



## Original article

# The effects of metabolic syndrome and its components on arterial stiffness in relation to gender



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## ABSTRACT

**Objectives:** The influence of gender-dependent metabolic risk factors on arterial stiffness has not been fully determined. This study was performed to investigate the relationship between components of metabolic syndrome and brachial-ankle pulse wave velocity (baPWV) according to gender.

**Methods:** A total of 537 subjects ( $54.4 \pm 7.5$  years and 70.6% men) who underwent baPWV measurement during routine check-ups were analyzed.

**Results:** BaPWV was  $1363 \pm 229$  cm/s in men and  $1387 \pm 269$  cm/s in women ( $p = 0.313$ ). The prevalence of metabolic syndrome was not different according to gender (23% in men versus 27% in women,  $p = 0.335$ ). In multiple linear regression analyses, after adjustment for age, baPWV was significantly associated with systolic and diastolic blood pressures, fasting glucose, and triglyceride in both genders. Waist circumference was associated with baPWV in women but not in men. High-density lipoprotein levels were not associated with baPWV in either gender. Subjects with metabolic syndrome had a higher baPWV than those without metabolic syndrome for women aged <55 years, but not for all men and women aged  $\geq 55$  years. As the number of the components of metabolic syndrome increased, baPWV increased proportionally in both genders. However, this correlation was more strong in women than that in men ( $\beta = 0.408$  versus  $\beta = 0.146$  after adjustment for age).

**Conclusion:** In middle-aged Koreans, women showed stronger associations between each component of metabolic syndrome and baPWV than men. The association of each component of metabolic syndrome to arterial stiffness may differ between men and women.

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## Introduction

Metabolic syndrome is associated with increased risk of mortality, cardiovascular disease, and diabetes [1–3]. It has been reported that about one-quarter of adults have metabolic syndrome, and that its prevalence is increasing persistently [4]. Therefore, metabolic syndrome is a big public health burden worldwide.

Arterial stiffness reflects vascular aging and atherosclerosis [5]. Increased arterial stiffness has been advocated as an independent risk factor for cardiovascular mortality and morbidity [6–9]. Arterial stiffness can be measured using pulse wave velocity (PWV). Although carotid-femoral PWV (cfPWV) is considered as the gold standard measure of arterial stiffness, difficulty in performing the test limits its clinical use, whereas, brachial-ankle

PWV (baPWV) is performed more easily than cfPWV, so that it has been used as an effective tool for screening vascular damage and cardiovascular risk in various populations [10–14], and its usefulness was demonstrated in a meta-analysis [6].

Metabolic risk factors lead to an increase in arterial stiffness. There have been many studies on the association between metabolic syndrome and arterial stiffness [15,16]. However, the impact of gender on the association between metabolic syndrome and arterial stiffness has not yet been fully assessed. This study was performed to investigate the relationship between each component of metabolic syndrome and baPWV according to gender.

## Methods

## Study subjects

Between October 2009 and July 2013, a total of 537 consecutive subjects underwent baPWV measurement as a part of self-paid health examination at Seoul National University Boramae Medical

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Center (Seoul, Korea) and their data were retrospectively reviewed. There were no exclusion criteria. All study subjects were relatively healthy and medically stable at the time of examination. Information on medical history, including hypertension, diabetes, dyslipidemia, stroke, and coronary artery disease, and smoking habits, were obtained using a standardized questionnaire. All subjects underwent measurement of body weight, height, and waist and hip circumference. Body fat composition was also obtained using a bioimpedance spectroscopy analyzer (InBody 720; Biospace Co., Ltd., Seoul, Korea), and was presented as percentages (%). Body mass index (BMI) was calculated as body weight (kg) divided by the square of body height (m). Blood pressure was measured on the right upper arm using an automatic digital blood pressure monitor. Venous blood was collected from the antecubital vein in the morning after overnight fasting. The blood levels of hemoglobin, fasting glucose, uric acid, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride, serum creatinine, and C-reactive protein were measured. Estimated glomerular filtration rate (eGFR) was calculated using following formula:  $eGFR = 175 \times \text{serum creatinine (mg/dL)} - 1.154 \times \text{age} - 0.203 (\times 0.742, \text{ if woman})$  [17]. Approval for the study protocol was obtained from the Institutional Review Board of Seoul National University Boramae Medical Center (Seoul, Korea).

#### Metabolic syndrome

Metabolic syndrome was defined as a waist circumference level  $\geq 85$  cm in women and  $\geq 90$  cm in men and 2 or more of the following four risk factors: (1) an elevated systolic/diastolic blood pressure of  $\geq 130/85$  mmHg, or previously diagnosed hypertension, (2) an elevated triglyceride level of  $\geq 150$  mg/dL, or specific treatment of this lipid abnormality, (3) a reduced HDL cholesterol level  $< 40$  mg/dL in men and  $< 50$  mg/dL in women, and specific treatment of this lipid abnormality, and (4) an elevated fasting glucose level of  $\geq 100$  mg/dL or previously diagnosed type 2 diabetes mellitus [18].

#### baPWV measurement

The baPWV measurement protocol has been described previously [19]. All study subjects had received no drug treatment on the day of measurement. Patients were examined in the supine position after resting for five or more minutes. BaPWV was measured using a volume-plethysmographic apparatus (VP-1000; Colin Co., Ltd., Komaki, Japan) in accordance with the manufacturer's instructions. Cuffs were wrapped on both arms and ankles. Phonogram, pulse volume waveform, blood pressure, and heart rate were simultaneously recorded. PWV was calculated by measuring the time for the pulse wave to travel between the brachial and posterior tibial arteries (velocity = distance/time). The mean value between left and right baPWV was used for study analysis. All measurements were performed by the same experienced operator blinded to patients' information.

#### Statistical analysis

Continuous variables were presented as mean  $\pm$  standard deviation (SD), and categorical variables were expressed as percentages. Continuous variables were compared using Student's *t*-test, and categorical variables were compared using the Chi-square test between both genders. Pearson's correlation analysis and scatter plots were used to show the association between two continuous parameters. Multiple linear regression analyses were performed to assess associations between baPWV and each component of metabolic syndrome, independent of age. The interactions between

**Table 1**

Baseline characteristics of study subjects.

	Men (n = 379)	Women (n = 158)	<i>p</i>
Age (years)	53.8 $\pm$ 7.5	55.9 $\pm$ 7.5	0.004
Body mass index (kg/m <sup>2</sup> )	24.4 $\pm$ 3.1	24.2 $\pm$ 3.4	0.570
Body fat (%)	23.2 $\pm$ 5.2	33.8 $\pm$ 6.0	<0.001
Waist circumference (cm)	84.4 $\pm$ 7.7	77.5 $\pm$ 9.1	<0.001
Hip circumference (cm)	95.1 $\pm$ 5.6	93.5 $\pm$ 6.5	0.003
Hypertension, n (%)	125 (34.5)	44 (29.1)	0.236
Diabetes, n (%)	39 (10.8)	13 (8.6)	0.459
Dyslipidemia, n (%)	74 (20.4)	39 (25.8)	0.180
Current smoking, n (%)	125 (38.0)	8 (6.5)	<0.001
Previous CAD, n (%)	11 (3.0)	2 (1.3)	0.363
Previous stroke, n (%)	5 (1.4)	3 (2.0)	0.699
SBP (mmHg)	123 $\pm$ 13	118 $\pm$ 16	<0.001
DBP (mmHg)	82.3 $\pm$ 9.7	78.5 $\pm$ 10.0	<0.001
Hemoglobin (g/dL)	15.3 $\pm$ 0.9	13.2 $\pm$ 0.8	<0.001
Fasting plasma glucose (mg/dL)	98.3 $\pm$ 18.5	96.1 $\pm$ 18.3	0.209
Uric acid (mg/dL)	5.76 $\pm$ 1.29	4.44 $\pm$ 1.09	<0.001
Total cholesterol (mg/dL)	191 $\pm$ 32	200 $\pm$ 41	0.012
LDL cholesterol (mg/dL)	119 $\pm$ 31	125 $\pm$ 39	0.141
HDL cholesterol (mg/dL)	48.7 $\pm$ 11.9	54.9 $\pm$ 12.0	<0.001
Triglyceride (mg/dL)	113 $\pm$ 61	103 $\pm$ 54	0.059
Estimated GFR (mL/min/1.73 m <sup>2</sup> )	81.6 $\pm$ 13.1	83.0 $\pm$ 14.9	0.254
C-reactive protein (mg/dL)	0.12 $\pm$ 0.20	0.15 $\pm$ 0.29	0.306
baPWV (cm/s)	1363 $\pm$ 229	1387 $\pm$ 269	0.313

CAD, coronary artery disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; GFR, glomerular filtration rate; baPWV, brachial-ankle pulse wave velocity.

the number of metabolic components and gender in relation to baPWV were assessed using cross-product term in the regression model. A *p*-value of  $< 0.05$  was considered statistically significant. All statistical analyses were conducted using SPSS 18.0 (Chicago, IL, USA).

## Results

### Baseline characteristics

Of the enrolled subjects, 379 (70.6%) were men. Baseline clinical characteristics according to gender are shown in Table 1. Women were older than men (55.9  $\pm$  7.5 years versus 53.8  $\pm$  7.5 years, *p* = 0.004). BMI was similar between both genders. Waist and hip circumferences were greater in men than in women. The percentage of body fat was higher in women than in men. The prevalence of traditional risk factors, including hypertension, diabetes, dyslipidemia, previous coronary artery disease, and stroke, were similar in both genders. The proportion of current smokers was significantly higher in men than in women. Systolic and diastolic blood pressures were higher in men than in women. Laboratory test results showed that men had a higher level of uric acid and a lower level of HDL cholesterol than women. Total cholesterol level was higher in women than in men. BaPWV values were 1363  $\pm$  229 cm/s in men and 1387  $\pm$  269 cm/s in women (*p* = 0.313). The distributions of baPWV of men and women are shown in Fig. 1.

### Association between age and baPWV

Although it is not a component of metabolic syndrome, age has been reported to be one of the most powerful indicators of arterial stiffness [20]. Our results also showed that there were significant positive linear correlations between age and baPWV in both genders (*r* = 0.411 in men and 0.495 in women, *p* < 0.001 for each) (Fig. 2).

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