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Sex and Age Differences in the Impact of Metabolic Syndrome and Its Components including A Body Shape Index on Arterial Stiffness in the General Population

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Aim: We investigated the effects of metabolic syndrome (MetS) and its components, including a body shape index (ABSI), on increased arterial stiffness measured using the cardio-ankle vascular index (CAVI) according to sex and age strata.

Methods: A total of 7127 asymptomatic Korean participants aged 21–90 years (men, 69.4%) were included. Age–sex-specific increased CAVI was defined as having the highest quartile of CAVI in each age group.

Results: The CAVI increased with age and was higher in men. MetS was associated with an increased risk of high CAVI by 1.30 times in men and 1.45 times in women. The risk of high CAVI with an increasing MetS risk score was greater in women. MetS was significantly associated with increased CAVI in men only aged 51–70 years and in women aged ≥ 51 years, and the size of association increased with age (odds ratio (OR) of 1.41 in 51–70 years vs. OR of 2.96 in ≥ 71 years of women). Among MetS components, triglyceride (men, all ages), hypertension (men, 51–70 years; women, ≤ 70 years), glucose intolerance (men, 51–70 years; women, ≥ 51 years), and HDL-cholesterol (women, ≥ 71 years) were associated with increased CAVI.
Unlike increased waist circumference (WC), increased ABSI revealed an association with high CAVI. MetS diagnosed with ABSI instead of WC was more significantly associated with increased CAVI in all age–sex groups.

Conclusion: The association of MetS and its components with increased CAVI differed with age and sex, which might provide a new insight for the management of MetS risk factors to promote vascular health.

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Key words: Metabolic syndrome, Arterial stiffness, Cardio-ankle vascular index, Sex, A body shape index

Introduction

Metabolic syndrome (MetS) is defined as a cluster of risk factors leading to diabetes and cardiovascular disease (CVD), and reports suggest that each component of MetS, including abdominal obesity, dyslipidemia, hypertension, and glucose intolerance, is a significant risk factor for CVD and associated mortality[1, 2]. The worldwide prevalence of MetS is increasing, and this is consistent with the increasing prevalence of obesity, which has also been observed in Asian countries, including Korea[3, 4]. Accordingly, accurate identification of this syndrome and the development of effective interventions have become important public health issues[5].

Arterial stiffness is a subclinical atherosclerotic marker associated with CVD and related mortality[6]. The cardio-ankle vascular index (CAVI) reflects the stiffness of the whole arterial tree from the aorta to the ankle, independent of blood pressure (BP) during the measurement, and it has been recognized as a reliable, noninvasive screening tool for arterial stiffness[7, 8].

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Previous studies have shown a significant association of the CAVI with arteriosclerotic diseases such as carotid and coronary atherosclerosis[9, 10], cerebrovascular disease[11], chronic kidney disease[12], and also cardiovascular risk factors, including hypertension[13], diabetes mellitus[14], and dyslipidemia[15].

Several studies examining the relationship between MetS and arterial stiffness in different ethnic groups have been conducted; however, findings regarding the association of MetS and its components with arterial stiffness have been inconsistent according to age, sex, and measurement methods[16-22]. Additionally, in most studies using the CAVI as a marker of arterial stiffness, a set score of 8 or 9 was chosen as the cutoff for the increased CAVI irrespective of age or sex[19, 21, 23, 24].

CAVI reportedly shows a positive correlation with the visceral fat area measured using computed tomography (CT), the gold standard for body adiposity measurement[25]. On the other hand, the waist circumference (WC) is not necessarily associated with CAVI[17, 19, 26], with the body mass index (BMI) showing a negative correlation in several studies[8, 18, 26, 27]. Whether WC and BMI are appropriate indicators of visceral obesity, which causes MetS, remains unclear[28]. Krakauer *et al.* presented a new index of body adiposity, a body shape index (ABSI), which is calculated using the following equation: ABSI = WC/[$BMI^{2/3} \times height^{1/2}$]. ABSI corresponds to a more central body volume concentration[29]. In several subsequent studies, ABSI was shown to be a good index of body adiposity[30], and it was significantly associated with CAVI and the presence of MetS[31].

This study aimed to examine the distribution of the CAVI according to sex and age strata and investigate the effects of MetS and its components, including ABSI as a new abdominal obesity marker, on age–sex-specific increased CAVI in the Korean general population to identify strategies to promote vascular health.

Methods

Study Population

This study was based on a retrospective review of medical records. We retrieved data from 7179 asymptomatic Korean adults without known valvular heart disease or arrhythmia who underwent CAVI measurement during a routine health check-up program for screening purposes at the Seoul National University Hospital Healthcare System Gangnam Center between 2012 and 2020. The exclusion criteria were as follows: ankle–brachial index (ABI) <0.9 ($n=51$), age >90 years, ($n=1$). Finally, a total of 7127 subjects aged 21–90 years were included in the analysis. Based on subject-recorded questionnaires, data regarding past medical history, comorbidities, current medication, and smoking status were obtained.

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, as revised in 1983, and was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. H-1804-053-936). The requirement for informed consent was waived because of the retrospective design of the study and because of the use of an anonymized database and medical records.

Measurement of Anthropometric and Laboratory Parameters

Body weight, height, and WC were measured on the day of the examination. WC was measured at the midpoint between the lower costal margin and the iliac crest by a suitably trained person using a tape ruler, as recommended by the World Health Organization. BMI was calculated by dividing weight (kg) by the square of height (m^2). ABSI was calculated using the following formula: ABSI = WC/[$BMI^{2/3} \times height^{1/2}$]. A cutoff value of 0.080 was used for the definition of increased ABSI[29, 32].

All subjects fasted for at least 12 h prior to the laboratory tests. All blood tests were performed using standard laboratory methods. The glomerular filtration rate was calculated according to the Modification of Diet in Renal Disease equation as follows: glomerular filtration rate (GFR) (mL/min/1.73 m^2) = $186 \times serum\ creatinine^{-1.154} \times age^{-0.203} \times 0.742$ (if women).

Definition of Comorbidities

Hypertension (HTN) was defined as systolic BP ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, or taking antihypertensive medications; diabetes (DM) was defined as fasting blood sugar (FBS) ≥ 126 mg/dL or HbA1c ≥ 6.5% or as use of any glucose-lowering agents; and dyslipidemia was defined as total cholesterol ≥ 240 mg/dL or triglyceride (TG) ≥ 200 mg/dL, or low-density lipoprotein (LDL)–cholesterol ≥ 160 mg/dL, or high-density lipoprotein (HDL)–cholesterol ≤ 40 mg/dL, or as use of lipid-lowering agents. Chronic kidney disease (CKD) was defined as having GFR $<$ 60 mL/min/1.73 m^2.

Definition of MetS

A diagnosis of MetS was based on the presence of three or more of the following criteria[33]: abdominal obesity (WC of ≥ 90 cm in men or ≥ 85 cm in women[34]), increased BP (BP ≥ 130/85 mmHg determined after

performing two measurements separated by a 10 min resting period or use of BP-lowering treatment), FBS ≥ 100 mg/dL or HbA1c ≥ 6.5% or use of glucose-lowering treatment, TG ≥ 150 mg/dL, and HDL-cholesterol <40 mg/dL (men) or <50 mg/dL (women). The MetS risk score (MSS) is the number of MetS components that a single individual has. When the criterion of increased WC was replaced with increased ABSI as the indicator of abdominal obesity, it was defined as "MetS with ABSI."

Measurement of Arterial Stiffness Using CAVI

A VaSera VS-1000 (Fukuda Denshi Co. Ltd., Tokyo, Japan) was used to measure the CAVI, using the methods described previously[7, 8]. Cuffs were applied to the four extremities in both the upper arms and ankles. A phonocardiogram was placed at the right sternum border in the second intercostal space, and electrocardiogram leads were attached to both wrists. Pulse wave velocity (PWV) was calculated by dividing the vascular length by the time taken for the pulse wave to propagate from the aortic valve to the ankle. The CAVI was determined using the following equation: $CAVI = a[(2\rho/Ps - Pd) \times \ln(Ps/Pd) \times PWV^2] + b$,

where Ps and Pd are the average values of the two readings of the systolic and diastolic BP, respectively; ρ is the blood density; and a and b are constants. The mean values of the right and left CAVI were used for analysis.

Definition of Increased CAVI

We defined age–sex-specific increased CAVI in this study. The age categories were ≤ 40, 41–50, 51–60, 61–70, and ≥ 71 years, as there were fewer subjects included at both extremes of the age ranges. The CAVI distribution in each age–sex stratum was evaluated, and subjects who had a mean CAVI higher than the 4th quartile [quartile 4, Q4] were defined as having increased CAVI; others were defined as having normal CAVI [quartile 1–3, Q1–3].

Statistical Analysis

Numerical variables are expressed as mean ± standard deviation and/or median (interquartile range). Categorical variables are presented as numbers and percentages. Comparisons of baseline characteristics according to the normal (age strata, sex-specific Q1–3) and increased (age strata, sex-specific Q4) CAVI, was conducted using independent *t*-test or Wilcoxon rank-sum test according to the normality of the parameter distribution. Categorical variables were compared using chi-square analysis. A general linear model was applied to evaluate the relationship of all continuous and categorical variables in determining the CAVI in subjects who were not taking any medication; these variables included age, sex, anthropometric parameters, and other known cardiovascular risk factors. To identify the odds ratio (OR) of MetS, MSS, and each MetS component on increased CAVI, we used univariate and multivariate logistic regression analyses after adjusting for related parameters. All statistical analyses were performed using the Statistical Package for the Social Sciences (version 23.0; SPSS Inc., Chicago, IL, USA), and a *p*-value of <0.05 was considered statistically significant.

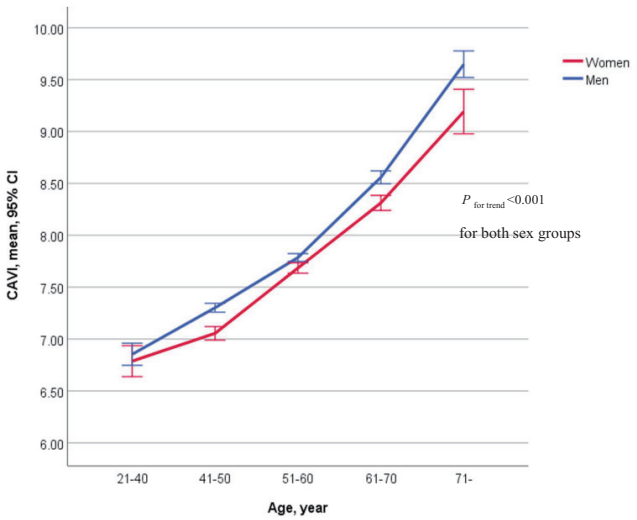

Fig. 1. Distribution of CAVI in men and women

Results

CAVI Distribution in Each Age and Sex Group

Among the 7127 participants (mean age, 56.3 years; men, 69.4%), the mean CAVI was 7.9 ± 1.12 and increased gradually with age in both sexes (*p*-value for trend <0.001 for both sexes) **(Fig. 1)**. The mean CAVI was higher in men compared to women across all ages, and these differences were statistically significant after the age of 40 (all *p*-values <0.05; *p* = 0.488 for ≤ 40-year-old subjects). The cutoff point for increased CAVI (4th quartile value) in each age–sex group was 7.40 vs. 7.20 (≤ 40 years), 7.75 vs. 7.45 (41–50 years), 8.30 vs. 8.20 (51–60 years), 9.20 vs. 8.86 (61–70 years), and 10.35 vs. 9.69 (≥ 71 years), respectively in men and women **(Supplementary Table 1)**. The mean CAVI values were lower in populations who did not take any medications for HTN, DM, or dyslipidemia **(Supplementary Table 2, Supplementary Fig. 1)**.

Baseline Characteristics between Normal CAVI and Increased CAVI Groups

Table 1 presents the detailed clinical characteristics according to CAVI. Compared with the normal CAVI group, subjects with an increased CAVI were significantly older ($p<0.001$) and had similar WC ($p=0.190$) despite lower BMI ($p<0.001$). The ABSI, systolic and diastolic BP, FBS, HbA1c, TG, and hs-CRP levels were significantly higher in the increased CAVI groups (all $p<0.001$), although total cholesterol, LDL- and HDL-cholesterol levels, blood urea nitrogen, creatinine, and GFR did not differ between the groups. HTN, DM, dyslipidemia, and CKD were more prevalent in the increased CAVI group than in the normal CAVI group ($p \leq 0.001$ for all three comorbidities, $p=0.001$ for CKD). In the increased CAVI group, the prevalence of former and current smoking status was higher than that in the normal CAVI group (35.8% vs. 34.2% for former smoking, 18.8% vs. 16.6% for current smoking, $p=0.010$).

MetS was identified in 2286 (32.1%) and the prevalence of MetS and MSS was significantly higher in the increased CAVI group than in the normal CAVI group (37.4% vs. 30.2%, $p<0.001$, 2.1±1.3 vs. 1.8±1.3, $p<0.001$). Increased ABSI, BP, increased FBS, and increased TG were significantly more common in the increased CAVI group than in the normal CAVI group (65.8% vs. 53.8% for increased ABSI, 61.4% vs. 50.2% for increased BP, 59.1% vs. 48.7% for increased FBS, 29.2% vs. 22.5% for increased TG; all $p<0.001$). Increased WC and decreased HDL-cholesterol did not differ significantly between the increased and normal CAVI groups.

Men and women group comparisons revealed that the women in our study were significantly older than the men (57.4±9.4 vs. 55.9±9.2, $p<0.001$) **(Supplementary Table 3)**. However, except for total cholesterol, LDL-cholesterol, and ABSI, all parameters including the CAVI were unfavorable in men. The prevalence of comorbidities and MetS was significantly higher in men (32.1% in all subjects; 37.0% in men vs. 20.8% in women, $p<0.001$). In both men and women, the increased CAVI group was characterized by older age; lower BMI; higher ABSI; higher prevalence of HTN, DM, and dyslipidemia; higher systolic and diastolic BP; higher FBS, HbA1c, TG, and hs-CRP levels; and higher prevalence of MetS and its components (except for increased WC and decreased HDL-cholesterol). LDL-cholesterol was significantly lower in women with increased CAVI than in the normal CAVI group (121.8±32.5 vs. 125.9±32.2, $p=0.010$), but the proportion of women using dyslipidemia medication was much higher than that in the normal CAVI group. In women, GFR was significantly lower in the higher CAVI group than in the normal CAVI group (89.6±16.9 vs. 91.3±15.7, $p=0.038$).

Association between Cardiovascular Risk Factors and the CAVI in Subjects not Using Any Medication

A total of 3061 subjects (42.9%) in the study population were undergoing treatment with at least one of the following three medications for cardiovascular risk factors: 2125 (29.8%) subjects using HTN medication, 775 (10.9%) subjects using DM medication, and 1700 (23.9%) subjects using dyslipidemia medication. Thus, to analyze the linear relationship between the CAVI and cardiovascular and anthropometric parameters, excluding the effects of medication on these parameters, only subjects not taking any medication were analyzed ($n=4066$, 57.1%). The following were associated with increased arterial stiffness in all subjects: age, men, higher WC, increased systolic and diastolic BP, higher TG, FBS, and HbA1c levels, lower BMI, and lower GFR. Current smoking, increased diastolic BP, and higher LDL-cholesterol were associated with increased CAVI only in men. When ABSI was used as an obesity index, replacing WC and BMI, a positive association with CAVI was revealed **(Table 2)**.

Significance of MetS and its Components in Relation to the Increased CAVI

Logistic regression analyses were performed to evaluate the impact of MetS and MSS as ordinal variables and their individual components on increased CAVI after adjusting for clinically relevant factors that were significantly associated with increased CAVI in all subjects and each sex group **(Table 3)**. In the analysis of all subjects, age, sex, CKD, and smoking status in the multivariate model were included. In the multivariate analyses, in men, age, CKD, and smoking status were included, and in women, only age was included. In all subjects and in each sex group, MetS was significantly associated with an increased risk of increased CAVI (OR 1.32, 95% confidence interval (CI) 1.18–1.48 for all subjects, OR 1.30, 95% CI 1.14–1.49 for men, OR 1.45, 95% CI 1.15–1.84 for women). As MSS increased, the risk of higher CAVI was increased in all subjects and in each sex group (p for trend <0.001 for all three groups) and the impact of MSS on increased CAVI was greater in women than in men **(Table 3, Fig. 2(A))**. Among MetS risk factors, increased BP (OR 1.53, 95% CI 1.37–1.71 for all subjects, OR 1.39, 95% CI 1.22–1.60 for men, OR 1.93, 95% CI 1.57–2.37 for women), increased FBS (OR 1.48, 95%

Table 1. Baseline characteristics of the study subjects

Parameters	Total (*n* = 7127)	Normal CAVI [Q123] (*n* = 5296)	Increased CAVI [Q4]* (*n* = 1831)	*p*-value
CAVI	7.90 ± 1.12	7.52 ± 0.83	9.02 ± 1.09	< 0.001
Age, years	56.3 ± 9.3	56.1 ± 9.2	57.1 ± 9.4	< 0.001
Men	4949 (69.4)	3663 (69.2)	1286 (70.2)	0.392
Obesity Indices				
BMI, kg/m²	24.1 ± 3.0	24.2 ± 3.0	23.6 ± 2.8	< 0.001
WC, cm	86.8 ± 8.4	86.9 ± 8.5	86.6 ± 8.2	0.190
ABSI	0.081 ± 0.003	0.080 ± 0.003	0.081 ± 0.004	< 0.001
Systolic BP, mmHg	119.0 ± 13.9	118.0 ± 13.3	122.1 ± 15.1	< 0.001
Diastolic BP, mmHg	78.6 ± 9.7	78.0 ± 9.4	80.3 ± 10.5	< 0.001
Laboratory parameters				
FBS, mg/dL	105.2 ± 22.5	103.4 ± 19.7	110.6 ± 28.5	< 0.001
HbA1c, %	5.8 ± 0.8	5.8 ± 0.7	6.0 ± 0.9	< 0.001
Total cholesterol, mg/dL	192.1 ± 36.8	192.1 ± 36.4	192.1 ± 38.0	0.983
LDL-cholesterol, mg/dL	122.2 ± 32.5	122.6 ± 32.1	121.3 ± 33.7	0.150
HDL-cholesterol, mg/dL	54.8 ± 15.1	54.9 ± 15.4	54.5 ± 14.2	0.343
TG, mg/dL	102 (73-149)	100 (71-145)	112 (79-161)	< 0.001
BUN, mg/dL	14.5 ± 3.9	14.5 ± 3.8	14.6 ± 4.0	0.159
Creatinine, mg/dL	0.86 ± 0.19	0.86 ± 0.18	0.87 ± 0.20	0.054
hs-CRP, mg/dL,	0.06 (0.03-0.12)	0.05 (0.03-0.11)	0.06 (0.03-0.14)	< 0.001
GFR, mL/min/1.73m²	87.2 ± 15.2	87.4 ± 14.9	86.6 ± 16.0	0.071
Comorbidities,				
Hypertension	2805 (39.4)	1930 (36.4)	875 (47.8)	< 0.001
Hypertension medication	2125 (29.8)	1498 (28.3)	627 (34.2)	< 0.001
Diabetes mellitus	1250 (17.5)	770 (14.5)	480 (26.2)	< 0.001
Diabetes mellitus medication	775 (10.9)	469 (8.9)	306 (16.7)	< 0.001
Dyslipidemia	3761 (52.8)	2173 (51.2)	1048 (57.2)	< 0.001
Dyslipidemia medication	1700 (23.9)	1206 (22.8)	494 (27.0)	< 0.001
Chronic kidney disease	181 (2.6)	116 (2.2)	65 (3.5)	0.003
Smoking status				0.010
Never	3440 (48.3)	2609 (49.3)	831 (45.4)	
Former	2465 (34.6)	1809 (34.2)	656 (35.8)	
Current	1222 (17.1)	878 (16.6)	344 (18.8)	
MetS	2286 (32.1)	1602 (30.2)	684 (37.4)	< 0.001
MetS with ABSI	2501 (35.7)	1685 (32.3)	816 (45.5)	< 0.001
MetS components				
Increased WC	2874 (40.3)	2142 (40.4)	732 (40.0)	0.725
Increased BP or on medication	3784 (53.1)	2659 (50.2)	1125 (61.4)	< 0.001
Increased FBS or on medication	3661 (51.4)	2578 (48.7)	1083 (59.1)	< 0.001
Increased TG	1727 (24.2)	1192 (22.5)	535 (29.2)	< 0.001
Decreased HDL-cholesterol	1171 (16.4)	877 (16.6)	294 (16.1)	0.617
Increased ABSI	3991(56.9)	2811 (53.8)	1180(65.8)	< 0.001
MetS risk score	1.9 ± 1.3	1.8 ± 1.3	2.1 ± 1.3	< 0.001
MSS 0	1269 (17.8)	1026 (19.4)	243 (13.3)	
MSS 1	1766 (24.8)	1356 (25.6)	410 (22.4)	
MSS 2	1806 (25.3)	1312 (24.8)	494 (27.0)	
MSS 3	1452 (20.4)	1037 (19.6)	415 (22.7)	
MSS 4	687 (9.6)	468 (8.8)	219 (12.0)	
MSS 5	147 (2.1)	97 (1.8)	50 (2.7)	
MetS risk score with ABSI	2.0 ± 1.2	1.9 ± 1.2	2.3 ± 1.2	< 0.001
MSS 0	792 (11.3)	644 (12.3)	148 (8.3)	
MSS 1	1719 (24.5)	1404 (26.9)	315 (17.6)	
MSS 2	2002 (28.5)	1489 (28.5)	513 (28.6)	
MSS 3	1673 (23.9)	1173 (22.5)	500 (27.9)	
MSS 4	688 (9.8)	425 (8.1)	263 (14.7)	
MSS 5	140 (2.0)	87 (1.7)	53 (3.0)	

Values are mean ± standard deviation, median (interquartile range; IQR) or *n* (%).

*Increased CAVI was defined as CAVI ≥ highest quartile for their age-sex-strata; MetS risk score as the number of MetS components that a single individual has; chronic kidney disease (CKD) as having GFR < 60 mL/min/1.73m², Increased ABSI was defined as having ABSI ≥ 0.080.

CAVI, cardio-ankle vascular index; SD, standard deviation; BMI, body mass index; WC, waist circumference; ABSI, a body shape index; BP blood pressure; FBS, fasting blood sugar; HbA1C, glycated hemoglobin; LDL, low density lipoprotein; HDL, high density lipoprotein; TG, triglyceride; BUN, blood urea nitrogen; hs-CRP, high sensitivity C reactive protein; GFR, glomerular filtration rate; MetS. Metabolic syndrome

Table 2. The association of cardiovascular risk factors with CAVI in subjects without any medication

	All (n = 4066)			Men (n = 2654)			Women (n = 1412)		
	Estimate	Standard Error	p- value	Estimate	Standard Error	p- value	Estimate	Standard Error	p- value
Age, year	0.056	0.002	<0.001	0.059	0.002	<0.001	0.050	0.003	<0.001
Men	0.159	0.039	<0.001						
Smoking									
Former smoker	0.037	0.090	0.686	0.031	0.037	0.409	0.032	0.080	0.694
Current smoker	-0.019	0.107	0.860	0.114	0.044	0.009	-0.025	0.095	0.795
Obesity Indices									
BMI, kg/m^2	-0.136	0.009	<0.001	-0.135	0.012	<0.001	-0.137	0.013	<0.001
WC, cm	0.021	0.003	<0.001	0.023	0.004	<0.001	0.018	0.005	<0.001
ABSI*	27.103	3.975	<0.001	31.775	5.454	<0.001	22.470	5.558	<0.001
Systolic BP, mmHg	0.008	0.001	<0.001	0.006	0.002	<0.001	0.012	0.002	<0.001
Diastolic BP, mmHg	0.004	0.002	0.020	0.007	0.002	0.006	-0.001	0.003	0.787
Laboratory parameters									
Total cholesterol, mg/dL	-0.003	0.002	0.084	-0.005	0.002	0.023	0.000	0.002	0.888
TG, mg/dL	0.001	0.000	<0.001	0.002	0.000	<0.001	0.001	0.001	0.015
HDL-cholesterol, mg/dL	0.002	0.002	0.244	0.004	0.002	0.063	-0.001	0.002	0.628
LDL-cholesterol, mg/dL	0.002	0.002	0.136	0.005	0.002	0.027	-0.001	0.002	0.631
FBS, mg/dL	0.004	0.001	0.002	0.002	0.001	0.093	0.006	0.002	0.002
HbA1c, %	0.088	0.034	0.009	0.118	0.043	0.006	0.062	0.059	0.295
GFR, mL/min/1.73 m^2	-0.003	0.001	0.001	-0.003	0.001	0.016	-0.003	0.001	0.016
hs-CRP, mg/dL	-0.008	0.026	0.768	0.024	0.033	0.473	-0.082	0.044	0.061

Abbreviations as Table 1.
*BMI, WC was excluded when ABSI was included in the model

CI 1.32–1.65 for all subjects, OR 1.45, 95% CI 1.26–1.66 for men, OR 1.58, 95% CI 1.28–1.94 for women), and increased TG had a significant association with increased CAVI (OR 1.46, 95% CI 1.29–1.65 for all subjects, OR 1.47, 95% CI 1.28–1.70 for men, OR 1.41, 95% CI 1.08–1.84 for women). Increased BP was more strongly associated with increased CAVI in women (OR 1.93) than in men (OR 1.39). Although increased WC was not associated with increased risk of high CAVI, the increased ABSI showed a significant association with high CAVI in both sex groups. Additionally, the sizes of ORs of MetS with ABSI were larger than those of MetS with high CAVI in both men and women **(Table 3)**.

Significance of MetS and its Components in Relation to CAVI according to Age in both Sex Groups

To further determine the differences in the association of MetS and its components with increased CAVI according to age, we divided the subjects into three age groups: ≤ 50 years (Group I), 51–70 years (Group II), and ≥ 71 years (Group III)[35]. When the subjects were divided into three age groups, there was no difference in the prevalence of MetS in men, but the prevalence increased significantly with age in women. When ABSI of ≥ 0.080 was used instead of WC as the abdominal obesity criterion[31], the prevalence of MetS (MetS with ABSI) also increased significantly with age in men **(Supplementary Table 4)**. The mean CAVI values were higher in all populations with MetS than in those without MetS; when divided by sex, values were higher in 51–70-year-old men and ≥ 51-year-old women **(Supplementary Table 5)**.

There were differences in the size of the OR and significant risk components according to age and sex. MetS was significantly associated with increased CAVI in both men and women aged 51–70 years (OR 1.50, 95% CI 1.27–1.77 for men, OR 1.41, 95% CI 1.07–1.86 for women) **(Table 4, Fig. 2(B))**. The MetS components that showed significant association were increased BP, FBS, and TG in men and increased BP, FBS in women in the 51–70-year-old group. In men, there was no significant association between MetS and increased CAVI in other age groups; however, increased TG was associated with increased CAVI in all age subgroups (OR 1.29, 95% CI 1.01–1.65 for

Table 3. Association of metabolic syndrome and metabolic syndrome components with increased arterial stiffness

	All		Men		Women	
	Adjusted OR[a] (95% CI)	*p*-value	Adjusted OR[b] (95% CI)	*p*-value	Adjusted OR[c] (95% CI)	*p*-value
MetS	1.32 (1.18-1.48)	<0.001	1.30 (1.14-1.49)	<0.001	1.45 (1.15-1.84)	0.002
MetS with ABSI	1.69 (1.51-1.90)	<0.001	1.68 (1.47-1.92)	<0.001	1.78 (1.43-2.23)	<0.001
MetS risk score		<0.001†		<0.001†		<0.001†
0	1 (Reference)		1 (Reference)		1 (Reference)	
1	1.27 (1.06-1.52)	0.011	1.10 (0.86-1.39)	0.461	1.49 (1.13-1.97)	0.005
2	1.54 (1.29-1.85)	<0.001	1.35 (1.07-1.70)	0.011	1.88 (1.39-2.53)	<0.001
3	1.61 (1.33-1.94)	<0.001	1.42 (1.12-1.80)	0.003	2.05 (1.46-2.86)	<0.001
4	1.93 (1.55-2.41)	<0.001	1.80 (1.38-2.34)	<0.001	1.97 (1.28-3.05)	0.002
5	2.05 (1.41-2.99)	<0.001	1.62 (1.04-2.50)	0.031	3.93 (1.76-8.78)	0.001
MetS risk score with ABSI		<0.001†		<0.001†		<0.001†
0	1 (Reference)		1 (Reference)		1 (Reference)	
1	0.96 (0.77-1.19)	0.709	0.86 (0.64-1.14)	0.280	1.18 (0.83-1.66)	0.346
2	1.45 (1.17-1.79)	0.001	1.31 (1.00-1.71)	0.049	1.80 (1.27-2.55)	0.001
3	1.76 (1.42-2.18)	<0.001	1.59 (1.22-2.08)	0.001	2.30 (1.58-3.35)	<0.001
4	2.60 (2.04-3.31)	<0.001	2.51 (1.87-3.38)	<0.001	2.63 (1.67-4.13)	<0.001
5	2.44 (1.64-3.61)	<0.001	1.88 (1.18-3.01)	0.008	4.99 (2.33-10.69)	<0.001
MetS component						
Increased WC	0.94 (0.84-1.05)	0.235	0.93 (0.82-1.06)	0.297	0.98 (0.79-1.22)	0.856
Increased BP	1.53 (1.37-1.71)	<0.001	1.39 (1.22-1.60)	<0.001	1.93 (1.57-2.37)	<0.001
Increased FBS	1.48 (1.32-1.65)	<0.001	1.45 (1.26-1.66)	<0.001	1.58 (1.28-1.94)	<0.001
Increased TG	1.46 (1.29-1.65)	<0.001	1.47 (1.28-1.70)	<0.001	1.41 (1.08-1.84)	0.012
Decreased HDL-cholesterol	0.97 (0.84-1.12)	0.656	0.91 (0.76-1.10)	0.316	1.08 (0.85-1.37)	0.540
Increased ABSI	1.61 (1.43-1.81)	<0.001	1.72 (1.49-1.97)	<0.001	1.38 (1.11-1.71)	0.004

Increased arterial stiffness was defined as CAVI of age-sex-strata specific highest quartile, and MetS risk score as the number of MetS components that a single individual has; Increased ABSI was defined as having ABSI ≥ 0.080

[a]ORs have been adjusted for age, gender, CKD (GFR <60 mL/min/1.73m^2) status, smoking status never/former/current,

[b]ORs have been adjusted for age, CKD status, smoking status never/former/current,

[c]ORs have been adjusted for age

[a, b, c]All variables with $P<0.05$ in univariate analysis and clinically relevant variables were included in a multivariate logistic regression model.

†*p* value for the test of trends of odds

OR, odds ratio; CI, confidence interval; other abbreviations as Table 1.

group I, OR 1.54, 95% CI 1.29–1.84 for Group II, and OR 2.15, 95% CI 1.13–4.07 for Group III). In women, MetS was significantly associated with increased CAVI after the age of 50 years, and the size of association was observed to increase with age (OR of 1.41 in Group II vs. OR of 2.96 in Group III). As for the MetS components, increased BP in ≤ 70 years (OR 1.95, 95% CI 1.23–3.09 for group I, OR 1.96, 95% CI 1.54–2.50 for Group II), increased FBS after the age of 50 years (OR 1.54, 95% CI 1.21–1.96 for Group II, OR 3.51, 95% CI 1.59–7.74 for Group III), and decreased HDL-cholesterol in ≥ 71 years (OR 2.28, 95% CI 1.01–5.12) were associated with increased CAVI. The association between increased TG and increased CAVI in all women lost statistical significance when the analysis was conducted according to the three age groups, although we could still observe a marginal association. Increased ABSI was significantly associated with increased CAVI in men ≤ 70 years of age and women 51–70 years of age. Furthermore, MetS with ABSI was significantly associated with high CAVI in men ≤ 70 years of age and in women ≥ 50 years of age (Table 4).

Discussion

In this study, the highest quartile of the CAVI by age (each decade) and sex was defined as increased arterial stiffness, and the effect of MetS on increased arterial stiffness was investigated using large-scale data from an apparently healthy general population. The main findings were as follows:

1) The CAVI increased gradually with age, and the mean value was greater in men than in women.

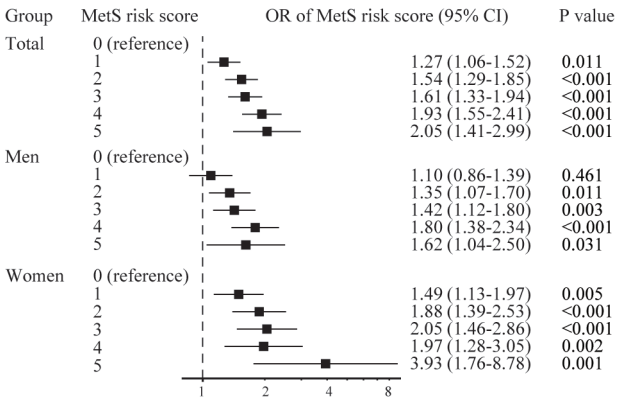

Fig. 2(A). Association of MetS risk score with increased arterial stiffness in all subjects and each sex group

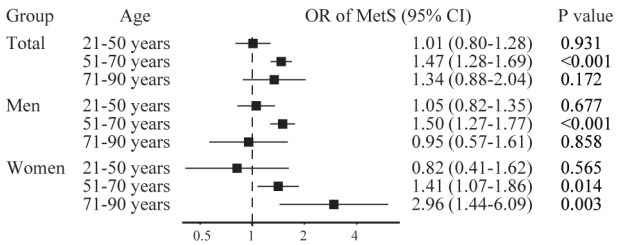

Fig. 2(B). Association of MetS with increased arterial stiffness according to age and sex groups

Our study also provides a reference value for the CAVI on the basis of a large number of subjects drawn from the general Korean population.

2) The impact of MetS and the associated risk components differed according to age and sex. In men aged 51–70 years and women aged ≥ 51 years, MetS was associated with an increased risk of high CAVI, and women were more affected by MetS.

3) The ABSI is a more suitable indicator than WC to show the association between visceral fat and CAVI.

Our research team previously reported an age-associated linear increase of the CAVI in healthy normotensive people not using medication for HTN, DM, and dyslipidemia to evaluate the effect of aging on CAVI; the difference between the two sexes lost significance at both extremities of the age groups (< 30 years and ≥ 60 years)[8]. In this study involving a larger real-world general population, the mean CAVI values were significantly higher in men than in women of all ages over 40 years, which is consistent with previous reports[18, 21, 36].

MetS was significantly associated with an increased risk of high CAVI in both sexes, and the association was stronger in women (by 1.30 times in men vs. by 1.45 times in women). Notably, in women, MetS consistently increased the risk of increased arterial stiffness after the age of 50 years, and the risk was greater with increasing age (by approximately 1.4 times in women aged 51–70 years and by approximately 3 times in women aged ≥ 71 years). In a previous Korean study, MetS was significantly associated with the CAVI only in women[21]. Previous reports that arterial stiffness measured by PWV was more significantly associated with MetS in women than in men are also consistent with the findings of this study[16, 22]. The reason why arterial stiffness is affected more by MetS in women remains unclear. It is postulated that estrogen, which has a favorable effect on the elasticity of blood vessels premenopausally[37], rapidly decreases during the transition to the postmenopausal period and that arterial stiffness accelerates to a level that could pose a greater risk than in men. Additionally, as MetS, which is significantly related to arterial stiffness, increases rapidly after menopause[38], arterial stiffness also increases significantly thereafter.

Among MetS risk factors, increased BP, FBS, and TG were significantly associated with a high CAVI and this finding is consistent with a reported Korean study[39]. The associations of increased CAVI with increased BP and increased FBS but not TG were more pronounced in women (OR 1.39 vs. 1.93 for increased BP and OR 1.45 vs. 1.58 for increased FBS). This corroborates previously reported large cohort studies that found a higher risk of acute

Table 4. Association of metabolic syndrome and metabolic syndrome components with increased arterial stiffness in three age groups

	All		Men		Women	
	Adjusted OR[a] (95% CI)	*p*-value	Adjusted OR[b] (95% CI)	*p*-value	Adjusted OR[c] (95% CI)	*p*-value
Group I (≤50 years)						
MetS	1.01 (0.80-1.28)	0.931	1.05 (0.82-1.35)	0.677	0.82 (0.41-1.62)	0.565
MetS with ABSI	1.42 (1.13-1.79)	0.003	1.45 (1.13-1.86)	0.003	1.38 (0.75-2.52)	0.302
MetS component						
Increased WC	0.84 (0.67-1.05)	0.125	0.90 (0.71-1.15)	0.402	0.59 (0.32-1.10)	0.099
Increased BP	1.22 (0.98-1.51)	0.074	1.07 (0.84-1.37)	0.566	1.95 (1.23-3.09)	0.005
Increased FBS	1.16 (0.93-1.45)	0.182	1.19 (0.93-1.52)	0.164	1.09 (0.65-1.84)	0.734
Increased TG	1.31 (1.04-1.65)	0.022	1.29 (1.01-1.65)	0.046	1.69 (0.90-3.15)	0.102
Decreased HDL-cholesterol	0.92 (0.69-1.22)	0.550	0.94 (0.68-1.30)	0.708	0.88 (0.51-1.53)	0.658
Increased ABSI	1.69 (1.37-2.08)	<0.001	2.05 (1.60-2.61)	<0.001	0.95 (0.62-1.45)	0.795
Group II (51-70 years)						
MetS	1.47 (1.28-1.69)	<0.001	1.50 (1.27-1.77)	<0.001	1.41 (1.07-1.86)	0.014
MetS with ABSI	1.81 (1.57-2.08)	<0.001	1.89 (1.60-2.22)	<0.001	1.63 (1.25-2.11)	<0.001
MetS component						
Increased WC	1.00 (0.88-1.15)	0.954	1.00 (0.85-1.17)	0.970	1.03 (0.80-1.33)	0.804
Increased BP	1.77 (1.54-2.04)	<0.001	1.68 (1.42-2.00)	<0.001	1.96 (1.54-2.50)	<0.001
Increased FBS	1.63 (1.41-1.87)	<0.001	1.64 (1.38-1.96)	<0.001	1.54 (1.21-1.96)	<0.001
Increased TG	1.51 (1.29-1.76)	<0.001	1.54 (1.29-1.84)	<0.001	1.34 (0.97-1.84)	0.074
Decreased HDL-cholesterol	0.94 (0.78-1.13)	0.506	0.87 (0.68-1.10)	0.245	1.05 (0.79-1.40)	0.744
Increased ABSI	1.62 (1.40-1.87)	<0.001	1.63 (1.37-1.94)	<0.001	1.59 (1.22-2.08)	0.001
Group III (≥71 years)						
MetS	1.34 (0.88-2.04)	0.172	0.95 (0.57-1.61)	0.858	2.96 (1.44-6.09)	0.003
MetS with ABSI	2.00 (1.29-3.12)	0.002	1.42 (0.83-2.42)	0.200	4.15 (1.88-9.14)	<0.001
MetS component						
Increased WC	0.67 (0.44-1.02)	0.062	0.53 (0.31-0.89)	0.016	1.36 (0.66-2.79)	0.400
Increased BP	1.12 (0.68-1.83)	0.659	0.89 (0.49-1.61)	0.695	1.70 (0.72-4.05)	0.229
Increased FBS	1.78 (1.12-2.85)	0.016	1.36 (0.76-2.44)	0.295	3.51 (1.59-7.74)	0.002
Increased TG	2.05 (1.22-3.45)	0.007	2.15 (1.13-4.07)	0.019	1.76 (0.73-4.28)	0.210
Decreased HDL-cholesterol	1.75 (1.04-2.94)	0.034	1.43 (0.72-2.84)	0.302	2.28 (1.01-5.12)	0.047
Increased ABSI	1.24 (0.64-2.43)	0.523	1.27 (0.56-2.88)	0.562	1.21 (0.38-3.92)	0.746

Increased arterial stiffness was defined as CAVI of age-gender-strata specific highest quartile. Increased ABSI was defined as having ABSI ≥ 0.080
[a]ORs have been adjusted for age, gender, CKD (GFR <60 mL/min/1.73m^2) status, smoking status never/former/current, [b]ORs have been adjusted for age, CKD status, smoking status never/former/current, [c]ORs have been adjusted for age
[a, b, c]All variables with $p<0.05$ in univariate analysis and clinically relevant variables were included in a multivariate logistic regression model.
OR, odds ratio; CI, confidence interval; other abbreviations as Table 1.

myocardial infarction associated with hypertension, and an approximately 30%–40% higher risk of coronary artery disease with diabetes in women than in men[40]. Additionally, the Atherosclerosis Risk in Communities study reported two times greater risk of the development of CVD in women and a 1.45 times greater risk in middle-aged men with MetS over 11 years[41]. Our results could explain some of the sex-related differences in the effects of metabolic risk factors on CVD.

In this study, men were more likely to have MetS than were women, as previously reported[21, 39, 42]. Among the MetS risk factors, increased TG was significantly associated with increased arterial stiffness in men of all ages. Additionally, among men not using dyslipidemia medication, LDL-cholesterol was associated with a higher CAVI in the analyses of linear relationships **(Table 2)**. This finding suggests that there is a need to focus on lifestyle management and control of the lipid profile in men. Contrary to men, the association between increased TG and increased CAVI lost significance in age subgroups but maintained the direction of the relationship, emphasizing that the monitoring and control of TG

should not be overlooked in women.

A notable finding in our study was that increased BP was significantly associated with increased arterial stiffness in women aged ≤ 70 years. Based on this observation, we assumed that hypertension could affect arterial stiffness in premenopausal women. A study published in 2020 suggests sex-related differences in the presentation of hypertension, with a more rapid increase in BP in women compared with men, beginning in subjects as young as 30–40 years[43]. Thus, there is a need to pay greater attention to reproductive-aged women with increased BP, as this condition would be the earliest and most important cardiovascular risk factor among MetS components requiring evaluation and monitoring, as highlighted in the recently released fact sheet from the Korean Society of Hypertension[44]. The effect of BP disappeared in both sexes in subjects aged ≥ 71 years, and this may be explained by the fact that almost three-quarters of the population in this age group (75.6% of men and 73% of women, respectively) have this component (increased BP) **(Supplementary Table 4)**.

A negative correlation was observed between the BMI, which is commonly used as an indicator of obesity along with WC, and the CAVI, consistent with previous studies[11, 27, 45]. Additionally, WC showed a positive correlation with the CAVI in linear regression analyses **(Table 2)**. This finding is consistent with the widely accepted positive correlation between increased visceral fatness and increased CVD risk. Nevertheless, when the increased WC was analyzed as a categorical variable as one component of MetS, a positive correlation between increased WC and increased CAVI was not observed in this population. Moreover, there was a negative correlation in men aged ≥ 71 years. As the BMI includes both fat and muscle mass by definition, it does not reflect body composition. Although questions remain about the relationship between body composition, including lean body mass or adiposity, and CAVI, as conflicting results have been found for the associations between CAVI and skeletal muscle mass, visceral fat, subcutaneous fat, and epicardial fat[46, 47], CAVI is reported to be correlated with visceral fat area measured with CT[25]. Additionally, a newly proposed obesity index ABSI[29, 48], which was not correlated with BMI, was shown to be associated with high CAVI[32]. When we used ABSI instead of WC, we could observe significant associations with high CAVI in our study group, confirming that ABSI is a more suitable indicator than WC to show the association between visceral fat and CAVI[48, 49].

Regarding the relationship of MetS and its components with CAVI, an ethnic difference is observed mainly in the relationship with WC. Although most studies in Korea and Japan report positive correlations between increased adiposity and high CAVI[8, 26], an inverse correlation between WC and arterial stiffness were reported in Caucasian populations in studies conducted in Spain and multicenter Europe[17, 19]. Whether the relevance will change if the ABSI is used instead of WC in those populations would require further investigation.

As the number of MetS risk factors increased, the risk of higher CAVI also increased, which means that even if the diagnostic criteria for MetS are not met, the risk of high CAVI increases with the number of metabolic risk factors. This association is significant in men, with at least two risk factors, and in women, with at least one risk factor, with an increasing OR with each additional MetS component[39]. On the other hand, the increase in the OR according to the increase in the MSS in both sexes did not follow a continuous linear incremental pattern, which may be attributed to the fact that increased WC and decreased HDL-cholesterol were not significantly associated with the risk of higher CAVI in this population.

This study has several advantages over previous studies. Our study included a significant number of subjects from the general asymptomatic population with a homogeneous ethnicity and gained information on comorbidities and medical history to differentiate patients with established vascular diseases. We used the CAVI to measure arterial stiffness, which reflects both functional and organic stiffness, independent of BP changes during measurement, and is now established as a screening tool for arterial stiffness measurement. Additionally, we used an age–sex group-specific definition of higher CAVI as there is no standardized cutoff point over which the risk is abnormally increased, particularly according to age groups. This classification could be useful, although there may be a limitation in that the value is dependent on the study population. There were other limitations to our study. The study subjects undergoing health evaluation on their own initiative may not represent the general Korean population and there may be a bias toward individuals with medium to high socioeconomic status. Second, we did not evaluate the effect of different lifestyle factors, such as dietary habits (including alcohol consumption) and physical exercise, which may affect the prevalence of MetS or arterial stiffness. Additionally, the cross-sectional nature of the present study limits the interpretation of causal inferences, and we cannot present a pathophysiological explanation for this relationship. Thus, further prospective cohort studies

are required to observe changes in the prevalence of MetS and its components or of the CAVI over time and its association with MetS or improvement following treatment.

Our results show a consistent and significant association between MetS and increased CAVI. MetS, MSS, and three components of MetS (increased BP, FBS, and TG) were significantly associated with increased CAVI in men and women. Women were more affected by MetS, and there were different associations between MetS and each component according to age and sex. We suggest that attention should be paid to managing MetS risk factors in sex-specific strategies to promote vascular health.

Author Contribution

Conception and design: S.Y.C., H.E.P., H.L.; data acquisition: S.Y.C., H.E.P., H.L.; data analysis and interpretation: S.K., S.Y.C., J.J.K.; statistical analysis S.K., S.Y.C.; drafting and finalizing the paper: S.K., S.Y.C.; critical revision of the paper for important intellectual content: J.J.K., H.L., H.E.P.

Conflict of Interest

The authors declared no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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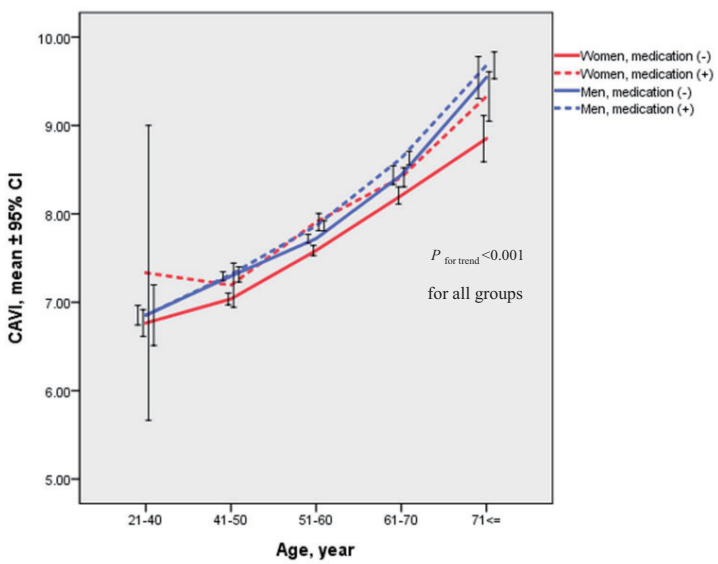
Supplementary Table 1. Distribution of CAVI in all subjects and each sex

Age groups, years	All		≤ 40		41-50		51-60		61-70		≥ 71	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
n	4949	2178	173	76	1222	404	2173	928	1021	574	360	196
Mean ± SD	7.93 ± 1.13	7.84 ± 1.08	6.85 ± 0.71	6.79 ± 0.65	7.30 ± 0.76	7.06 ± 0.67	7.79 ± 0.90	7.69 ± 0.78	8.56 ± 1.01	8.31 ± 0.89	9.65 ± 1.24	9.19 ± 1.52
p-value	0.001		0.488		< 0.001		0.002		< 0.001		< 0.001	
25 percentile	7.15	7.15	6.35	6.36	6.80	6.60	7.18	7.15	7.85	7.65	8.90	8.50
50 percentile	7.75	7.70	6.85	6.85	7.25	7.10	7.70	7.60	8.45	8.25	9.55	9.10
75 percentile	8.55	8.45	7.40	7.20	7.75	7.45	8.30	8.20	9.20	8.86	10.35	9.69

Supplementary Table 2. Distribution of CAVI in all subjects and each sex without taking any medication

Age groups, years	All		≤ 40		41-50		51-60		61-70		≥ 71	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
n	2654	1412	146	73	848	358	1191	642	384	283	85	56
Mean ± SD	7.70 ± 1.10	7.58 ± 0.89	6.85 ± 0.68	6.77 ± 0.65	7.30 ± 0.73	7.04 ± 0.64	7.72 ± 0.86	7.59 ± 0.74	8.44 ± 1.04	8.21 ± 0.82	9.54 ± 1.10	8.85 ± 0.98
p-value	0.001		0.356		< 0.001		< 0.001		0.001		< 0.001	
25 percentile	7.05	6.95	6.39	6.35	6.80	6.65	7.15	7.05	7.75	7.65	8.83	8.21
50 percentile	7.55	7.50	6.83	6.80	7.25	7.10	7.65	7.55	8.30	8.15	9.65	9.00
75 percentile	8.20	8.10	7.36	7.20	7.74	7.40	8.20	8.05	9.10	8.75	10.35	9.44



Supplementary Fig. 1. Distribution of CAVI in subjects with any-medication and no-medication for hypertension, diabetes mellitus, or dyslipidemia according to each sex

Supplementary Table 3. Basal characteristics with increased arterial stiffness in each sex group

Parameters	Men Total *n* = 4949	Normal CAVI [Q1-3] *n* = 3663	Increased CAVI [Q4] *n* = 1286	*p*-value	Women Total *n* = 2178	Normal CAVI [Q1-3] *n* = 1633	Increased CAVI [Q4] *n* = 545	*p*-value
CAVI §	7.93 ± 1.13	7.53 ± 0.84	9.08 ± 1.06	< 0.001	7.84 ± 1.08	7.49 ± 0.79	8.88 ± 1.14	< 0.001
Age, years†	55.9 ± 9.2	55.6 ± 9.1	56.6 ± 9.3	0.001	57.4 ± 9.4	57.1 ± 9.2	58.2 ± 9.8	0.029
Obesity indices								
BMI, kg/m²†	24.7 ± 2.7	24.9 ± 2.8	24.2 ± 2.6	< 0.001	22.5 ± 3.0	22.7 ± 3.0	22.2 ± 2.8	0.004
WC, cm †	89.2 ± 7.4	89.3 ± 7.4	88.8 ± 7.2	0.020	81.3 ± 8.1	81.3 ± 8.2	81.3 ± 8.1	0.980
ABSI †	0.080 ± 0.003	0.080 ± 0.003	0.081 ± 0.003	< 0.001	0.081 ± 0.004	0.081 ± 0.004	0.082 ± 0.004	< 0.001
Systolic BP, mmHg†	119.7 ± 13.3	118.8 ± 12.7	122.2 ± 14.6	< 0.001	117.5 ± 15.0	116.1 ± 14.3	121.7 ± 16.3	< 0.001
Diastolic BP, mmHg†	80.0 ± 9.5	79.4 ± 9.2	81.6 ± 10.0	< 0.001	75.5 ± 9.7	74.9 ± 9.1	77.3 ± 10.9	< 0.001
Laboratory parameters								
FBS, mg/dL†	107.9 ± 23.4	105.9 ± 20.3	113.6 ± 29.8	< 0.001	99.2 ± 19.1	97.8 ± 17.1	103.6 ± 23.6	< 0.001
HbA1c, %†	5.9 ± 0.8	5.8 ± 0.7	6.0 ± 1.0	< 0.001	5.8 ± 0.7	5.7 ± 0.6	5.9 ± 0.8	< 0.001
Total cholesterol, mg/dL†	188.4 ± 36.4	188.1 ± 35.9	189.3 ± 37.7	0.316	200.4 ± 36.4	201.0 ± 35.8	198.6 ± 38.0	0.173
LDL-cholesterol, mg/dL†	121.1 ± 32.5	121.1 ± 31.9	121.0 ± 34.2	0.963	124.9 ± 32.3	125.9 ± 32.2	121.8 ± 32.5	0.010
HDL-cholesterol, mg/dL†	51.6 ± 12.6	51.6 ± 12.5	51.6 ± 12.9	0.989	62.1 ± 17.5	62.3 ± 18.3	61.3 ± 14.8	0.246
TG, mg/dL†	112 (80-161)	109 (79-156)	122 (85-174)	< 0.001	85 (61-121)	82 (60,117)	90 (66.5-131)	< 0.001
BUN, mg/dL†	14.8 ± 3.7	14.8 ± 3.6	14.9 ± 4.1	0.403	13.8 ± 4.1	13.7 ± 4.2	13.9 ± 3.9	0.274
Creatinine, mg/dL†	0.94 ± 0.15	0.94 ± 0.14	0.94 ± 0.18	0.256	0.69 ± 0.15	0.69 ± 0.16	0.70 ± 0.11	0.174
hs-CRP, mg/dL†	0.06 (0.03-0.13)	0.06 (0.03-0.12)	0.07 (0.03-0.15)	< 0.001	0.05 (0.02-0.11)	0.05 (0.02-0.10)	0.05 (0.03-0.13)	0.008
GFR, mL/min/1.73m²†	85.6 ± 14.5	85.6 ± 14.2	85.3 ± 15.4	0.525	90.9 ± 16.0	91.3 ± 15.7	89.6 ± 16.9	0.038
Comorbidities								
Hypertension†	2152 (43.5)	1509 (41.2)	643 (50.0)	< 0.001	653 (30.0)	421 (25.8)	232 (42.6)	< 0.001
Hypertension medication†	1633 (33.0)	1170 (31.9)	463 (36.0)	0.008	492 (22.6)	328 (20.1)	164 (30.1)	< 0.001
Diabetes mellitus†	988 (20.0)	621 (17.0)	367 (28.5)	< 0.001	262 (12.0)	149 (9.1)	113 (20.7)	< 0.001
Diabetes mellitus medication†	619 (12.5)	383 (10.5)	236 (18.4)	< 0.001	156 (7.2)	86 (5.3)	70 (12.8)	< 0.001
Dyslipidemia†	2777 (56.1)	2003 (54.7)	774 (60.2)	0.001	984 (23.8)	710 (43.5)	274 (50.3)	0.006
Dyslipidemia medication§	1216 (24.6)	872 (23.8)	344 (26.7)	0.035	484 (22.2)	334 (20.5)	150 (27.5)	0.001
Chronic kidney disease	134 (2.7)	85 (2.3)	49 (3.8)	0.013	47 (2.2)	31 (1.9)	16 (2.9)	0.239
Smoking †				0.016				0.517
Never	1437 (29.0)	1101 (30.1)	336 (26.1)		2003 (92.0)	1508 (92.3)	495 (90.8)	
Former	2362 (47.7)	1736 (47.4)	626 (48.7)		103 (4.7)	73 (4.5)	30 (5.5)	
Current	1150 (23.2)	826 (22.5)	324 (25.2)		72 (3.3)	52 (3.2)	20 (3.7)	
MetS†	1832 (37.0)	1291 (35.2)	541 (42.1)	< 0.001	454 (20.8)	311 (19.0)	143 (26.2)	< 0.001
MetS with ABSI†	1950 (40.0)	1319 (36.5)	631 (50.0)	< 0.001	551 (25.8)	366 (22.8)	185 (35.0)	< 0.001
MetS components								
Increased WC†	2193 (44.3)	1635 (44.6)	558 (43.4)	0.439	681 (31.3)	507 (31.0)	174 (31.9)	0.701
Increased BP or on medication†	2859 (57.8)	2032 (55.5)	827 (64.3)	< 0.001	925 (42.5)	627 (38.4)	298 (54.7)	< 0.001
Increased FBS or on medication†	2894 (58.5)	2049 (55.9)	845 (65.7)	< 0.001	767 (35.2)	529 (32.4)	238 (43.7)	< 0.001
Increased TG†	1429 (28.9)	987 (26.9)	442 (34.4)	< 0.001	298 (13.7)	205 (12.6)	93 (17.1)	0.008
Decreased HDL-cholesterol †	727 (14.7)	550 (15.0)	177 (13.8)	0.275	444 (20.4)	327 (20.0)	117 (21.5)	0.469
Increased ABSI †	2693 (55.2)	1868 (51.6)	825 (65.3)	< 0.001	1298 (60.8)	943 (58.8)	355 (67.1)	0.001
MetS risk score†	2.0 ± 1.3	2.0 ± 1.3	2.2 ± 1.3	< 0.001	1.4 ± 1.3	1.3 ± 1.2	1.7 ± 1.3	< 0.001
MSS 0	641(13.0)	510 (13.9)	131 (10.2)		628 (28.8)	516 (31.6)	112 (20.6)	
MSS 1	1142 (23.1)	885 (24.2)	257 (20.0)		624 (28.7)	471 (28.8)	153 (28.1)	
MSS 2	1334 (27.0)	977 (26.7)	357 (27.8)		472 (21.7)	335 (20.5)	137 (25.1)	
MSS 3	1157 (23.4)	833 (22.7)	324 (25.2)		295 (13.5)	204 (12.5)	91 (16.7)	
MSS 4	554 (11.2)	375 (10.2)	179 (13.9)		133 (6.1)	93 (5.7)	40 (7.3)	
MSS 5	121 (2.4)	83 (2.3)	38 (3.0)		26 (1.2)	14 (0.9)	12 (2.2)	
MetS risk score with ABSI†	2.2 ± 1.2	2.1 ± 1.2	2.4 ± 1.2	< 0.001	1.7 ± 1.2	1.6 ± 1.2	2.0 ± 1.3	< 0.001
MSS 0	446 (9.1)	358 (9.9)	88 (7.0)		346 (16.2)	286 (17.8)	60 (11.3)	
MSS 1	1061 (21.7)	875 (24.2)	186 (14.7)		658 (30.3)	529 (33.0)	129 (24.4)	
MSS 2	1423 (29.2)	1065 (29.4)	358 (28.3)		579 (27.1)	424 (26.4)	155 (29.3)	
MSS 3	1307 (26.8)	923 (25.5)	384 (30.4)		366 (17.2)	250 (15.6)	116 (21.9)	
MSS 4	535 (11.0)	325 (9.0)	210 (16.6)		153 (7.2)	100 (6.2)	53 (10.0)	
MSS 5	108 (2.2)	71 (2.0)	37 (2.9)		32 (1.5)	16 (1.0)	16 (3.0)	

NOTE. Values are mean ± standard deviation, median (interquartile range; IQR) or n (%). Increased CAVI was defined as CAVI of age-gender-strata specific highest quartile; MetS risk score as the number of MetS components that a single individual has; chronic kidney disease (CKD) as having glomerular filtration rate (GFR) < 60 mL/min/1.73m², Increased ABSI was defined as having ABSI ≥ 0.080

CAVI, cardio-ankle vascular index; SD, standard deviation; IQR, interquartile range; BMI, body mass index; WC, waist circumference; ABSI, a body shape index; BP blood pressure; FBS, fasting blood sugar; HbA1C, glycated hemoglobin; LDL, low density lipoprotein; HDL, high density lipoprotein; TG, triglyceride; BUN, blood urea nitrogen; hs-CRP, high sensitivity C reactive protein; GFR, glomerular filtration rate; MetS, metabolic syndrome

†parameters with significant different mean values between men and women, *p*-value of < 0.05

§parameters with significant different mean values between men and women, *p*-value of < 0.001

Supplementary Table 4. Prevalence of metabolic syndrome by age group and sex

Age groups, years *n* (%)	≤ 50 (*n* = 1875)	51-70 (*n* = 4696)	≥ 71 (*n* = 556)	*p*-value
All				
MetS	566 (30.2)	1509 (32.1)	211 (37.9)	0.003
MetS with ABSI	531 (28.6)	1683 (36.4)	287 (53.5)	<0.001
Increased WC	709 (37.8)	1896 (40.4)	269 (48.4)	<0.001
Increased BP or on medication	798 (42.6)	2571 (54.7)	415 (74.6)	<0.001
Increased FBS or on medication	799 (42.6)	2508 (53.4)	354 (63.7)	<0.001
Increased TG	588 (31.4)	1052 (22.4)	87 (15.6)	<0.001
Decreased HDL-cholesterol	321 (17.1)	754 (16.1)	96 (17.3)	0.494
Increased ABSI	798 (42.6)	2571 (54.7)	415 (74.6)	<0.001
Men	(*n* = 1395)	(*n* = 3194)	(*n* = 360)	
MetS	513 (36.8)	1183 (37.0)	136 (37.8)	0.939
MetS with ABSI	472 (34.2)	1279 (40.6)	199 (57.0)	<0.001
Increased WC	632 (45.3)	1400 (43.8)	161 (44.7)	0.644
Increased BP or on medication	687 (49.2)	1900 (59.5)	272 (75.6)	<0.001
Increased FBS or on medication	707 (50.7)	1938 (60.7)	249 (69.2)	<0.001
Increased TG	537 (38.5)	837 (26.2)	55 (15.3)	<0.001
Decreased HDL-cholesterol	237 (17.0)	437 (13.7)	53 (14.7)	0.014
Increased ABSI	571 (41.3)	1821 (57.8)	301 (86.2)	<0.001
Women	(*n* = 480)	(*n* = 1502)	(*n* = 196)	
MetS	53 (11.0)	326 (21.7)	75 (38.3)	<0.001
MetS with ABSI	59 (12.4)	404 (27.4)	88 (47.1)	<0.001
Increased WC	77 (16.0)	496 (33.0)	108 (55.1)	<0.001
Increased BP or on medication	111 (23.1)	671 (44.7)	143 (73.0)	<0.001
Increased FBS or on medication	92 (19.2)	570 (37.9)	105 (53.6)	<0.001
Increased TG	51 (10.6)	215 (14.3)	32 (16.3)	0.065
Decreased HDL-cholesterol	84 (17.5)	317 (21.1)	43 (21.9)	0.199
Increased ABSI	192 (40.5)	944 (64.1)	162 (86.6)	<0.001

Abbreviations as Supplementary Table 3.

Supplementary Table 5. Distribution of CAVI by metabolic syndrome and metabolic syndrome with ABSI status

Age groups, years CAVI	MetS (+)	MetS (-)	*p*-value	MetS with ABSI (+)	MetS with ABSI (-)	*p*-value
All	2286 (32.1)	4841 (67.9)		2501 (35.7)	4513 (64.3)	
	8.06 ± 1.26	7.83 ± 1.03	< 0.001	8.21 ± 1.26	7.72 ± 0.98	< 0.001
Men	1832 (37.0)	3117 (63.0)		1950 (40.0)	2930 (60.0)	
	8.01 ± 1.22	7.88 ± 1.07	< 0.001	8.19 ± 1.24	7.75 ± 1.01	< 0.001
≤ 50	513 (36.8)	882 (63.2)		472 (34.2)	910 (65.8)	
	7.23 ± 0.87	7.26 ± 0.71	0.554	7.36 ± 0.88	7.19 ± 0.70	< 0.001
51-70	1183 (37.0)	2011 (63.0)		1279 (40.6)	1870 (59.4)	
	8.15 ± 1.08	7.96 ± 0.95	< 0.001	8.24 ± 1.08	7.89 ± 0.92	< 0.001
≥ 71	136 (37.8)	224 (62.2)		199 (57.0)	150 (43.0)	
	9.74 ± 1.28	9.59 ± 1.21	0.294	9.79 ± 1.23	9.43 ± 1.16	0.006
Women	454 (20.8)	1724 (29.2)		551 (25.8)	1583 (74.2)	
	8.23 ± 1.40	7.73 ± 0.95	< 0.001	8.30 ± 1.32	7.67 ± 0.92	< 0.001
≤ 50	53 (11.0)	427 (89.0)		59 (12.4)	415 (87.6)	
	7.02 ± 0.66	6.93 ± 0.71	0.342	7.04 ± 0.75	7.01 ± 0.66	0.804
51-70	326 (21.7)	1176 (78.3)		404 (27.4)	1069 (72.6)	
	8.11 ± 0.92	7.87 ± 0.86	< 0.001	8.20 ± 0.90	7.82 ± 0.84	< 0.001
≥ 71	75 (38.3)	121 (61.7)		88 (47.1)	99 (52.9)	
	9.67 ± 2.10	8.89 ± 0.89	0.003	9.63 ± 1.98	8.83 ± 0.86	< 0.001

NOTE. Values are *n* (%), and mean ± standard deviation of CAVI
Abbreviations as Supplementary Table 3.