included subjects

Characteristics	CAD N=213	non-CAD N=1266	t or χ^2	P-value
Age (years)	68.26±0.71	59.64±0.40	251.86	<0.001
Gender				
Male	95(44.60)	524(41.39)		
Female	118(55.40)	742(58.61)	1.14	0.29
BMI (kg/m^2)	26.18±0.28	25.44±0.13	61.52	<0.001
Waist-hip ratio	0.86±0.13	0.86±0.09	0	0.50
Smoking status				
No	156(73.24)	922(77.03)		
Yes	57(26.76)	275(22.97)	1.44	0.23
Drinking status				
No	190(89.20)	1031(86.13)		
Yes	23(10.80)	166(13.87)	1.47	0.23
Diabetes				
No	151	1059		
Yes	62	207	19.94	<0.001
Hypertension				
No	84(39.91)	778(65.0)		
Yes	129(60.09)	419(35.01)	49.72	<0.001
Fasting glucose (mmol/L)	5.40±0.13	5.31±0.06	16.16	<0.001
Uric acid (umol/L)	302.08±5.75	285.39±2.43	70.99	<0.001
Total cholesterol (mmol/L)	4.91±0.07	4.98±0.03	24.29	<0.001
HDL cholesterol (mmol/L)	1.35±0.03	1.40±0.01	45.28	<0.001
LDL cholesterol (mmol/L)	3.01±0.05	2.99±0.02	10.05	<0.001
Hs-CRP (mg/dL)	0.50±0.07	0.32±0.02	73.74	<0.001
cfPWV (cm/s)	12.52±0.23	11.25±0.10	133.11	<0.001
caPWV (cm/s)	8.94±0.15	8.91±0.07	4.64	<0.001

BMI: Body Mass Index; HDL cholesterol: high density lipoprotein cholesterol; LDL cholesterol: Low Density Lipoprotein cholesterol; Hs-CRP: high-sensitivity C-reactive protein; caPWV: Carotid Femoral Pulse Wave Velocity.

Table 2. Multiple logistic regression analysis for potential risk factors of CAD

Characteristics	Adjust OR	95% Confident Interval (CI)	P value
Age			
BMI	1.03	0.98-1.07	0.22
Waist-hip ratio	0.99	0.91-1.08	0.84
Smoking status	1.43	0.95-2.14	0.09
Drinking status	0.98	0.60-1.60	0.94
Hypertension	1.47	1.25-1.74	<0.001
Fasting glucose	0.97	0.88-1.07	0.56
Uric acid	1.17	1.01-1.26	0.006
Total cholesterol	0.81	0.50-1.33	0.41
HDL cholesterol	0.58	0.40-0.83	0.003
LDL cholesterol	1.31	0.72-2.39	0.89
Hs-CRP	1.35	1.10-1.67	0.005
CfPWV	1.15	1.09-1.19	<0.001
caPWV	1.07	1.01-1.15	0.007

BMI: Body Mass Index; HDL cholesterol: high density lipoprotein cholesterol; LDL cholesterol: Low Density Lipoprotein cholesterol; Hs-CRP: high-sensitivity C-reactive protein; caPWV: Carotid Femoral Pulse Wave Velocity.

Table 3. Pearson correlation of cfPWV with other risk factors of CAD

Characteristics	cfPWV	
	Pearson's coefficient	*P* value
Age	0.166	<0.001
BMI	0.014	0.60
Waist-hip ratio	-0.016	0.54
Smoking status	0.034	0.20
Drinking status	0.003	0.90
Hypertension	0.074	0.005
Fasting glucose	-0.005	0.86
Uric acid	0.031	0.24
Total cholesterol	0.036	0.17
Triglyceride	0.022	0.41
HDL cholesterol	-0.011	0.67
LDL cholesterol	0.057	0.03
Hs-CRP	0.021	0.47
CaPWV	0.384	<0.000

BMI: Body Mass Index; HDL cholesterol: high density lipoprotein cholesterol; LDL cholesterol: Low Density Lipoprotein cholesterol; Hs-CRP: high-sensitivity C-reactive protein; caPWV: Carotid Femoral Pulse Wave Velocity.

Conflicts of interest

The authors had no conflicts of interest to declare in relation to this article.

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