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Research Paper

Relationship between brachial-ankle pulse wave velocity and metabolic syndrome components in a Chinese population

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Abstract

The purpose of this study was to assess the relationship between arterial stiffness, as measured by brachial-ankle pulse wave velocity (baPWV), and the presence of the metabolic syndrome (MS) in a Chinese population. A total of 4,445 subjects were enrolled. The prevalence of MS in our study population was 21.7%, 17.2% and 25.6% for the general population, males and females, respectively. With adjustments for age, gender, cigarette smoking, heart rate, total cholesterol, low-density lipoprotein (LDL) cholesterol, and the use of anti-hypertensive drug, the stepwise regression analysis showed that baPWV had a significant relationship with components of MS, including systolic blood pressure ($P < 0.001$), diastolic blood pressure ($P < 0.001$), glucose ($P < 0.001$), high-density lipoprotein (HDL) cholesterol ($P = 0.04$), and triglycerides ($P < 0.001$), but no relationship with waist circumference ($P = 0.25$). With an increase in the number of the MS components, baPWV increased significantly both in women and men. This study indicated that the MS is indeed a risk factor for arterial stiffness. Monitoring of baPWV in patients with MS may help in identifying persons at high risk for cardiovascular disease.

Keywords: arterial stiffness, brachial-ankle pulse wave velocity, metabolic syndrome

INTRODUCTION

Metabolic syndrome (MS) represents a clustering of several cardiovascular risk factors including abdominal obesity, impaired glucose intolerance, dyslipidemia, and hypertension[1,2]. MS is associated with a marked increase in the risk of atherosclerotic cardiovascular disease. MS affects 24% of adults in the US and 13.8% of adults in China[3–5]. Arterial stiffness is a marker of arterial damage and its increase has been shown to be associated with an increased risk of cardiovascular events[6–9]. Brachial-ankle pulse wave velocity (baPWV) is an effective index of the arterial stiffness of large arteries and is widely used for noninvasive assessment of vascular function. The present study investigates the relationship between arterial stiffness, as measured by baPWV, and the components of the MS in a Chinese population.

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SUBJECTS AND METHODS

Study population

The method of study population enrollment has been published previously[10,11]. Briefly, stratified random sampling was used to select a representative sample from the towns of Baqiao and Songqiao in Gaoyou, a city 170 km north of Nanjing, China. From the local authorities, we obtained the population data which included 10,008 inhabitants from all the villages of Baqiao and 3,763 inhabitants from 2 Songqiao villages. Five-thousand subjects from Baqiao and 1,000 subjects from Songqiao, aged 18 to 74 years old, were selected and invited to participate in the study. We did not apply any other inclusion and exclusion criteria in our study. Between January and May, 2010, 4536 subjects participated in the study, including 3918 subjects in Baqiao and 618 subjects in Songqiao; the response rates were 78.4% and 61.8%, respectively. We excluded 91 subjects because of incomplete anthropometric measurements (n = 36), a lack of information on their baPWV (n = 45), or missing value of biochemical measurements (n = 10), resulting in a total of 4,445 subjects who were suitable for statistical analysis. This study complied with the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the First Affiliated Hospital with Nanjing Medical University. All subjects gave informed written consent

Field work

The subjects fasted overnight and abstained from caffeine, tea, tobacco and alcohol for at least 1 hour prior to measurement. We used a standardized questionnaire to collect information on the subject's medical history, smoking habits, alcohol intake and use of medications. Blood pressure was measured by trained examiners using a mercury sphygmomanometer according to a standard protocol. After each subject rested for at least 5 minutes in the sitting position, his or her blood pressure was measured three times on the right arm with the arm cuff maintained at the heart level. These three readings were averaged for analysis. Hypertension was diagnosed if the average of the three blood pressure readings was at least 140 mm Hg for systolic blood pressure (SBP) or 90 mm Hg for diastolic blood pressure (DBP), or if the subjects were on antihypertensive medication. Diabetes was diagnosed if the fasting plasma glucose concentration was at least 7.0 mmol/L or, if the subject was on an anti-diabetic medication or insulin treatment. Weight and height were measured with the subjects wearing light indoor clothing without shoes. Body mass index (BMI) was calculated using the subject's weight in kilograms divided by height in meters squared (kg/m^2). The waist-to-hip ratio was calculated using the smallest circumference at the waist divided by the largest circumference at the hip. For detailed information, refer to our previous study[10,11].

Pulse wave velocity measurement

The baPWV was assessed non-invasively using a VP-1000 automated PWV/ABI analyzer (Colin Co. Ltd., Komaki, Japan), which simultaneously measured the pulse volumes in the brachial and ankle arteries using an oscillometric method as well as the bilateral arm and ankle blood pressures. The subjects were examined in a supine position after a period of rest of at least 5 minutes. The cuffs were wrapped on both sides of the brachium and ankle and contained a plethysmographic sensor that determined the waveform data. The mean of the right and left baPWV values was used for the analysis.

Laboratory measurements

Routine biochemical measurements of lipid profiles, including triglycerides, total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol, were performed in the central laboratory of the First Affiliated Hospital with Nanjing Medical University (Nanjing, China) by an automated analyzer (Chemistry Analyzer AU2700, Olympus Medical Engineering Co., Tokyo, Japan).

MS

We defined MS according to the Adult Treatment Panel III criteria[1]. MS was diagnosed if a subject had at least three of the five following characteristics: (1) waist circumference $>$ 102 cm in men and $>$ 88 cm in women; (2) triglycerides $\geqslant$ 1.7 mmol/L; (3) high-density lipoprotein (HDL) cholesterol $<$ 1.04 mmol/L in men and $<$1.3 mmol/L in women; (4) blood pressure $\geqslant$ 130/85 mmHg or the use of antihypertensive drugs; (5) fasting plasma glucose $\geqslant$ 6.1 mmol/L or the presence of diabetes mellitus. Subjects taking medications for any of these components were also considered to have the corresponding risk factor.

Statistical analysis

For database management and statistical analysis, we used the SAS software, version 9.2 (SAS Institute, Cary, NC, USA). Continuous variables are expressed as mean $\pm$ SD. Common logarithmic transformations were performed for distributions that were

Table 1 **Age-stratum-specific population structure in total population and selected study population.**

	Total population (n = 13,771)		Selected study population (n = 4,445)	
Age range (years)	Male (n,%)	Female (n,%)	Male (n,%)	Female (n,%)
18–34	847 (6.2%)	1,194 (8.7%)	133 (3.0%)	239 (5.4%)
35–44	1,453 (10.6%)	2,115 (15.4%)	410 (9.2%)	660 (14.8%)
45–54	1,129 (8.2%)	1,557 (11.3%)	413 (9.3%)	541 (12.2%)
55–64	1,760 (12.8%)	1,761 (12.8%)	691 (15.5%)	631 (14.2%)
65–74	1,050 (7.6%)	905 (6.6%)	427 (9.6%)	300 (6.7%)
All	6,239 (45.3%)	7,532 (54.7%)	2,074 (46.7%)	2,371 (53.3%)

significantly skewed before analysis. Differences among the groups were tested using ANOVA with post-hoc least significant difference (LSD) t-tests. Pearson′s correlation coefficients were used to examine the bivariate associations between variables. Stepwise regression analyses were used to evaluate which factors were independently associated with baPWV in the whole population; P values for covariates to be included in the model were set at 0.15. P values $<$ 0.05 were considered statistically significant and all tests were two-tailed.

RESULTS

In this study, proportionately stratified random sam–pling was used to select a representative sample from the total population. The gender specific population structures in total population and selected study popu–lation are shown in ***Table 1***. Characteristics of the study population are shown in ***Table 2***. The study population included 2074 (46.7%) men and 2371 (53.3%) women. Men and women were comparable BMI, pulse pressure, total cholesterol, LDL cholesterol

Table 2 **Gender specific characteristics of the study population.**

Parameters	Male (n = 2,074)	Female (n = 2,371)	P
Anthropometric measurements			
Age (years)	54.2±12.0	50.3±12.2	<0.001
Weight (kg)	67.5±10.3	59.6±8.5	<0.001
BMI (kg/m^2)	24.5±3.1	24.6±3.2	0.25
Waist circumference (cm)	84.3±9.5	80.8±8.9	<0.001
Waist-to-hip ratio	0.87±0.07	0.84±0.06	<0.001
Peripheral arterial measurements			
SBP (mmHg)	138.7±20.1	134.4±21.3	<0.001
DBP (mmHg)	87.3±10.5	83.6±10.4	<0.001
Pulse pressure (mmHg)	51.4±15.1	50.8±15.3	0.20
Heart rate (beats per minute)	71.1±12.0	74.0±11.2	<0.001
Metabolic variables			
Glucose (mmol/L)	5.8±1.3	5.7±1.2	0.02
Total cholesterol (mmol/L)	4.9±1.0	4.9±1.0	0.64
Triglycerides (mmol/L)	1.6±1.6	1.5±1.2	<0.01
HDL cholesterol (mmol/L)	1.3±0.3	1.4±0.3	<0.001
LDL cholesterol (mmol/L)	3.0±0.7	3.0±0.7	0.47
Logarithm of triglycerides (mmol/L)	0.10±0.27	0.10±0.23	<0.001
baPWV (cm/s)	1531.0±297.3	1442.5±348.2	<0.001
Hypertension, n(%)	1138(54.9)	972(41)	<0.001
Diabetes mellitus, n(%)	136(6.6)	148(6.2)	0.67
Cigarette smoking (%)	1348(65.0)	49(2.1)	<0.001

Data are presented as the mean ± SD or the percentage of patients.

Logarithm of triglycerides indicates the common logarithmic transformation of serum triglycerides level.

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; baPWV: brachial-ankle pulse wave velocity.

Table 3 **Differences in gender specific parameters according to the presence of MS.**

	Male (n = 2,074)		Female (n = 2,371)		All (n = 4,445)	
Parameters	No MS (n = 1,717)	With MS (n = 357)	No MS (n = 1,765)	With MS (n = 606)	No MS (n = 3,482)	With MS (n = 963)
Anthropometric measurements						
Age (years)	54.5±12.2	53.0±11.1*	48.4±12.3	55.5±10.4***	51.4±12.6	54.6±10.7***
Weight (kg)	66.0±9.5	74.5±10.7***	57.9±7.9	64.6±8.4***	61.9±9.6	68.2±10.5***
BMI (kg/m^2)	24.0±2.9	26.8±3.1***	23.8±2.8	26.8±3.1***	23.9±2.9	26.8±3.1***
Waist circumference (cm)	82.7±8.7	92.1±8.9***	78.4±7.7	88.0±8.4***	80.5±8.5	89.5±8.8***
Waist-to-hip ratio	0.86±0.06	0.92±0.07***	0.83±0.06	0.89±0.06***	0.84±0.06	0.90±0.06***
Peripheral arterial measurements						
SBP (mmHg)	137.2±20.2	145.8±18.0***	129.8±19.8	147.5±20.0***	133.5±20.3	146.9±19.3***
DBP (mmHg)	86.2±10.4	92.5±9.5***	81.4±9.8	89.8±9.5***	83.8±10.4	90.8±9.6***
Pulse pressure (mmHg)	51.0±15.1	53.3±15.5***	48.4±14.2	57.7±16.3***	49.7±14.7	56.1±16.2***
Heart rate (beats per minute)	70.3±11.4	74.9±13.8**	73.4±10.9	75.8±12.0***	71.8±11.3	75.5±12.7***
Metabolic variables						
Glucose (mmol/L)	5.6±1.0	6.6±1.9***	5.4±0.7	6.4±1.8***	5.5±0.9	6.4±1.9***
Total cholesterol (mmol/L)	4.9±0.9	5.2±1.1***	4.8±0.9	5.2±1.1***	4.8±0.9	5.2±1.1***
Triglycerides (mmol/L)	1.2±0.9	3.4±2.7***	1.2±0.6	2.4±1.7***	1.2±0.8	2.8±2.2***
HDL cholesterol (mmol/L)	1.3±0.3	1.0±0.2***	1.4±0.3	1.1±0.2***	1.4±0.3	1.1±0.2***
LDL cholesterol (mmol/L)	2.9±0.7	3.2±0.7***	2.9±0.7	3.2±0.8***	2.9±0.7	3.2±0.7***
Logarithm of triglycerides (mmol/L)[#]	0.03±0.22***	0.44±0.25***	0.02±0.18**	0.32±0.22**	0.03±0.20***	0.37±0.24***
baPWV (cm/s)	1,511.9±286.4	1623.0±330.5***	1,372.9±310.8	1,645.2±371.7***	1,441.5±306.9	1,637.0±357.0***

Data are presented as the mean ± SD. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

[#] Logarithm of triglycerides indicates the common logarithmic transformation of serum triglycerides level.

MS: metabolic syndrome; BMI: body mass index; SBP, : systolic blood pressure; DBP: diastolic blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; baPWV: brachial-ankle pulse wave velocity.

and prevalence of diabetes mellitus. Men, compared to woman, had greater age, weight, waist circumference, waist-to-hip ratio, SBP, DBP, baPWV, and glucose, and triglycerides, but had lower heart rate and HDL cholesterol. Men had a higher prevalence of hypertension ($P < 0.001$) and higher rate of cigarette smoking ($P < 0.001$). The age-stratum-specific characteristics of the study population are provided as ***supplemental Table 1*** in the online appendix.

The prevalence of MS in our study population was 21.7%, 17.2% and 25.6% for the general population, males and females, respectively ($P < 0.001$). Differences in gender specific parameters, according to the presence of MS, are shown in ***Table 3***. Compared

Table 4 **Gender specific multiple regression analysis of baPWV**

	baPWV (cm/s)								
	Male			Female			All		
Parameters	B	SE	*P*	B	SE	*P*	B	SE	*P*
SBP (mmHg)	10.67	0.33	<0.001	11.87	0.35	<0.001	11.47	0.24	<0.001
DBP (mmHg)	-3.30	0.65	<0.001	-2.62	0.71	<0.001	-2.76	0.49	<0.001
Waist circumference (cm)	-1.67	0.59	<0.001	1.43	0.61	0.019	0.49	0.42	0.25
Glucose (mmol/L)	22.23	3.92	<0.001	34.57	4.27	<0.001	29.33	2.93	<0.001
HDL cholesterol (mmol/L)	1.37	15.90	0.931	52.71	16.74	0.002	24.18	11.65	0.04
Triglycerides (mmol/L)	8.37	3.34	0.012	22.41	4.67	<0.001	12.25	2.77	<0.001

Adjusted for age, gender, cigarettes smoking, heart rate, BMI, total cholesterol, LDL cholesterol, and the use of anti-hypertensive drugs.

baPWV: brachial-ankle pulse wave velocity; B: partial regression coefficient; SE: standard error; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

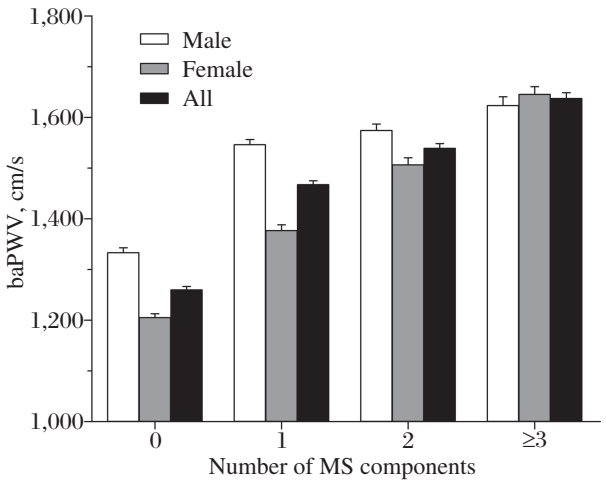

Fig. 1 **BaPWV and the number of the metabolic syndrome components.**

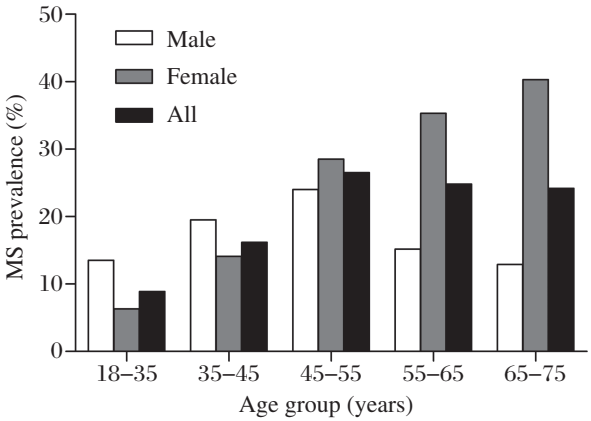

Fig. 2 **The prevalence of metabolic syndrome according to age.**

to patients with no MS, patient with MS had higher age, weight, BMI, waist circumference, waist-to-hip ratio, SBP, DBP, pulse pressure, heart rate, glucose, triglycerides, and baPWV, but lower HDL cholesterol. Additionally, men with MS had lower age, which was opposite to women and general populations. The differences in age-stratum-specific parameters, according to the presence of MS, are also provided as supplemental files. After adjusting for age, gender, cigarette smoking, heart rate, total cholesterol, LDL cholesterol, and the use of anti-hypertensive drug, the regression analysis showed that baPWV had a significant relationship with components of MS, including SBP ($P < 0.001$), DBP ($P < 0.001$), glucose ($P < 0.001$), HDL cholesterol ($P = 0.04$), and triglycerides ($P < 0.001$), but no relationship with waist circumference ($P = 0.25$) (***Table 4***). But, the gender specific multiple regression analysis of baPWV showed that baPWV had significant relationship with all these parameters in men, except for HDL cholesterol ($P = 0.931$).

Table 5 **Effects of specific clusters of MS components on clinical characteristics of study population.**

	Number of MS components				
Parameters	0 (n = 798)	1 (n = 1,623)	2 (n = 1,061)	⩾3 (n = 963)	*P*
Anthropometric measurements					
Age (years)	46.4±13.1	52.4±12.4	53.7±11.4	54.6±10.7	<0.001
Weight (kg)	58.5±8.5	61.6±9.2	64.9±10.2	68.2±10.5	<0.001
BMI (kg/m^2)	22.6±2.5	23.8±2.7	25.1±2.9	26.8±3.1	<0.001
Waist circumference (cm)	76.4±7.3	80.0±8.0	84.3±8.5	89.5±8.8	<0.001
Waist-to-hip ratio	0.82±0.06	0.84±0.06	0.87±0.06	0.90±0.06	<0.001
Peripheral arterial measurements					
SBP (mmHg)	116.7±8.1	136.8±20.1	141.0±19.1	146.9±19.3	<0.001
DBP (mmHg)	75.6±6.0	85.0±10.5	87.9±9.4	90.8±9.6	<0.001
Pulse pressure (mmHg)	41.1±6.7	51.7±15.3	53.0±15.5	56.1±16.2	<0.001
Heart rate (beats per minute)	71.4±11.1	71.2±11.2	73.1±11.4	75.5±12.7	<0.001
Metabolic variables					
Glucose (mmol/L)	5.2±0.4	5.5±0.8	5.8±1.1	6.4±1.9	<0.001
Total cholesterol (mmol/L)	4.7±0.8	4.8±0.9	5.0±1.0	5.2±1.1	<0.001
Triglycerides (mmol/L)	0.9±0.3	1.1±0.6	1.6±1.0	2.8±2.2	<0.001
HDL cholesterol (mmol/L)	1.5±0.3	1.4±0.3	1.3±0.3	1.1±0.2	<0.001
LDL cholesterol (mmol/L)	2.7±0.6	2.9±0.7	3.0±0.7	3.2±0.7	<0.001

All data are expressed as the mean ± SD.

MS: metabolic syndrome; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

With an increase in the number of the MS components, characteristics of the participants-including all the components of the MS increased or decreased significantly (***Table 5*** and ***Fig. 1***). ***Fig. 1*** shows that, in our study population, an increasing number of MS disorders were associated with an increasing baPWV in both males and females. ***Fig. 2*** shows that, with increase in the age, the prevalence of MS changed accordingly. From the total population and the men, the prevalence of MS had the highest level in the middle-aged group (from 45–55 years), but this tendency was not observed in women.

DISCUSSION

In recent years, along with in-depth understanding of cardiovascular disease, people gradually realized that the structure and function of the vascular wall lesions are closely related to the development of cardiovascular disease. Studies have shown that vascular morphological and functional changes occurred before clinical damage. MS is associated with increased risk of cardiovascular disease. As an indicator of vascular function, PWV abnormality can be found in early vascular wall injury and it has been demonstrated that the PWV is an independent prognostic factor in subjects with either hypertension or diabetes mellitus, both of which are MS disorders[12–17]. The proposed underlying mechanisms for this association are as follows: an increase in the PWV, which is related to the severity of atherosclerosis, results in an increased cardiac ventricular load, reduced ejection fraction, increase in the myocardial oxygen demand, impaired coronary blood flow, and a direct aggravation of atherosclerosis via increased stress on the arterial wall[18]. The brachial-ankle PWV reflects arterial stiffness through the central and peripheral arteries. Measuring baPWV is very simple to perform and can be performed even in large study populations. It is also strongly correlated with the aortic PWV. Thus, baPWV can be very reliably used as a convenient marker of arterial stiffness in the central aorta[19,20].

Sipila et al. examined the independent influences of MS, its components, and other cardiovascular risk factors on arterial stiffness as well, to compare 2 definitions for MS (National Cholesterol Education Program [NCEP] and International Diabetes Federation [IDF]) in their ability to identify subjects with arterial stiffness. The NCEP and IDF definitions were similarly associated with PWV and did not differ in their ability to identify subjects with increased arterial stiffness[21]. Satoh et al. analyzed the relationship between MS and the severity of arterial stiffness using baPWV in 3,102 subjects. The results showed that subjects with MS had significantly greater mean values of baPWV than those without MS among both male and female subjects. MS was identified as a significant and independent risk factor for increased arterial stiffness in both the male and female general population in Japan[22]. Xu et al. measured 1,122 subjects from a substudy of the Guangzhou Biobank Cohort Study and found that MS was associated with subclinical atherosclerosis independent of insulin resistance. The presence of an increasing number of MS risk factors appeared to be more important than the diagnosis of MS in predicting subclinical atherosclerosis. Early screening for MS risk factors might identify those at greater cardiovascular risk[23]. Li et al. measured 1,518 community-dwelling subjects at baseline and re-examined them within a mean follow-up period of 3 years. It was found that subjects with MS had significantly greater baPWV at the endpoint than those without MS, after adjusting for age, gender, education, hypertension medication and mean arterial pressure. Arterial stiffness increased as the number of MS components increased[24]. Zhu et al. enrolled a total of 5,476 subjects from annual health checkups and demonstrated that the values of baPWV and its change rates in MS patients were both higher than those in non-MS subjects. MS patients have early alterations of arterial wall elasticity and function[25].

Our study showed that the prevalence of MS was 21.7%, 17.2% and 25.6% for the general population, males and females, respectively in Gaoyou, and baPWV was significantly correlated with the components of MS. Compared to subjects with no MS, subjects with MS had higher baPWV and, with the increase of numbers of MS components, the baPWV was gradually elevated accordingly.

There are several limitations to this study. First, a prospective study to confirm that an increasing baPWV is a marker to predict future cardiovascular events in cases with MS is required; second, this is a single center study, and the study subjects lack control of confounding factors, thereby reducing the statistical power and precluding temporality and causal inference.

In conclusion, baPWV, representing arterial stiffness, is closely associated with the number of components for MS. Monitoring of baPWV in patients with MS may be helpful in identifying persons at high risk for cardiovascular disease.

Acknowledgments

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