Journal *of*
Cardiovascular Imaging JCVI

Original Article

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Conflict of Interest
The authors have no financial conflicts of interest.

Prevalence and Prediction of Aneurysmal Dilatation of the Abdominal Aorta in Koreans: Results of Screening During Transthoracic Echocardiographic Examination

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ABSTRACT

BACKGROUND: Aortic aneurysm (AA) is an enlargement of the aorta to greater than 1.5 times normal size. Although the US guideline recommends ultrasound screening for abdominal AA (AAA) in men older than 65 years regardless of symptoms, limited data describe the prevalence of AAA in Korea. In this study, we screened patients for AAA during transthoracic echocardiographic examination (TTE).

METHODS: We screened for AAA in all consecutive subjects older than 60 years who underwent TTE. We defined AAA as an abdominal aorta with the diameter greater than 30 mm.

RESULTS: We analyzed 5,679 persons (2,272 females, 74 ± 8 years old). The mean size of the abdominal aorta was 19.0 ± 6.1 mm. The prevalence of AAA was 2.9% (165/5,679) and was significantly higher in males (4.7% vs. 1.1%, p < 0.001). AAA was significantly associated with male sex (odds ratio [OR] = 3.098, 95% confidence interval [CI] = 1.971-4.870, p < 0.001), older age (OR = 1.074, 95% CI = 1.050-1.097, p < 0.001), non-diabetes (OR = 1.886, 95% CI = 1.264-2.813, p < 0.001), dyslipidemia (OR = 1.475, 95% CI = 1.019-2.135, p = 0.040), ever-smoker (OR = 2.090, 95% CI = 1.448-3.015, p < 0.001), chronic kidney disease (CKD, OR = 1.757, 95% CI = 1.182-2.612, p = 0.005), and coronary artery disease (CAD, OR = 2.452, 95% CI = 1.742-3.451, p < 0.001). A prediction score with a multivariate model (range: 3.34-10.51) detected AAA with a sensitivity of 79.4% and a specificity of 66.8% with a reference value > 6.8 (area under the curve = 0.799).

CONCLUSIONS: In Korea, the prevalence of AAA was 2.9% in subjects older than 60 years during TTE, and AAA was significantly associated with older age, male sex, non-diabetes, dyslipidemia, ever-smoker, CKD, and CAD. Prediction score (> 6.8%) detected AAA with a sensitivity of 79.4% and a specificity of 66.8%.

Keywords: Abdominal aortic aneurysm; Echocardiography; Mass screening

INTRODUCTION

Aortic aneurysm is a dilation of the aorta more than 1.5 times than its normal size. It is a relatively common disease, but it can be fatal when complications occur.[1)2)] The abdominal

aorta is the most common location of aortic aneurysm, especially the lower part of both renal arteries. Large abdominal aortic aneurysm (AAA) is associated with rupture and sudden death, especially in elderly persons, with an overall mortality rate of nearly 85%-90% with rupture.[3] Rupture of AAA causes about 15,000 deaths/year in the United States and 8,000 deaths/year in the United Kingdom.[4][5]

Screening for AAA is the most efficient method to reduce associated morbidity and mortality. According to the established guidelines, males over 65 years of age who have smoked at least 100 cigarettes in their lives should undergo one-time screening for AAA.[6] After detection of AAA, prophylactic surgery or procedure can reduce mortality and morbidity if the aneurysm has reached 5.5 cm or showed rapid expansion (0.5 cm within six months).[7-9] However, the current AAA screening guidelines are based on population studies from Western countries. Few data describe the prevalence and characteristics of the aortic aneurysmal disease in a Korean population.[10][11] Thus, we evaluated the prevalence of AAA and identified its risk factors in a general Korean population.

METHODS

Study population
A cohort study was conducted at a single tertiary hospital in Korea (Chungnam National University Hospital) from October 2016 to June 2019. All patients over age 60 were screened for AAA during transthoracic echocardiographic examination (TTE) regardless of the initial indications for TTE. We evaluated baseline demographic data of age, sex, cardiovascular risk factors, and past history from medical records. The presence of hypertension was identified as the use of medication to reduce blood pressure for > 6 months. We also defined hypertension in patients who were diagnosed and treated only with lifestyle modifications. Diabetes was defined in those receiving active treatment with oral hypoglycemic medications or insulin. A diagnosis of diabetes was also confirmed in patients with an abnormal fasting blood glucose level ($\geq$ 126 mg/dL) or an abnormal blood glucose level 2 hours after a meal ($\geq$ 200 mg/dL) in those treated only with dietary modification. Dyslipidemia was defined as the use of medication for cholesterol-lowering or an abnormal cholesterol profile (total cholesterol $\geq$ 200 mg/dL) upon examination. Chronic kidney disease (CKD) was defined as the estimated glomerular filtration rate < 30 mL/min/1.73 m^2 or need for hemodialysis. The presence of coronary artery disease (CAD) was defined as > 50% diameter stenosis on the coronary angiogram. The study was approved by the institutional review board of our institution (IRB No. 2020-01-040) and conducted according to the principles of the Declaration of Helsinki. The IRB waived the requirement for informed consent.

Identification of AAA
Measurement of AAA was performed by commercially-available echocardiographic machines with a sector probe with 3.5MHz. TTE was performed with the subjects in the left decubitus position. The abdominal aorta was visualized in the supine position, and the size of the aorta was measured above the level of the umbilicus. In the axial plane, both transverse and anteroposterior diameters with outer-to-outer measurements were established between the renal arteries and the aortic bifurcation. AAA was defined as an abdominal aorta with a size of 30 mm or greater in maximum diameter. If AAA was observed, its maximal anteroposterior diameter was measured on the section perpendicular to its axis.

Statistical analysis

Continuous variables were presented as mean ± standard deviation and categorical variables as number and percentage. The Chi-square test was used for between-group comparison of categorical variables, and Student's t-test was used for comparison of numeric data. Associations between AAA and cardiovascular risk factors or other comorbidities, assessed by odds ratio (OR), were determined using a multivariate binary logistic regression with 95% confidence interval (CI), and two-sided p values were used. The prediction score was derived as a summation of the scores after multiplying the B value and variable of the multivariate analysis. The optimal cutoff value of the prediction score for detecting AAA was determined by receiver operating characteristic (ROC) curve analysis. We used commercial software, SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA) for statistical analyses. In all cases, a p-value < 0.05 was considered statistically significant.

RESULTS

Clinical characteristics of the study population

A total of 5,770 subjects were included in this study and had a mean age of 74.4± 7.6 years, and 2,908 were male (50.4%). The size of the abdominal aorta was calculated in 5,679 subjects (98.4%), including 2,845 males (50.1%). Their baseline characteristics are summarized in **Table 1**. Among the cardiovascular risk factors, hypertension was the most common (64.7%). CAD was found in 1,173 subjects (20.7%).

Size of the abdominal aorta and prevalence of AAA

The mean size of the abdominal aorta was 19.1 ± 5.8 mm. The distribution of abdominal aorta size of the total subjects is shown in **Figure 1A**. Total prevalence of AAA was 2.9% (n = 165). In males, the mean size of the abdominal aorta was 20.1 ± 6.8 mm (**Figure 1B**), whereas in females 18.1 ± 4.4 mm (**Figure 1C**). On average, the abdominal aortas in male subjects were bigger than those of the women by 2.0 mm. Among all AAA patients, 80.6% were males, and 19.4% were females. The prevalence of AAA was higher in men (4.7% vs. 1.1%, p < 0.001) and increased with age (**Figure 2**). The mean diameter of AAA was 43.6 ± 13.4 mm (range: 30 – 91.9 mm).

Prediction of AAA

Comparison of baseline characteristics according to the presence of AAA is listed in **Table 1**. In univariate analysis, age, male sex, hypertension, dyslipidemia, CKD, CAD, and ever-smoker were significantly associated with AAA. The presence of diabetes was negatively associated with AAA. The results of multivariate analysis are summarized in **Table 2**. Age (OR

Table 1. Comparison of baseline clinical characteristics according to presence of AAA

Characteristics	All (n = 5,679)	AAA (−) (n = 5,514)	AAA (+) (n = 165)	OR	95% CI	p value
Age (years)	74.4 ± 7.6	74.3 ± 7.6	78.1 ± 7.6	1.067	1.046–1.089	< 0.001
Male sex	2,845 (50.1)	2,712 (49.1)	133 (80.6)	4.294	2.909–6.339	< 0.001
Body mass index (kg/m²)	23.9 ± 3.4	23.9 ± 3.5	23.6 ± 2.9	1.750	0.997–1.003	0.974
Hypertension	3,676 (64.7)	3,556 (64.5)	120 (72.7)	1.468	1.038–2.077	0.030
Diabetes	1,658 (29.2)	1,628 (29.5)	30 (18.1)	0.530	0.356–0.791	0.002
Dyslipidemia	1,251 (22.0)	1,202 (21.7)	50 (30.3)	1.561	1.113–2.190	0.010
CKD	738 (13.0)	698 (12.6)	40 (24.2)	2.207	1.533–3.179	< 0.001
CAD	1,173 (20.7)	1,098 (71.7)	74 (86.0)	2.413	1.298–4.485	0.005
Ever-smoker	1,632 (28.7)	1,538 (28.6)	94 (56.9)	3.289	2.403–4.502	< 0.001

Data shown are number (%) unless otherwise specified.
AAA: abdominal aortic aneurysm, CAD: coronary artery disease, CI: confidence interval, CKD: chronic kidney disease, OR: Odd ratio.
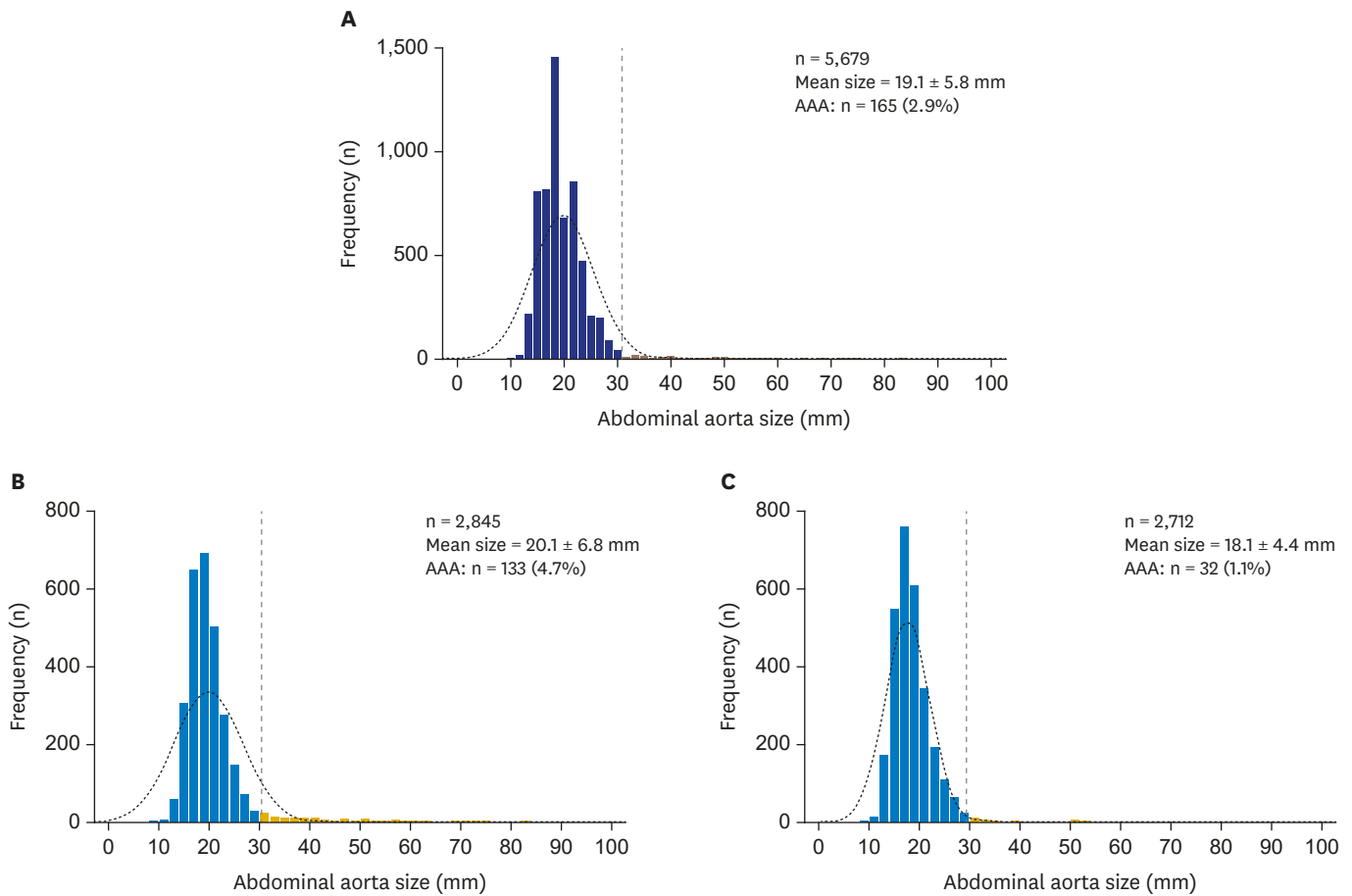
Figure 1. Distribution of abdominal aorta size during transthoracic echocardiography. The prevalence of abdominal aortic aneurysm (AAA) was 2.9% in the entire population (A), with 4.7% in males (B) and 1.1% in females (C).
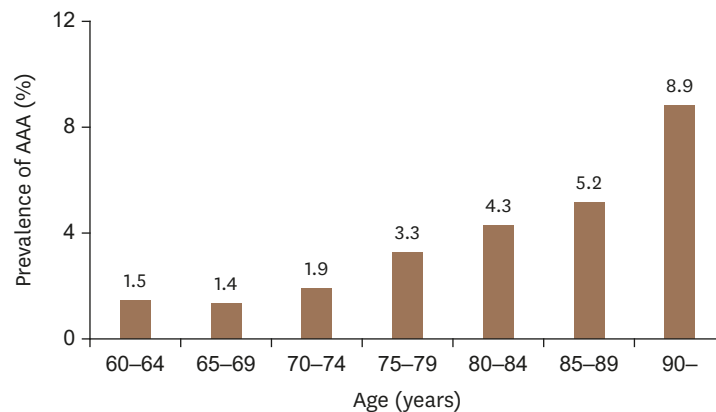

Figure 2. The prevalence of abdominal aortic aneurysm (AAA) by age. The prevalence of AAA increased with age.

= 1.074, 95% CI = 1.050 - 1.097, p < 0.001), male sex (OR = 3.098, 95% CI = 1.971 − 4.870, p < 0.001), dyslipidemia (OR = 1.475, 95% CI = 1.019 − 2.135, p = 0.040), CKD (OR = 1.757, 95% CI = 1.182 − 2.612, p = 0.005), CAD (OR = 2.452, 95% CI = 1.742 − 3.451, p < 0.001), and ever-smoker (OR = 2.090, 95% CI = 1.448 − 3.015, p < 0.001) showed significant positive correlations with AAA. However, diabetes had an inverse relation to AAA (OR = 0.370, 95% CI = 0.242 − 0.565, p < 0.001).

**Table 2.** Multivariate analysis for prediction of abdominal aortic aneurysm

Characteristics	B	Odds ratio	95% confidence interval	p value
Age (years)	0.071	1.074	1.050–1.097	< 0.001
Male sex	1.131	3.098	1.971–4.870	< 0.001
Hypertension	0.335	1.398	0.966–2.021	0.075
Diabetes	−0.994	0.370	0.242–0.565	< 0.001
Dyslipidemia	0.388	1.475	1.019–2.135	0.040
Chronic kidney disease	0.564	1.757	1.182–2.612	0.005
Coronary artery disease	0.897	2.452	1.742–3.451	< 0.001
Ever-smoker	0.737	2.090	1.448–3.015	< 0.001

We calculated prediction scores with the results of multivariate analyses: 0.071 for age; 1.131 for male sex; 0.335 for hypertension; -0.994 for diabetes; 0.388 for dyslipidemia; 0.564 for CKD; 0.897 for CAD; and 0.737 for ever-smoker. If a subject had diabetes, we subtracted 0.994 points from the total prediction score. The prediction score ranged from 3.34 to 10.51, according to the B value of each variable. With ROC curve analysis, AAA can be detected with a sensitivity of 79.4% (95% CI = 72.4 - 85.3) and a specificity of 66.8% (95% CI = 65.5 - 68.1) with a reference value > 6.8 (area under the curve = 0.799, **Figure 3**).

DISCUSSION

In this study, the prevalence of AAA was 2.9%, and AAA was significantly associated with age, male sex, non-diabetes, dyslipidemia, CKD, CAD, and ever-smoker. A prediction score (> 6.8) derived from multivariate analysis can detect AAA with a sensitivity of 79.4% and a specificity of 66.8% in Korean population age > 60 years.

According to summaries in which major AAA screening programs were included in a meta-analysis,[12] most cardiologist and vascular surgeon societies agreed that men over 65 years with a smoking history should be screened once in a lifetime for AAA. However, the guidelines differ for women. The American College of Cardiology and American Heart Association (ACC/AHA), American College of Preventive Medicine (ACPM), European

Reference > 6.8
Sensitivity: 79.4%
Specificity: 66.8%
Area under curve: 0.799
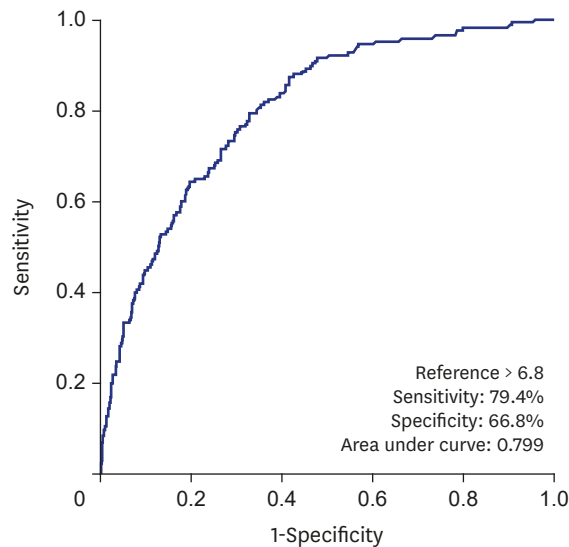
Figure 3. Receiver operating characteristic curve analysis for prediction of abdominal aortic aneurysm.

Society for Vascular Surgery (ESVS), and US Preventive Services Task Force (USPSTF) state not to screen women for AAA, while Screen for Abdominal Aortic Aneurysm Very Efficiently (SAAVE) Act and Society for Vascular Surgery (SVS) recommend screening women with family history.[12] A previous report demonstrated that population-based AAA screening with an ultrasound scan in asymptomatic males > 65 years significantly reduced AAA-related mortality.[13] However, there was no benefit for one-time AAA screening in females.[13] It is crucial to point out that all major nationwide screening programs only included men over 65 years, except one in Chichester, UK, with 9,342 women.[14] There is a need for more research in older females with a high cardiovascular risk profile.

The prevalence of AAA is estimated at 3.5% to 7.7% of men aged 65 to 74 years[15)17] and 1.0% to 1.5% of women of that age.[16)17]. However, a nationwide AAA screening program is expensive, considering the low prevalence of the disease. Furthermore, it is not cost-effective to screen and find small aneurysms, which have a minimal risk of rupture.

Screening for AAA during TTE can provide benefits. In one meta-analysis that included a total of 43,341 participants (23,291 men and 20,050 women), the prevalence of AAA was 3.3% in the entire population (4.6% in men and 1.4% in women).[18] Although we performed this study in subjects with higher risk than the normal population, the prevalence of AAA was 2.9% (4.7% in males and 1.1% in females), which is similar to previous studies. However, the prevalence of AAA in our study was much higher than that of an earlier study performed in Korea patients undergoing echocardiographic examination (27/4939 patients, 0.5%).[10] The age difference (74 ± 8 years vs. 61 ± 13 years) between our study and the previous study could be one possible explanation for the difference. In another study that included patients with significant CAD, the prevalence of AAA was 2.4% (22/920 patients).[11] The prevalence of AAA in our patients who underwent percutaneous coronary intervention was 6.2% (74 cases/1186 patients). The differences in the prevalence of AAA could come from discrepancies of inclusion criteria, including age and significant CAD.

TTE was a good modality for screening AAA and demonstrated high sensitivity (94% to 100%) and specificity (98% to 100%) for detecting AAA. A previous study reported that visualization of the abdominal aorta during TTE was possible in 86% of the total screened cases.[18] In our study, the abdominal aorta was found in 98.4% of the subjects at the time of TTE.

We designed a prediction score using eight parameters from multivariate analysis for use in the selection of high-risk patients who need AAA screening during TTE. Of the parameters, older age, hypertension, dyslipidemia, CKD, CAD, and smoking were positively associated with AAA. However, diabetes had an inverse relation with AAA in our study, like in previous studies. For example, there was a significant inverse association between diabetes and AAA in 17 large population prevalence studies (OR = -0.80, 95% CI = 0.70-0.90, $p < 0.001$).[19] Also, diabetic patients exhibit a slower growth rate of AAA and lower incidence of AAA rupture.[20)21] The exact mechanisms of this inverse correlation are unknown. One possible explanation is that common antidiabetic medications can inhibit the growth of AAA.[20]

Limitations

There are several limitations to this study. First, this was a single-center study with only a limited number of screened subjects in a limited time period compared to the large sample populations in previous studies. Thus, it may be problematic to directly apply these results to the general population. Second, there was a problem with missing or incomplete

information in electronic medical records because patient history was based on patient self-reporting. Third, the study was conducted in a single tertiary healthcare center in which a large proportion of patients had already been diagnosed with other cardiovascular diseases. Thus, systemic error or selection bias is present to some extent. A large study with a general population is needed to evaluate the prevalence of AAA to overcome these limitations.

In conclusion, the prevalence of AAA was 2.9% in subjects age > 60 years during TTE (4.7% in males and 1.1% in females), and AAA was significantly associated with older age, male sex, non-diabetes, dyslipidemia, ever-smoker, CKD, and CAD. A prediction score based on multivariate analysis (> 6.8%) can detect AAA with a sensitivity of 79.4% and a specificity of 66.8%.

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