Original Article

Ankle-Arm Blood Pressure Index and Cardiovascular Risk Factors in Elderly Japanese Men

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Low ankle-arm systolic blood pressure index (AAI) correlates with various cardiovascular risk factors and with risk of subsequent coronary heart disease and stroke in Western countries. However, few epidemiological data are available among Japanese, in whom the reported prevalence of peripheral artery disease is low. We examined the relationship between AAI and cardiovascular risk factors among 1,219 men aged 60 to 79 years in two Japanese communities in 1999 and 2000. The prevalence of AAI<0.90 was 5% in both communities. Hypertension, major ECG abnormality, current smoking, and history of stroke were associated with two- to four-fold higher prevalence of AAI<0.90. One-standard deviation increments of body mass index and high density lipoprotein-cholesterol levels were associated with 60% and 40% lower prevalence of AAI<0.90, respectively. Although the prevalence of low AAI in Japanese elderly men is lower than that reported in the Unites States and European studies, similar correlations of low AAI with cardiovascular risk factors were observed among different ethnic groups. Low AAI is suggested to be a predictor for stroke among Japanese men, which should be confirmed by a prospective study.
(*Hypertens Res* 2003; 26: 377–382)

***Key Words*: ankle-arm index, cardiovascular risk factors, cross-sectional studies, Japanese**

Introduction

Atherosclerotic cardiovascular disease is a major health problem in developed countries. In Japan, cardiovascular disease accounted for 30% of all deaths in 1999 (*1*). Atherosclerotic peripheral arterial disease in the lower extremities is associated with aging, smoking, diabetes, hypertension, and hypercholesterolemia (*2*–*4*). Peripheral arterial disease is associated with increased risk of mortality from cardiovascular disease and all causes (*5*, *6*). The ratio of ankle-to-arm systolic blood pressure (SBP) measured by a Doppler ultrasound device, *i.e*., the ankle-arm index (AAI), has been used to estimate the presence of peripheral arterial disease (*2*, *3*, *6*, *7*). Previous angiography studies have indicated that an AAI of below 0.90 is well correlated with the presence of peripheral arterial disease (*8*). Furthermore, low AAI has been associated with carotid atherosclerosis (*2*), and is a consistent risk factor for incident cardiovascular disease (*9*). However, these observational data were predominantly based on studies from the United States and Europe, and few data are available from Asian countries, where the prevalence of peripheral arterial disease has been reported to be low (*10*). Therefore, we conducted a cross-sectional population-based study of Japanese elderly men to examine the distribution of AAI and its relation to cardiovascular risk factors.

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This study was supported by a Grant-in-Aid for Scientific Research (B) (2) from the Japanese Society for the Promotion of Science (No. 12470092 in 2000–2001).
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Received September 25, 2002; Accepted in revised form January 8, 2003.

Methods

Subjects

The study group was derived from population-based samples of Japanese men aged 60 to 79 years, who lived in two rural communities of Ikawa, northeast Japan (census population of men aged 60–79 in 1995: $n=642$) and Kyowa, central Japan ($n=1{,}492$). Annual cardiovascular risk surveys have been conducted since 1963 in Ikawa and since 1981 in Kyowa by a research team of the Osaka Medical Center for Health Science and Promotion, and the University of Tsukuba. Participants aged 60 to 79 years in the 1999 and 2000 surveys were included in the present study. The numbers of participants were 377 in Ikawa (participation rate=59%) and 842 in Kyowa (56%). We restricted the subjects to men, since men have been reported to have a three-fold higher prevalence of peripheral arterial disease than women (*11*), and thus were considered to be at greater risk. Informed consent was obtained from all participants.

Measurement of Ankle-Arm Index

The AAI ratio was determined by trained technicians using a standard protocol (*2*). In 1999, systolic blood pressure (SBP) was measured at the right brachial artery using a standard sphygmomanometer, and at the right and left posterior tibial arteries using a bi-directional Doppler ES-100V II (Hayashi Denki Co., Kawasaki, Japan). Standard 12-cm blood pressure cuffs were applied to both ankles, and an appropriate size cuff was applied to the right arm. After 5 min of rest and while the subject was in the supine position, SBP levels were measured in the right arm and both ankles and then repeated 30 s later. The cuff was inflated rapidly to 20 mmHg above the palpated SBP and deflated at 2 mmHg per pulse. The first appearance of Korotkoff sound was recorded as SBP. In 2000, AAI was measured automatically using a FORM PWV/ABI device (Colin Co., Komaki, Japan) (*12*, *13*) consisting of an automatic sphygmomanometer (BP-203RPE) and standard 12-cm blood pressure cuffs that were applied to both ankles and one arm to calculate AAI automatically. The lowest AAI in either leg was used for the analysis (*4*).

The comparability of the two measurement systems was tested in 36 subjects. There was no significant difference between the AAI values measured by the two techniques; the mean AAI measured by the manual system was 1.07 ± 0.17 ($\pm$SD) and that by the automatic system was 1.08 ± 0.18 ($p=0.81$; Pearson correlation coefficient=0.82). We therefore used the data on AAI measured in 1999 and 2000 for the analysis.

Measurement of Cardiovascular Risk Factors

Cardiovascular risk factors were measured in both the 1999 and 2000 surveys. Height in stocking feet and weight in light clothing were measured. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2). Seated SBP and diastolic blood pressure (DBP) were measured by trained observers using standard mercury sphygmomanometers on the right arm of participants who had rested for 5 min (*14*). Hypertension was defined as SBP of $\geqq160$ mmHg, and/or DBP of $\geqq95$ mmHg, and/or current treatment with antihypertensive medication, while normotension was defined as SBP of <140 mmHg and DBP of <90 mmHg and no antihypertensive medication. Subjects with blood pressure levels between the above two categories were classified as having borderline hypertension.

A resting ECG was obtained with the subject supine and was coded according to the Minnesota Code, second version (*15*). Major ECG abnormalities were defined and included a ventricular conduction defect (codes 7-1 or 7-2), major Q and QS abnormalities (codes 1-1 or 1-2), minor Q or QS codes (*1–3*) with major ST-T wave abnormalities (codes 4-1 to 4-3 or 5-1 to 5-3), left ventricular hypertrophy [codes (3-1) and (4-1 to 4-3 or 5-1 to 5-3)], isolated major ST-T-wave changes, atrial fibrillation (code 8-3), and first-degree atrioventricular block (code 6-1). A color photograph of the right fundus was taken and graded according to Scheie's classification (*16*). Hypertension- or arteriosclerotic-related changes of grades 2 or higher were regarded as a significant hypertensive change in the retinal arterioles.

For measurement of serum lipids and glucose, non-fasting blood was drawn from seated participants into a plain, siliconized glass tube, and the serum was separated. The serum was transported on dry ice to the Osaka Medical Center for Health Science and Promotion, and stored at -70 ºC until measurement. Total cholesterol and high density lipoprotein (HDL)-cholesterol were measured using enzymatic methods by an automatic analyzer (Hitachi 7250; Hitachi Medical Corp., Hitachi, Japan) at the Osaka Medical Center for Health Science and Promotion, an international member of the US National Cholesterol Reference Method Laboratory Network (CRMLN). This laboratory has been standardized since 1975 by the CDC-NHLBI Lipid Standardization Program provided by the Centers for Disease Control and Prevention (Atlanta, USA) and successfully met the criteria for both precision and accuracy of cholesterol and triglycerides measurements (*17*). Serum glucose was measured by the hexokinase method using the same instrument.

An interview was conducted to ascertain the alcohol intake per day, number of cigarettes smoked per day, use of medication for diabetes mellitus, and past history of stroke and coronary heart disease. Persons who smoked $\geqq1$ cigarette per day were defined as current smokers, and those who had not smoked for 3 months or more were defined as ex-smokers. An interviewer assessed the usual weekly intake of alcohol in units of "go" (a traditional Japanese unit of volume corresponding to 23 g of ethanol) (*18*, *19*). Diabetes mellitus was defined as a fasting glucose level of 7.8 mmol/l

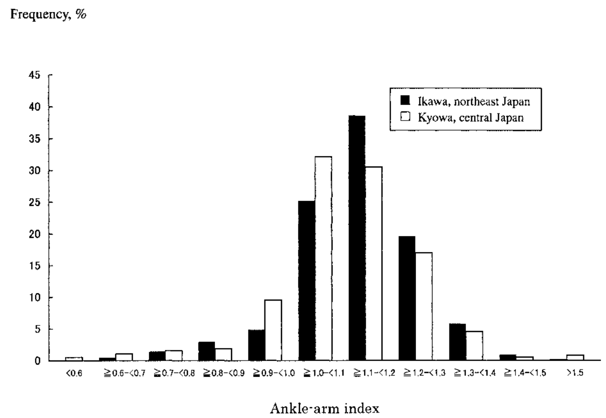

Fig. 1. *Distribution of ankle-arm index (AAI) values among population-based samples of Japanese elderly men in two communities.*

or more, a non-fasting glucose level of 11.1 mmol/l or more, or use of medication for diabetes. Information on the past history of stroke and coronary heart disease was supplemented by systemic surveillance data for the incidence of these endpoints since 1963. In that surveillance system, the final diagnoses were made by the standardized criteria based on clinical symptoms, ECG, cardiac enzymes, and CT and/or MRI (*19*, *20*).

Statistical Analysis

Age and community-adjusted mean values and prevalence of cardiovascular disease risk factors were examined according to six AAI categories: $<$0.90, 0.90–0.99, 1.00–1.09, 1.10–1.19, 1.20–1.29 and ≧1.30, and differences across the categories were tested by the analysis of covariance and χ^2 tests. Multiple linear regression analysis was used to estimate predicted changes in AAI associated with changes in selected cardiovascular risk factors. The odds ratio of AAI $<$0.90 was also calculated using multiple logistic regression analysis. All analyses were conducted using the SAS statistical package version 6.12 (SAS Institute Inc., Cary, USA). All p values for statistical tests were two-tailed, and values of $p<0.05$ were regarded as indicating statistical significance.

Results

The frequency distribution of AAI is shown in Fig. 1. The prevalence of AAI$<$0.90 was 5% in both communities.

Table 1 shows the mean age and the age- and community-adjusted values of cardiovascular risk factors according to six AAI categories. There was a positive linear correlation between BMI and AAI, and an inverse linear correlation between current smoking and AAI. Compared with men with AAI≧0.90, those with AAI$<$0.90 had lower mean values of BMI and HDL-cholesterol, and were more likely to have a current smoking habit, hypertension, major ECG abnormalities, and history of stroke and coronary heart disease. There were no differences in the mean values of SBP, DBP, total cholesterol, or alcohol intake, or in the prevalence of retinal changes, ex-smoking, or diabetes mellitus between men with AAI$<$0.90 and those with higher AAI.

We also examined predicted changes in AAI associated with increments of cardiovascular risk factors and calculated odds ratios (95% confidence interval (CI)) of AAI$<$0.90 associated with cardiovascular risk factors, adjusted for community (Table 2). BMI and HDL-cholesterol levels were positively associated with AAI. Age, total cholesterol, current smoking, ex-smoking and history of stroke were inversely associated with AAI. As for the odds ratio of AAI$<$0.90, 1-SD increments of BMI and HDL-cholesterol levels were associated with 60% and 40% lower prevalence of AAI$<$0.90, respectively. Hypertension, current smoking, and history of stroke were associated with three- to four-fold higher prevalence of AAI$<$0.90. When hypertension was defined as SBP≧140 mmHg and/or DBP≧90 mmHg, the multivariate adjusted odds ratio (95% CI) of low AAI for hypertension was 2.2 (1.1, 4.1) (not shown in the table).

Major ECG abnormalities were associated with a two-fold higher prevalence of low AAI; history of coronary heart disease was also associated with a two-fold higher prevalence of low AAI, but this trend did not reach the level of statistical significance due to the low prevalence of coronary heart disease.

Discussion

The present population-based study showed that the prevalence of low AAI ($<$0.90) was 5% among Japanese men aged 60–79 years. The prevalence in our study was lower than those reported by studies in the United States and Europe: 12% in the Cardiovascular Health Study of American men and women aged 65 and over (*2*), 14% in Danish men and women aged 60 (*11*), 10% in Italian men and women aged 65 and over (*21*), 19% in the Rotterdam Study of Netherlandic men and women aged 55 and over (*3*), and 9% in the Edinburgh Artery Study of Scottish men and women aged 55–74 (*4*). In spite of the low prevalence of low AAI among rural Japanese men, the correlation between cardiovascular risk factors and low AAI was similar and even stronger than that reported in previous studies of the United States and Europe, where low AAI was associated with subsequent risk of cardiovascular diseases (*2*, *3*, *11*, *21*). Our results showed that hypertension, current smoking, history of stroke, low HDL-cholesterol levels, and low BMI were strong determinants of low AAI.

Hypertension was associated with a three-fold higher prevalence of low AAI in the present study. The Cardiovascular Health Study (*2*) and the Rotterdam Study (*3*) showed that hypertension was associated with a two-fold higher prevalence of low AAI (AAI$<$0.90). The Framingham study

Table 1. Age-Adjusted Mean Values and Proportions of Cardiovascular Risk Factors According to Ankle-Arm Index (AAI) among 1,219 Men Aged 60–79 Years in Japanese Rural Communities

	AAI						*p* for overall difference
	<0.90	0.90–0.99	1.00–1.09	1.10–1.19	1.20–1.29	≧1.30	
Number	60	86	328	444	222	79	
Age (years)	70	69	69	68	68	67	0.04
Body mass index (kg/m²)	22.0	22.2	22.9	23.7	24.3	25.2	<0.001
Systolic blood pressure (mmHg)	144	138	139	139	140	138	0.28
Diastolic blood pressure (mmHg)	81	78	81	81	81	80	0.47
Hypertension (%*)	63	35	41	45	50	43	0.008
Major ECG abnormality (%)	34	17	14	16	15	24	0.005
Retinal changes† (%)	4	3	3	4	3	3	0.88
Total cholesterol (mmol/l)	4.97	4.95	5.08	5.07	5.10	4.79	0.08
HDL-cholesterol (mmol/l)	1.34	1.39	1.47	1.46	1.47	1.36	0.04
Current smoker (%)	56	49	44	41	31	32	<0.001
Ex-smoker (%)	38	37	42	44	46	38	0.63
History of stroke (%)	15	4	5	4	5	2	0.01
History of coronary heart disease (%)	6	0	1	2	3	3	0.06
Alcohol intake (g/day)	26	22	22	26	23	25	0.17
Diabetes mellitus (%)	15	16	10	12	11	6	0.31

*Percent populations among each category of AAI are presented. †Retinal changes denote hypertensive and/or arteriosclerotic changes in the fundus. HDL, high density lipoprotein.

Table 2. Multivariate-Adjusted Predicted Change in Ankle-Arm Index (AAI) and Odds Ratios (95% CI) of AAI<0.90 Associated with Changes in Cardiovascular Risk Factors among Men Aged 60–79 Years in Japanese Communities

	Predicted changes in AAI (95% CI)	Odds ratios of low AAI (95% CI)
Age, 5 years	−0.01 (−0.02, −0.01)***	1.2 (0.9, 1.6)
Body mass index, 3.1 kg/m²	0.04 (0.03, 0.05)***	0.4 (0.3, 0.6)***
Hypertension, yes	−0.02 (−0.03, −0.002)*	2.7 (1.4, 5.1)**
Major ECG abnormality, yes	−0.02 (−0.03, 0.01)	2.1 (1.1, 3.9)*
Retinal changes, yes	−0.03 (−0.07, 0.01)	1.1 (0.2, 5.6)
Total cholesterol, 0.88 mmol/l	−0.01 (−0.02, −0.01)***	1.2 (0.9, 1.7)
HDL-cholesterol, 0.41 mmol/l	0.02 (0.01, 0.02)***	0.6 (0.4, 0.8)**
Current smoker, yes	−0.04 (−0.07, −0.02)***	3.8 (1.1, 13.0)*
Ex-smoker, yes	−0.03 (−0.05, −0.01)***	2.6 (0.8, 9.4)
Alcohol intake, 24 g/day	−0.0001 (−0.01, 0.01)	1.1 (0.8, 1.4)
History of stroke, yes	−0.05 (−0.08, −0.01)***	2.9 (1.2, 6.8)*
History of coronary heart disease, yes	−0.01 (−0.05, 0.03)	2.3 (0.6, 8)
Diabetes mellitus, yes	−0.01 (−0.03, 0.01)	1.0 (0.4, 2.2)

Test for significance: * $p<0.05$, ** $p<0.01$, *** $p<0.001$. CI, confidence interval; HDL, high densty lipoprotein.

(*22*) showed that hypertension increased the risk of intermittent claudication 2.5-fold among men.

History of stroke was associated with a three-fold increase in the prevalence of low AAI in the present study, which was similar to the increase reported by the Cardiovascular Health Study (*2*). This finding is in line with the positive association between hypertension and low AAI, because hypertension is a strong risk factor for stroke. Other cross-sectional studies have reported that history of cardiovascular disease was associated with a two-fold higher prevalence of low AAI (*2*, *4*, *23*). Recent prospective studies (*24*, *25*) have shown that low AAI was strongly associated with the incident of ischemic stroke. In those studies, however, the relationship was substantially reduced after adjustment for major cardiovascular risk factors, probably because AAI is a marker of generalized atherosclerosis and the cumulative effects of cardiovascular risk factors.

Current smoking was associated with a four-fold higher prevalence of low AAI. Our results corroborate previous findings that current smoking resulted in a two- to three-fold increase in the risk of low AAI among individuals in the United States and Europe (*2*, *3*, *11*, *21*), as well as among

Japanese men (*26*). In previous studies, ex-smoking was associated with decreased AAI (*2*) and a two-fold higher risk of low AAI (*11*). In the present study, ex-smoking was associated with a three-fold higher prevalence of low AAI, but this trend did not reach the level of statistical significance.

Our study also showed that a 1-SD (0.4 mmol/l) increase in HDL-cholesterol levels was associated with a 40% lower prevalence of low AAI. In the Cardiovascular Health Study (*2*), the same increment of HDL-cholesterol was associated with a 15% lower prevalence of low AAI. These findings are consistent in that HDL-cholesterol levels were reduced in patients with peripheral arterial disease (*27*).

In this study, BMI was positively associated with AAI, as shown in previous studies (*2*, *26*, *28*). The exact reason for this finding is not clear. One possible explanation is that ankle blood pressure values may have been overestimated due to the larger circumferences of ankles among obese men (*29*).

In the present study, serum total cholesterol level was inversely associated with AAI, and the association between the odds ratio of low AAI and a 1-SD increment of total cholesterol was of borderline significance. This association was consistent with the results of previous studies (*2*, *3*).

Major ECG abnormality was associated with a two-fold higher prevalence of low AAI, which was consistent with a result from the Cardiovascular Health Study in the United States (*2*).

Several US and European studies have reported that diabetes mellitus is associated with a two- to four-fold higher prevalence of low AAI (*2*, *3*). However, such a relationship was not confirmed in our study, probably due to the low statistical power arising from the relatively lower prevalence of diabetes in Japan compared to Western countries (*30*).

In conclusion, we found similar correlations between low AAI and cardiovascular risk factors, except for diabetes, among elderly Japanese men as were previously reported for men and women in the United States and Europe, although low AAI was less prevalent among Japanese than among Western ethnic groups. Also, low AAI was suggested to be a predictor for stroke among Japanese men, which should be confirmed by a prospective study.

Acknowledgements

The authors are grateful to Prof. Aaron R. Folsom, University of Minnesota, Minneapolis, USA, for his valuable comments.

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