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The Relationship between Aortic Knob Width and Metabolic Syndrome

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Background: Both aortic knob width and metabolic syndrome are suggested to be related to atherosclerosis and cardiovascular diseases. However, the association between aortic knob width and metabolic syndrome is unknown. This study aimed to explore this relationship.
Methods: Participants were 3,705 Korean adults aged 18–79 years who visited the health promotion center of a general hospital. Data on chest radiography, physical measurements, medical and social history, and blood tests were collected. We defined metabolic syndrome according to the National Cholesterol Education Program Adult Treatment Panel III criteria. A single reviewer measured aortic knob width on chest radiography.
Results: Aortic knob width was significantly correlated with age; body mass index; waist circumference; systolic and diastolic blood pressures; total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting glucose, glycated hemoglobin, insulin, and uric acid levels; and homeostatic model assessment of insulin resistance values. Aortic knob width significantly increased as the number of metabolic syndrome components increased. Moreover, metabolic syndrome component values tended to increase across the quartile groups of aortic knob width after adjusting for age, exercise, smoking status, and alcohol use. Through receiver operating characteristic curve analysis, we determined the clinically useful cutoff value for aortic knob width to be 30.47 mm in premenopausal women.
Conclusion: Aortic knob width was found to be significantly related to metabolic syndrome and its individual components.

Keywords: Metabolic Syndrome; Aortic Knob Width; Thoracic Aorta; Chest Radiography

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INTRODUCTION

Radiography is one of the most inexpensive and easily accessible imaging modalities in the clinical setting. Despite the latest European guidelines on aortic diseases stating that chest radiography is of limited value for diagnosing acute aortic syndrome,[1] this modality provides valuable and fundamental information about the heart, the lungs, and bony structures.

The aortic knob width (AKW) is a radiographic configuration formed by a portion of the descending aorta and the foreshortened aortic arch.[2] An increase in the transverse diameter of the aortic arch has been associated with atherosclerosis and cardiovascular diseases (CVDs) such as target organ damage,[3] hypertension, cardiac dysfunction, aortic calcifications, and coronary artery disease (CAD).[4,5]

Dyslipidemia, diabetes, hypertension, and smoking status are known risk factors for CVDs.[6] Metabolic syndrome (MetS) is a collection of cardiovascular risk factors that increases cardiovascular mortality and morbidity beyond the sum of risk components.[7] As both AKW and MetS are significantly associated with CVDs, we hypothesized that AKW might be related to MetS. Previous studies examined the relationship between AKW and cardio-ankle vascular stiffness index[8] or carotid intima–media thickness (CIMT).[9] However, no studies to date have focused on the relationship between MetS and AKW. This study aimed to explore this relationship.

METHODS

1. Subjects

Study participants were 3,970 Korean adults aged 18–79 years who visited the health promotion center of a general hospital for regular checkups from January to December 2015. The following individuals were excluded from the study: (1) two with structural abnormalities such as mediastinal shift and a history of previous pneumonectomy; 2) 27 with chronic liver diseases (3 times the upper normal limits of aspartate aminotransferase/alanine aminotransferase, total bilirubin level >3 mg/dL); (3) eight with acute inflammation (white blood cell count >13,000/μL); (4) 101 with any history of cancers; (5) 40 with anemia (hemoglobin level <9 g/dL); (6) two with chronic renal diseases (estimated glomerular filtration rate[10] <30 mL/min/1.73 m^2); (7) 22 who were pregnant or did not undergo chest radiography; (8) 23 who did not undergo laboratory examination; (9) 46 with abnormal findings on thyroid function tests (thyroid-stimulating hormone level <0.1 or >10 μIU/mL); and (10) eight with outliers (fasting glucose level >300 mg/dL, insulin level >300 μIU/mL). Ultimately, 265 were excluded, leaving a total of 3,705 study participants for this analysis.

This is a retrospective study which does not require the Institutional Review Board approval. And all participants provided written informed consent.

2. Clinical Examination and Blood Assays

Lifestyle, social, and medical history data were collected through self-administrated questionnaires. Height and weight were measured using an automatic digital stadiometer. Body mass index (BMI) was defined as body weight divided by height squared (kg/m^2). Blood pressure (BP) was measured using an automated sphygmomanometer after the participants were comfortably seated for at least 10 minutes. Blood samples were drawn from the antecubital vein in the morning after fasting for more than 8 hours. Laboratory tests for total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, fasting glucose, insulin, uric acid, creatinine, and glycated hemoglobin (HbA1c) levels were performed. Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated using standard methods.[11]

MetS, in accordance with the National Cholesterol Education Program Adult Treatment Panel III criteria,[12-14] was defined as the presence of three or more of the following: elevated triglyceride level (≥150 mg/dL or use of triglyceride-lowering medications), low HDL cholesterol level (men <40 mg/dL, women <50 mg/dL, or use of HDL cholesterol-raising medications), elevated systolic BP (SBP) or diastolic BP (DBP) (≥130/85 mm Hg or use of antihypertensive medications), elevated fasting glucose level (≥100 mg/dL or use of antidiabetic medications), and increased waist circumference (≥90 cm in men, ≥85 cm in women).[13]

3. Measurement of Aortic Knob Width

On posteroanterior chest radiography, the widest point of the aortic knob was measured along the straight imaginary line from the lateral edge of the trachea to the left lateral wall of the aortic arch.[2,4,8,9,15,16] To minimize interpersonal differences, a single reviewer blinded to the participants' demographic data measured all AKW on chest radiography.

4. Statistical Analysis

All continuous variables except for triglyceride and insulin levels were analyzed using independent t-tests, whereas categorical variables were compared using chi-square test. Because triglyceride and insulin levels did not pass the normality tests, they were subjected to the Mann–Whitney U-test. Pearson correlation analysis was used to determine the association between metabolic parameters and AKW. For the same reason, triglyceride and insulin levels were determined using nonparametric Spearman correlation coefficients. To evaluate the AKW trends according to the number of MetS components and each MetS component according to AKW quartile, the P for trend was determined using a contrast test for the analysis of covariance (ANCOVA) after adjusting for age, alcohol use, smoking status, and exercise. Receiver operating characteristic (ROC) curves were used to assess the sensitivity and specificity of AKW to identify MetS. All statistical analyses were performed using PASW SPSS for Windows ver. 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The study included 2,002 men (54.04%) and 1,703 women (45.96%) aged 18–79 years. Mean AKW was 32.29±5.30 mm overall, 34.21±4.78 mm in men, and 30.03±4.98 mm in women. The mean age was 45.45±11.56 years, and the mean BMI was 23.88±3.35 kg/m^2 (Table 1).

AKW showed significant correlations with age; BMI; waist circumference; SBP; DBP; total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, fasting glucose, insulin, HbA1c, and uric acid levels; and HOMA-IR values (Table 2). All variables showed significant correlations with AKW, except for total cholesterol and uric acid levels in men and insulin level in women.

Analysis of variance showed a significant increase in AKW in accordance with the number of MetS components (Table 3). Moreover, ANCOVA after adjusting for age, exercise, smoking status, and alcohol use showed a significant increase in each MetS component according to AKW quartile (Table 4).

In the ROC curve analysis of the ability of AKW to predict MetS, we divided men into three groups based on age and women into two groups, considering 50 years as the average menopause age. The cutoff values were 33.49 mm overall (sensitivity, 68%; specificity, 67%; area under the curve [AUC], 0.74; 95% confidence interval [CI], 0.72–0.76; P<0.001) (Figure 1A), 32.05 mm in men aged 20–39 years (sensitivity, 52%; specificity, 69%; AUC, 0.61; 95% CI, 0.53–0.68; P<0.001) (Figure 1B), 34.39 mm in men aged 40–59 years (sensitivity, 64%; specificity, 57%; AUC, 0.64; 95% CI, 0.60–0.67; P<0.001) (Figure 1C), 36.98 mm in men aged 60–79 years (sensitivity, 80%; specificity, 40%; AUC, 0.58; 95% CI, 0.50–0.66; P<0.001) (Figure 1D), 30.47 mm in women aged 20–

Table 1. Characteristics of study participants

Characteristic	Total (n=3,705)	Men (n=2,002)	Women (n=1,703)	P-value
Aortic knob width (mm)	32.29±5.30	34.21±4.78	30.03±4.98	<0.001
Age (y)	45.45±11.56	46.82±10.68	43.84±12.32	<0.001
Body mass index (kg/m^2)	23.88±3.35	24.96±2.97	22.61±3.31	<0.001
Waist circumference (cm)	80.52±10.30	85.80±7.97	74.30±9.21	<0.001
Systolic blood pressure (mm Hg)	118.15±13.43	121.38±12.71	114.35±13.27	<0.001
Diastolic blood pressure (mm Hg)	71.50±9.86	73.65±9.49	68.97±9.68	<0.001
Total cholesterol level (mg/dL)	201.79±36.87	205.50±38.52	197.43±34.33	<0.001
Triglyceride level (mg/dL)	120.54±106.84	148.36±128.88	87.85±57.75	<0.001
High-density lipoprotein cholesterol level (mg/dL)	56.46±13.54	51.16±11.32	62.68±13.29	<0.001
Low-density lipoprotein cholesterol level (mg/dL)	121.71±33.03	127.16±33.49	115.30±31.30	<0.001
Fasting glucose level (mg/dL)	91.50±20.55	94.50±23.25	87.98±16.15	<0.001
Hemoglobin A1c level (%)	5.64±0.72	5.72±0.80	1.09±2.14	<0.001
Insulin level (μIU/mL)	4.92±5.72	5.04±4.03	4.77±7.25	<0.001
Homeostatic model assessment of insulin resistance	1.16±1.68	1.23±1.16	1.09±2.14	0.020
Uric acid level (mg/dL)	5.21±1.37	5.94±1.25	4.33±0.91	<0.001
Current smoker	790 (21.3)	737 (36.8)	53 (3.1)	<0.001

Values are presented as mean±standard deviation or number (%). All data except for triglyceride and insulin levels were analyzed by independent t-tests. Triglyceride and insulin levels were analyzed by Mann–Whitney U-test. P-value refers to comparison between men and women.

Table 2. Correlations between aortic knob width and variables

Variable	Total		Men		Women	
	R	P-value	R	P-value	R	P-value
Age (y)	0.616	<0.001	0.547	<0.001	0.694	<0.001
Body mass index (kg/m^2)	0.408	<0.001	0.256	<0.001	0.374	<0.001
Waist circumference (cm)	0.490	<0.001	0.294	<0.001	0.416	<0.001
Systolic blood pressure (mm Hg)	0.352	<0.001	0.202	<0.001	0.367	<0.001
Diastolic blood pressure (mm Hg)	0.330	<0.001	0.216	<0.001	0.319	<0.001
Total cholesterol level (mg/dL)	0.100	<0.001	-0.022	0.317	0.170	<0.001
Triglyceride level (mg/dL)	0.319	<0.001	0.113	<0.001	0.237	<0.001
High-density lipoprotein cholesterol level (mg/dL)	-0.279	<0.001	-0.080	<0.001	-0.187	0.001
Low-density lipoprotein cholesterol level (mg/dL)	0.118	<0.001	-0.053	0.017	0.182	<0.001
Fasting glucose level (mg/dL)	0.244	<0.001	0.168	<0.001	0.263	<0.001
Insulin level (μIU/mL)	0.104	<0.001	0.086	<0.001	0.032	0.215
Homeostatic model assessment of insulin resistance	0.094	<0.001	0.115	<0.001	0.073	0.005
Hemoglobin A1c (%)	0.250	<0.001	0.149	<0.001	0.332	<0.001
Uric acid level (mg/dL)	0.247	<0.001	0.000	0.983	0.054	0.029

All values except for triglyceride and insulin levels are presented as correlation coefficient by Pearson correlation analysis. Triglyceride and insulin levels are presented as nonparametric Spearman correlation coefficients.

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Table 3. Trends of aortic knob width according to the number of MetS components

Variable	No. of MetS components				P-value	P for trend
	0	1	2	≥3		
Total (mm)	29.73±4.51 (1,577)	33.05±4.69 (864)	34.06±5.01 (671)	35.98±5.06 (593)	<0.001	<0.001
Men (mm)	32.25±4.24 (551)	34.16±4.39 (529)	34.59±4.69 (467)	36.26±4.98 (455)	<0.001	<0.001
Women (mm)	28.39±4.06 (1,026)	31.30±4.61 (335)	32.84±5.49 (204)	35.04±5.22 (138)	<0.001	<0.001

Values are presented as mean±standard deviation (number). Analyzed by ANCOVA after adjusting for age, alcohol use, smoking status, and exercise. P for trend was determined using a contrast test for ANCOVA.
MetS, metabolic syndrome; ANCOVA, analysis of covariance.

Table 4. Trends of each metabolic syndrome component according to AKW quartile

Variable	1st AKW quartile	2nd AKW quartile	3rd AKW quartile	4th AKW quartile	P-value	P for trend
Total	14.16–28.49 mm	28.50–32.00 mm	32.01–35.60 mm	35.61–75.00 mm		
Waist circumference (cm)	74.38±0.35	79.51±0.29	82.49±0.30	86.04±0.33	<0.001	<0.001
SBP (mm Hg)	112.01±0.49	116.23±0.42	119.88±0.43	124.38±0.47	<0.001	<0.001
DBP (mm Hg)	66.49±0.36	69.98±0.31	73.44±0.31	76.04±0.35	<0.001	<0.001
Triglyceride level (mg/dL)	95.16±4.08	120.45±3.48	130.04±3.52	139.22±3.88	<0.001	<0.001
HDL cholesterol level (mg/dL)	62.22±0.50	56.32±0.43	54.10±0.43	53.07±0.48	<0.001	<0.001
Fasting glucose level (mg/dL)	88.96±0.79	90.06±0.68	92.10±0.69	95.29±0.76	<0.001	<0.001
Men	21.40–30.89 mm	30.90–33.79 mm	33.80–37.19 mm	37.20–75.00 mm		
Waist circumference (cm)	82.69±0.38	84.81±0.35	86.30±0.35	89.55±0.38	<0.001	<0.001
SBP (mm Hg)	117.94±0.61	119.63±0.56	122.62±0.56	125.28±0.60	<0.001	<0.001
DBP (mm Hg)	70.01±0.45	72.44±0.41	75.49±0.42	76.52±0.44	<0.001	<0.001
Triglyceride level (mg/dL)	131.65±6.33	139.98±5.83	165.16±5.86	158.89±6.25	0.001	<0.001
HDL cholesterol level (mg/dL)	52.95±0.55	51.39±0.50	50.63±0.51	49.72±0.54	0.001	<0.001
Fasting glucose level (mg/dL)	92.50±1.14	92.80±1.05	95.99±1.05	97.15±1.12	0.011	0.002
Women	14.16–26.49 mm	26.50–29.59 mm	29.60–33.02 mm	33.03–64.14 mm		
Waist circumference (cm)	71.18±0.49	72.89±0.43	74.65±0.43	78.24±0.49	<0.001	<0.001
SBP (mm Hg)	110.70±0.72	111.55±0.63	113.96±0.63	120.58±0.72	<0.001	<0.001
DBP (mm Hg)	65.23±0.53	67.24±0.47	69.70±0.47	73.54±0.53	<0.001	<0.001
Triglyceride level (mg/dL)	82.50±3.15	81.08±2.78	92.84±2.76	93.24±3.14	0.008	<0.001
HDL cholesterol level (mg/dL)	65.39±0.75	63.91±0.66	61.30±0.66	60.70±0.75	<0.001	<0.001
Fasting glucose level (mg/dL)	85.40±0.90	86.02±0.79	88.23±0.79	92.13±0.89	<0.001	<0.001

Values are presented as range or mean±standard deviation, unless otherwise stated. Analyzed by ANCOVA after adjusting for age, alcohol use, smoking status, and exercise. P for trend was determined using a contrast test for ANCOVA.
AKW, aortic knob width; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; ANCOVA, analysis of covariance.

49 years (sensitivity, 0.76%; specificity, 0.75%; AUC, 0.79; 95% CI, 0.73–0.85; P<0.001) (Figure 1E), and 36.14 mm in women aged 50–69 years (sensitivity, 0.50%; specificity, 0.76%; AUC, 0.66; 95% CI, 0.60–0.73; P<0.001) (Figure 1F). Considering the area under the ROC curve (i.e., AUC) values of 0.7–0.8 as fair and clinically useful,[17,18] the discriminatory power of AKW was moderate in premenopausal women.

DISCUSSION

This study showed that AKW was significantly correlated with multiple factors, including older age, higher BMI, abdominal obesity, hypertension, dyslipidemia, and insulin resistance. AKW showed an increasing trend based on the number of MetS components, and each MetS component showed increasing trends according to AKW quartile. An exception for this was the triglyceride level in several AKW quartile subgroups in men and women, but the overall trends were statistically significant. In addition, we confirmed moderate clinical usefulness for distinguishing MetS in premenopausal women with a cutoff value of 30.47 mm for AKW.

The normal human adult aortic wall comprises three layers: intima, media, and adventitia.[19] Atherosclerosis is characterized by intimal lesions called atheromata, or atheromatous or fibrofatty plaques, which protrude into the arterial lumen and weaken the underlying media often associated with calcification. With aging, presence of risk factors, and genetic predisposition,[20] this condition progresses to complicated lesions with surface defects, hemorrhage, and/or thrombosis.[21] The aortic knob can be enlarged because of increased pressure flow in the aorta or changes in the elasticity of its wall.[20]

A few similar studies have been published. One Japanese study involving hypertensive patients with known or suspected CAD suggested that AKW is an independent predictor of central SBP.[15] A Turkish study that compared AKW with cardio-ankle vascular stiffness index in the diagnosis of subclinical atherosclerosis suggested a cutoff value of 41 mm for AKW to detect subclinical atherosclerosis.[8] Another

Turkish study that compared AKW with CIMT in hypertensive patients showed a strong relationship between them. AKW, age, and SBP were also reported as independent predictors of CIMT.[9] A French study that focused on the relationship between MetS and age-related progression of aortic stiffness measured using aortic pulse wave velocity showed a positive result.[22]

A number of factors, including age, sex, body size, measurement method, and imaging methods used, affect "normal" aortic diame-

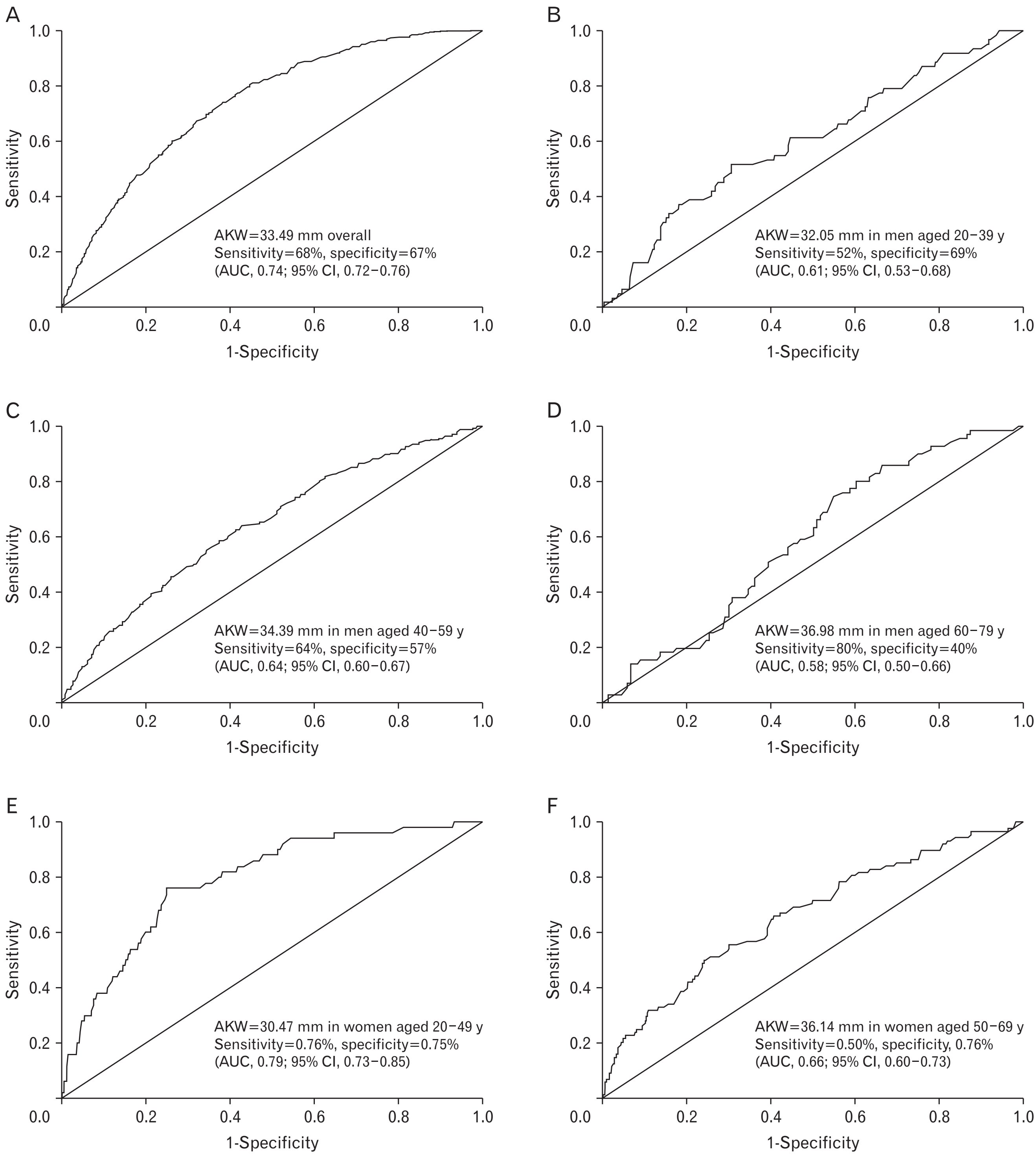

Figure 1. ROC curves in specified participants. (A) ROC curve in all participants. (B) ROC curve in men aged from 20 to 39. (C) ROC curve in men aged from 40 to 59. (D) ROC curve in men aged from 60 to 79. (E) ROC curve in women aged from 20 to 49. (F) ROC curve in women aged from 50 to 79. AKW, aortic knob width; ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval.

ter.[21] In healthy adults, aortic diameters are usually <40 mm and are larger in men, and they increase with age (0.9 mm in men and 0.7 mm in women for each decade of life), body size (height, weight, body surface area),[1,21] and BP.[1] One previous study with a small sample size reported that the mean AKW was 3.16±0.60 cm in men and 2.75±0.35 cm in women, with AKW differently defined as the minimum distance of the left edge of the aortic knob from the midline.[23] Another cross-sectional study on an Indian population indicated that the mean AKW was 3.10±3.34 cm in men and 3.08±3.90 cm in women and that it increased with age.[20] Another Turkish study involving patients on hemodialysis reported that AKW was independently related to male sex, age, and SBP.[24] In our study, AKW was greater in men than in women and increased with age, BMI, waist circumference, SBP, and DBP, which was similar to the results of previous studies.

After adjusting for age, alcohol use, smoking status, and exercise, significant increases in each MetS component according to AKW quartile in both men and women were observed. Moreover, AKW increased as the number of MetS components increased. These results support that MetS and each of its individual components were related to AKW.

The discriminatory ability of AKW to identify MetS was fair in premenopausal women and overall in this study. However, it seemed less useful in men and postmenopausal women (AUC <0.70). This suggested that AKW is a surrogate marker for MetS in premenopausal women.

Structural changes in the aorta seem irreversible, especially when calcifications develop, and patients with MetS were emphasized as a high-risk group for the development of CVDs.[12] Early identification of MetS is important for the preparation of decisive strategies for managing probable future major adverse cardiovascular events.[25] In particular, in clinical settings in which no laboratory tests but chest radiography are available, AKW could be helpful for predicting MetS.

The latest guidelines on aortic diseases recommend the use of computed tomography and/or magnetic resonance imaging for assessing external aortic diameter and echocardiography for assessing internal aortic diameter.[1] Moreover, minimizing radiation exposure was heavily emphasized.[21] From this point of view, chest radiography is the most cost-effective radiologic test with minimal concern for radiation-induced malignancy in the clinical setting. Therefore, for primary physicians, measuring AKW on routine chest radiography is cost-effective and safe enough for detecting MetS when it is clinically doubtful.

The limitations of this study must be considered. First, its cross-sectional design makes it difficult to demonstrate causal relationships. Second, selection bias was unavoidable owing to the use of a single center. Third, the participants might have paid closer attention to their health than the general population because they voluntarily attended a health checkup.

Nevertheless, this study also has important strengths. First, it was the first study designed to show the relationship between AKW and MetS. Second, the study population was comparatively large and included a high percentage of healthy adults without underlying disease. Most previous studies on AKW were confined to hypertensive individuals or those at risk for CVDs.[3,4,8,9,24]

In conclusion, this study showed a significant relationship between AKW and MetS. Chest radiography is cost-effective and readily accessible with minimal concern related to excessive radiation exposure. AKW is easily measured by primary physicians. Therefore, they can pay more attention to patients with a greater AKW than the cutoff values in this study on routine chest radiography, particularly in premenopausal women.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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