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The Prevalence of Aortic Calcification in Japanese Compared to White and Japanese-American Middle-Aged Men is Confounded by the Amount of Cigarette Smoking

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Abstract

Background—Prevalence of coronary artery calcification (CAC) in Japanese men is lower than in white and Japanese-American men. It is unclear if aortic calcification (AC) strongly linked to smoking is also lower in Japanese men who have many times higher smoking prevalence compared to US men.

Methods—We conducted a population-based study of 903 randomly-selected men aged 40–49 years: 310 Japanese men in Kusatsu, Japan, 301 white men in Allegheny County, U.S., and 292 Japanese men in Hawaii, U.S. (2002–2006). The presence of AC was assessed by electron-beam tomography. AC was defined as Agatston aortic calcium scores (AoCaS) >0 and 100.

Results—Japanese (35.8%) had significantly less AoCaS>0 compared to both white (68.8%, $p<0.001$) and Japanese-American (62.3%, $p<0.001$) but similar AoCaS 100 (19.4%, 18.3%, 22.6%, respectively, $p=0.392$). Pack-years of smoking, which was highest in Japanese, was the most important single associate of AC in all populations. Additionally age, low-density-lipoprotein cholesterol (LDL-C), and triglycerides in Japanese; body-mass index (BMI) in white; and BMI, LDL-C, hypertension, diabetes, and lipid medications in Japanese-American were

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independent associates of AC. The risk of AC using either cut points adjusted for pack-years of smoking and additional risk factors was lower in Japanese compared to both white and Japanese-American. AC and CAC had moderately positive and significant correlations in Japanese ($r=0.26$), white ($r=0.39$), and Japanese-American ($r=0.45$).

Conclusions—Prevalence of AC defined both >0 and >100 was significantly lower in Japanese than in white and Japanese-American men after adjusting for cigarette smoking and additional risk factors

Keywords

Epidemiology; risk factors; atherosclerosis; aorta; calcification; electron-beam tomography; Caucasian; Japanese; Japanese American

INTRODUCTION

Coronary artery calcification (CAC) is increasingly used as a marker of subclinical atherosclerosis. Aortic calcification (AC), a less widely used measure of atherosclerosis, has been linked in many reports to CAC [1, 2] and cardiovascular morbidity and mortality [3–5]. Unlike CAC, the prevalence of AC and its risk factors have received little attention especially in non-white populations. Moreover, the heterogeneity of available data as far as populations studied, aortic segment examined, and imaging techniques used, preclude fair comparisons between different populations. In fact, few studies used electron-beam tomography (EBT) scanning to detect AC compared to conventional computed tomography or plain X ray [6]. The different scoring systems between different imaging techniques and sometimes within the same imaging technique (for example, plain X-ray) further complicates across population comparisons.

Comparing geographical and racial differences in coronary heart disease (CHD) burden and attempts to interpret the reasons for these differences is an essential step in CHD prevention. CHD mortality remains very low in Japan compared to the US [7, 8] despite major dietary changes and increases in CHD risk factors [7, 9]. We have reported lower CAC in Japanese men (in Japan) compared to both white and Japanese-American men (in US) [10]. Epidemiologic data comparing Japanese-white EBT-detected AC is lacking. Therefore it is unclear whether AC that has been strongly linked to smoking in multiple races [11–14] is also lower in Japanese men who have many times higher smoking prevalence than both white and Japanese-American men [10, 15]. The objectives of the current study were to compare AC and its risk factors between Japanese, white and Japanese-American men using standardized methods and to examine the relation between AC and CAC in the three populations.

METHODS

I- Study population

The study protocol was described in detail elsewhere [10, 16]. Briefly, between 2002 and 2006 a population-based samples of 903 men aged 40–49 were randomly selected; 313 Japanese men from Basic Residents' Register of Kusatsu, Japan, 310 white men from voter registration list of Allegheny County, U.S., and 303 Japanese men from lists of offspring of Japanese American fathers participated in the Honolulu Heart Program in Hawaii, U.S. All participants were without clinical cardiovascular disease, type 1 diabetes, non-skin cancer, renal failure, and genetic familial hyperlipidemias. We excluded those with missing data. Our final sample was 310 Japanese, 301 whites, and 292 Japanese Americans. The study was approved by the Institutional Review Boards of Shiga University Medical Science,

Otsu, Japan; University of Pittsburgh, Pittsburgh, Pennsylvania, US; and Kuakini Medical Center, Honolulu, Hawaii. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology[17].

II- Exposure assessment

A self-administered questionnaire was used to obtain information on demography, smoking habits, alcohol drinking, medication use, and other factors. Current smoking was defined as smoking cigarettes over the last month. Pack-years of smoking were calculated as years of smoking multiplied by the number of cigarettes smoked per day divided by 20. Alcohol drinking was defined as drinking alcohol at least two days per week. Ethanol consumption per day (g/day) was estimated assuming that concentrations of alcohol were 5% for beer, 12% for wine, and 40% for liquor. Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or use of anti-hypertensive medications. Diabetes mellitus was defined as fasting serum glucose level ≥ 7.0 mmol/liter or use of anti-diabetic medications.

III- Outcome assessment

AC and CAC were assessed using EBT. As previously described,[10] EBT was done using a GE-Imatron C150 EBT scanner (GE Medical Systems, South San Francisco, U.S.) at the three centers using standardized methods. A total of 30–40 contiguous 3 mm thick transverse images were obtained from the level of the aortic root to the apex of the heart to evaluate CAC. Then, the scanner was set to acquire 6mm images from the aortic arch to the iliac bifurcation to evaluate AC. Scanners were calibrated regularly by technicians following a standardized protocol. One trained reader at the Cardiovascular Institute, University of Pittsburgh Medical Center in Pittsburgh, Pennsylvania read aortic and coronary scanning from all centers using the widely accepted Agatston scoring method [18]. The reader was blinded to participant's characteristics and the study centers. The reproducibility of aortic and coronary scans was very high (intraclass correlation of 0.98 and 0.99, respectively).

Statistical analyses

The distributions of Agatston aortic calcium scores (AoCaS) across the three populations were examined. The presence of AC was defined as AoCaS >0 [12, 13, 19] and ≥ 100 [19] as reported by studies using EBT. Similarly, CAC was defined as coronary calcium score (CCS) >0 and ≥ 10 [12, 13, 19]. Linear associations of categorical variables (e.g. hypertension frequency) with ordinal AoCaS groups (0, 1–99, and ≥ 100) were tested using gamma test. Linear associations of continuous variables with ordinal AoCaS groups were tested using analysis of variance (ANOVA) if normal and Jonckheere-Terpstra test if normality is violated. Population differences (e.g. White-Japanese) in AoCaS prevalence after adjusting for (stratification by) groups of pack-years of smoking were examined using Mantel-Haenszel Chi square.

The effect on AoCaS of all potential risk factors in all populations was examined by running race-specific crude and multiple-adjusted logistic regression models with AoCaS >0 and AoCaS ≥ 100 as an outcome and risk factors as potential associates. Population differences in AoCaS prevalence after adjusting for different sets of risk factors were examined using logistic regression models (Models 1 through 4 as shown in Table 3) with AoCaS >0 and AoCaS ≥ 100 as an outcome and race as a potential associate after adjusting for these risk factors. The discrimination capabilities of these models to detect high aortic calcium were evaluated by estimating the area under the Receiver Operating Characteristic (ROC) curve. The fit of data was evaluated using Hosmer and Lemeshow test. The correlation between AoCaS and CCS was examined using Spearman rho. P-values from all tests were two-tailed.

P-value <0.05 was considered as significant. SPSS software (release 17.0, SPSS Inc., Chicago, U.S.) was used for all statistical analyses.

RESULTS

With the exception of lower BMI and higher HDL cholesterol, Japanese men had a less favorable or similar profile of many risk factors compared to white men, including total and LDL cholesterol, triglycerides, hypertension, diabetes, current smoking, and pack-years of smoking. Japanese-American men who were similarly obese as white, had poorer risk factor profile compared to Japanese with the exception of cigarette smoking, and LDL cholesterol. Japanese-American men had significantly greater rates of hypertension and diabetes and levels of triglycerides and glucose than white men (data are not shown). The Japanese in this study consumed fish (at least two times a week) more than the whites and Japanese American (83.6%, 21.4%, 31.7%, respectively, $p<0.001$ for each).

The distribution of AoCaS in all populations was very skewed to the right, especially among Japanese who had the majority of AoCaS as zero (Figure 1). Japanese (35.8%) had significantly less AoCaS>0 compared to both white (68.8%, $p<0.001$) and Japanese-American (62.3%, $p<0.001$) but similar AoCaS 100 (19.4%, 18.3%, 22.6%, respectively, $p=0.392$) (Figure 1). In all populations, AoCaS had significant positive associations with age, triglycerides, serum glucose, current smoking, and pack-years of smoking (Table 1). Additionally, in Japanese men, AoCaS had significant positive associations with total and LDL cholesterol and fibrinogen. In both white and Japanese-American men, AoCaS had significant positive associations with body mass index (BMI), waist circumference, systolic and diastolic blood pressure, diabetes, serum insulin, and C-reactive protein (Table 1). HDL cholesterol and fibrinogen in white and hypertension and receiving lipid medication in Japanese-American were also associated with AoCaS (Table 1). Very similar results were obtained by crude logistic regression models (data are not shown).

There was a dose-response relationship between pack-years of smoking and prevalence of either AoCaS>0 or AoCaS 100 in all populations (Figure 2). Both white and Japanese-American had significantly higher AoCaS>0 and 100 compared to Japanese after adjusting for pack-years of smoking (Mantel-Haenszel p -value <0.001 for all). Pack-years of smoking, which was highest in Japanese, was the most important single independent associate of AoCaS in all populations irrespective of the cut point (Table 2). Additionally age, LDL cholesterol, and triglycerides in Japanese; BMI in White; and BMI, LDL cholesterol, hypertension, diabetes, and lipid medications in Japanese-American were independent associates of AoCaS using one or the other cut points (Table 2). Interestingly, no significant race-specific interaction terms have been detected between smoking and other important risk factors (data are not shown).

Japanese men had a significantly lower odds of having AoCaS>0 compared to white men in an age-adjusted model (OR=0.24; 95% CI 0.17, 0.34; $p<0.001$). Additional adjustment for pack-years of smoking and additional risk factors further reduced the already small OR (Table 3). Although Japanese men had similar odds of having AoCaS 100 compared to white men in an age-adjusted model (OR=1.06; 95% CI 0.70, 1.60; $p=0.797$), further adjusting for pack-years of smoking and additional risk factors resulted in a highly significant lower odds of having AoCaS 100 in Japanese compared to white men (OR=0.33; 95% CI 0.19, 0.59; $p<0.001$) (Table 3). The above results for both AoCaS>0 and AoCaS 100 were replicated when comparing Japanese to Japanese-American. The estimated area under the ROC curve ranged between 0.79 and 0.81 in the above fully adjusted models, indicating good discrimination capabilities of these models. Goodness-of-fit statistic showed well calibrated data in these models. On the other hand, white had higher

odds of AoCaS>0 but similar AoCaS 100 compared to Japanese-American irrespective of the degree of adjustment.

AC and CAC had moderately positive and significant correlations in Japanese ($r=0.26$, $p<0.001$), white ($r=0.39$, $p<0.001$), and Japanese-American men ($r=0.45$, $p<0.001$). For example, among those having AoCaS>0, 44.1% of Japanese, 58.9% of white, and 61.5% of Japanese-American men had CCS>0. Similarly among those having AoCaS 100, 25.0% of Japanese, 58.2% of white, and 60.6% of Japanese-American men had CCS 10.

DISCUSSION

To our knowledge, this is the first epidemiologic study to examine AC in Japanese, white, and Japanese-American men. While Japanese men in the current study had lower crude AC prevalence than both white and Japanese-American men using AoCaS>0 but not AoCaS 100, they had the lowest prevalence of AC using both cut points after adjusting for cigarette smoking and additional risk factors.

Available data describing AC in Japanese compared to other populations are derived from autopsy studies. In older autopsy studies, Japanese have lower atherosclerotic burden in both coronaries and aorta compared to US white or Japanese-American [20, 21]. Nevertheless, a relatively recent autopsy study [22] showed that Japanese men and women aged 15–34 years, who had lower atherosclerotic raised lesions in the coronaries, had similar abdominal aorta or even higher thoracic aorta atherosclerotic raised lesions compared to white and black Americans of similar age and sex. This could be due to the accelerated rate of AC compared to CAC [1, 23]. It is possible that westernization of life style in Japan, which was linked to progression of atherosclerosis,[24] would affect aorta at an accelerated rate than coronaries [14]. Closely related to our finding, Chinese in the Multi-Ethnic Study of Atherosclerosis (MESA) had similar AC but lower CAC compared to white populations [25].

The associations between AC and traditional cardiovascular risk factors were not uniform across studied populations. More frequent associations were observed in both white and Japanese-American than observed in Japanese men. Our findings in white were generally similar to previous EBT reports [1, 12, 13, 23, 26]. In these studies, age, smoking, hypertension, diabetes, hypercholesterolemia, lower HDL cholesterol but not BMI were frequently associated with AC. We could not identify any epidemiologic study describing associations of AC with cardiovascular risk factors among Japanese or Japanese-American men. However, our findings were generally consistent with findings from autopsy-based studies in both populations [14, 27]. Age, blood pressure, serum cholesterol and BMI in Japanese [27] as well as blood pressure, serum cholesterol, and smoking in Japanese-American were associated with aortic atherosclerosis [14].

Pack years of smoking was the single most important independent associate of AC in all studied populations. Smoking was reported to be an important risk factor for the presence and progression of AC in many populations [1, 4, 11–14, 26]. Moreover, smoking was a stronger risk for AC than CAC in many epidemiologic studies [1, 11–14]. It is not fully understood why the confounding effect of smoking on prevalence of AoCaS (at 100 cut point) among Japanese is not seen with CCS. However, the stronger relative risk [1, 11–14] and the accelerated atherosclerotic process at aorta compared to coronaries at all ages [1, 23] and the relatively younger age of our population (who started smoking at similar age) may partly explain why coronaries escaped such confounding effect of smoking. Moreover, the lower AC prevalence in Japanese compared to other populations after adjusting for pack-years of smoking suggest that Japanese may have some non-genetic protective factors

against AC. We have previously reported that higher levels of serum marine-derived n-3 fatty acids in Japanese than whites contribute to the difference in CAC [10]. However, neither high fish consumption nor higher levels of serum marine-derived n-3 fatty acids in Japanese contributed to the difference in AC (data not shown). This discrepancy may be due to the fact that aortic calcification represents mainly medial calcification whereas coronary calcification primarily represents intimal calcification of focal plaque and atheromatous burden in the coronary artery [28].

AoCaS and CCS were moderately and positively correlated in all studied populations. Similar findings were reported in the few studies that compared EBT measured AC and CAC scores in the US [1, 2]. Allison and colleagues [1] reported significant correlations between coronary and both proximal ($r=0.35$) and distal ($r=0.40$) aorta in middle aged US men. Despite having different risk factors, [12] MSEA researcher reported that AC is a strong predictor of CAC independent of CV risk factors in multiple ethnic groups [2]. We could not find studies comparing AC and CAC in the Japanese or Japanese-American men. AoCaS measured by CT may have a potential significance in CVD prevention. The earlier onset of AC than other subclinical markers of atherosclerosis including CAC [1, 23] could be an advantage in early disease. Moreover, the large size of the aorta and relative lack of image artifact from motion make it ideal for radiographic quantitative imaging.[12]

This report is original in comparing AC and AC risk factors in multiple populations using a standardized population-based data. However, several limitations should be noted. First, the study is cross-sectional in design and cannot establish causality between risk factors and AC. Second, the generalizability of the study results is limited to men of respective populations in their 40s. Third, white men in this study may be healthier than the general white population based on the rate of cigarette smoking. Fourth, obesity may cause image noises in EBT, resulting in higher prevalence of AC in white men. However, such effect is expected to be minimal since we adjusted for BMI that was reported to adequately control for this confounding [29].

In conclusion, unlike inconsistent crude results, prevalence of AC defined both >0 and >100 was significantly lower in Japanese than in white and Japanese-American men after adjusting for cigarette smoking and additional risk factors

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List of abbreviations

AC	Aortic Calcification
CAC	Coronary Artery Calcification
AoCaS	Aortic Calcium Score
CCS	Coronary Calcium Score
EBT	Electron-Beam Tomography
CHD	Coronary Heart Disease
BMI	Body-Mass Index
LDL	Low-Density-Lipoprotein Cholesterol

HDL High-Density-Lipoprotein Cholesterol

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Fig. 1A

Fig. 1B

Figure 1. Distribution of aortic calcium score (AoCaS) in Japanese, white, and Japanese-American men (2002–2006)

Very skewed AoCaS distributions in all populations (A). Japanese have significantly less AoCaS >0 compared to both white and Japanese-American but similar AoCaS ≥100 (B)

Fig. 2A

Fig. 2B

Figure 2. Prevalence of aortic calcium score (AoCaS) >0 and 100 by pack-years of smoking in Japanese, white, and Japanese-American men (2002–2006)

There is a significant dose-response relationship (as indicated by p for trend) between pack-years of smoking and prevalence of both AoCaS>0 (A) and AoCaS 100 (B) in all populations.

Table 1

Comparison of potential risk factors by aortic calcium score (AoCaS) groups in Japanese, white, and Japanese-American men (2002–2006)^a

	Japanese AoCaS (n=310)				White AoCaS (n=301)				Japanese-Americans AoCaS (n=292)			
	0 (n=199)	1–99 (n=51)	100 (n=60)	0 (n=94)	1–99 (n=152)	100 (n=55)	0 (n=110)	1–99 (n=116)	100 (n=66)	0 (n=110)	1–99 (n=116)	100 (n=66)
Age (years)	44.6±2.9	45.6±2.4	46.3±2.2 ***	44.5±2.7	44.9±2.9	45.9±2.5 **	45.7±3.0	46.0±2.8	46.8±2.3 *	45.7±3.0	46.0±2.8	46.8±2.3 *
BMI (Kg/m ²)	23.5±2.7	24.6±3.5	23.3±3.0	25.9±2.8	28.4±3.9	29.7±5.4 ***	26.2±4.0	29.2±4.1	28.6±4.3 ***	26.2±4.0	29.2±4.1	28.6±4.3 ***
Waist (cm)	84.9±8.0	88.5±8.6	83.9±7.5	92.4±7.9	100.4±10.5	103.7±13.5 ***	89.1±10.1	97.1±9.8	95.8±11.7 ***	89.1±10.1	97.1±9.8	95.8±11.7 ***
Hypertension (%)	23.1%	39.2%	28.3%	11.7%	13.8%	21.8%	19.1%	38.8%	47.0% ***	19.1%	38.8%	47.0% ***
SBP (mmHg)	124.7±15.1	124.2±16.0	127.5±18.8	119.8±11.0	122.8±10.9	125.8±11.2 **	125.0±11.9	129.2±12.9	129.0±12.7 *	125.0±11.9	129.2±12.9	129.0±12.7 *
DBP (mmHg)	76.1±11.3	77.1±12.9	77.8±12.7	71.1±8.8	73.4±8.1	75.3±9.3 **	75.5±8.8	79.5±10.0	78.1±8.0 *	75.5±8.8	79.5±10.0	78.1±8.0 *
Total cholesterol (mmol/L)	5.46±0.89	5.89±1.00	5.90±0.89 ***	5.42±0.99	5.52±0.97	5.54±0.96	5.21±0.90	5.40±0.93	5.48±1.07 *	5.21±0.90	5.40±0.93	5.48±1.07 *
LDL (mmol/L)	3.28±0.90	3.79±1.00	3.59±0.88 **	3.42±0.89	3.54±0.88	3.46±0.81	3.05±0.78	3.22±0.84	3.15±0.99	3.05±0.78	3.22±0.84	3.15±0.99
HDL (mmol/L)	1.41±0.34	1.35±0.34	1.39±0.40	1.33±0.35	1.20±0.31	1.16±0.33 **	1.36±0.35	1.27±0.30	1.31±0.29	1.36±0.35	1.27±0.30	1.31±0.29
Triglycerides (mmol/L) ^b	1.51 (1.10–2.03)	1.50 (1.28–1.81)	1.71 (1.31–2.42) *	1.33 (0.97–1.63)	1.47 (1.06–2.15)	1.67 (1.08–2.64) **	1.32 (0.95–2.00)	1.74 (1.21–2.66)	1.80 (1.07–3.60) **	1.32 (0.95–2.00)	1.74 (1.21–2.66)	1.80 (1.07–3.60) **
Diabetes (%)	5.5%	5.9%	8.3%	0.0%	2.6%	10.9% **	8.2%	10.3%	27.3% **	8.2%	10.3%	27.3% **
Glucose (mmol/L)	5.85±0.67	5.94±0.94	6.22±1.82 *	5.42±0.45	5.60±0.55	6.12±1.53 ***	5.98±0.84	6.27±1.26	6.60±1.40 **	5.98±0.84	6.27±1.26	6.60±1.40 **
Insulin (pmol/L)	70.8±29.0	77.3±35.5	68.2±30.4	90.1±39.9	108.2±57.4	123.1±74.2 ***	87.9±39.5	110.1±72.8	119.4±69.4 **	87.9±39.5	110.1±72.8	119.4±69.4 **
CRP (mg/L) ^b	0.28 (0.15–0.65)	0.36 (0.18–0.52)	0.36 (0.17–1.02)	0.78 (0.35–1.46)	1.18 (0.56–2.00)	0.99 (0.67–1.67) **	0.49 (0.24–1.02)	0.71 (0.41–1.32)	0.78 (0.35–1.57) **	0.49 (0.24–1.02)	0.71 (0.41–1.32)	0.78 (0.35–1.57) **
Fibrinogen (umol/L)	7.32±1.93	7.79±1.67	7.94±2.08 *	8.06±1.59	8.69±2.27	9.04±2.07 **	9.26±2.08	9.20±1.98	9.49±2.57	9.26±2.08	9.20±1.98	9.49±2.57
Smoker (%)	43.2%	49.0%	70.0% **	3.2%	6.6%	16.4% *	9.1%	11.2%	21.2% *	9.1%	11.2%	21.2% *
Pack-years ^b	13 (0.3, 25.0)	21 (9.0, 29.0)	31.5 (23.3, 44.8) ***	0 (0.0, 0.0)	0 (0.0, 0.9)	0 (0.0, 20.0) ***	0 (0.0, 0.8)	0 (0.0, 0.8)	3.5 (0.0, 14.6) ***	0 (0.0, 0.8)	0 (0.0, 0.8)	3.5 (0.0, 14.6) ***
Alcohol drinkers (%)	68.3%	58.8%	71.7%	46.8%	42.1%	45.5%	40.0%	36.2%	40.9%	40.0%	36.2%	40.9%
Ethanol (g/day) ^b	14.3 (2.6, 40.0)	12 (1.5, 50.0)	34.3 (3.8, 54.7)	5.0 (1.0, 17.6)	4.1 (0.9, 14.7)	4.1 (0.8, 16.0)	1.7 (0.0–26.1)	0.4 (0.0–24.7)	2.8 (0.0–31.8)	1.7 (0.0–26.1)	0.4 (0.0–24.7)	2.8 (0.0–31.8)
Lipid medications (%)	3.0%	3.9%	5.0%	11.7%	8.6%	21.8%	15.5%	21.6%	39.4% **	15.5%	21.6%	39.4% **

^aMean ± standard deviation unless mentioned otherwise

^bMedian and inter-quartile range

* p 0.05

p<0.01

p<0.001 (p for trend)

BMI: body-mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, LDL: low-density-lipoprotein cholesterol, HDL: high-density-lipoprotein cholesterol, CRP: C-reactive protein.

Table 2

Multiple-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for potential risk factors of aortic calcium score (AoCaS) >0 and 100 in Japanese, white, and Japanese-American men (2002–2006)^a

	AoCaS>0			AoCaS 100		
	Japanese N=308	White N=293	Japanese-Americans N=291	Japanese N=308	White N=293	Japanese-Americans N=291
Age (years)	1.12 [*] (1.01–1.24)	1.08 (0.97–1.19)	1.04 (0.95–1.14)	1.15 [*] (1.00–1.32)	1.09 (0.97–1.24)	1.10 (0.97–1.25)
BMI (Kg/m ²)	1.09 (0.68–1.75)	2.33 ^{***} (1.51–3.59)	1.88 ^{***} (1.28–2.74)	0.52 [*] (0.28–0.96)	1.25 (0.83–1.88)	0.76 (0.50–1.15)
Hypertension	1.55 (0.80–3.01)	0.98 (0.41–2.34)	2.10 [*] (1.07–4.13)	0.89 (0.39–2.03)	0.97 (0.38–2.47)	2.00 (0.93–4.33)
Diabetes	1.02 (0.32–3.23)	>10.00 (0, >10.00)	0.91 (0.36–2.32)	1.84 (0.38–8.87)	5.00 (0.98–25.45)	2.73 [*] (1.11–6.69)
LDL (mmol/L)	1.69 ^{***} (1.28–2.24)	1.16 (0.87–1.53)	1.47 [*] (1.06–2.04)	1.41 [*] (1.01–1.98)	1.15 (0.82–1.63)	1.24 (0.84–1.82)
HDL (mmol/L)	1.02 (0.76–1.39)	0.87 (0.62–1.21)	0.98 (0.70–1.38)	1.01 (0.70–1.47)	1.01 (0.68–1.51)	1.08 (0.72–1.63)
Triglycerides (mmol/L)	1.28 (0.87–1.90)	1.19 (0.78–1.81)	1.09 (0.85–1.39)	2.10 ^{***} (1.31–3.39)	1.25 (0.89–1.75)	1.10 (0.85–1.41)
CRP (mg/L)	0.81 (0.53–1.25)	1.16 (0.79–1.69)	1.25 (0.91–1.73)	0.99 (0.69–1.43)	0.83 (0.51–1.34)	1.30 (0.94–1.79)
Fibrinogen (umol/L)	1.06 (0.75–1.50)	1.22 (0.88–1.69)	0.76 (0.53–1.08)	0.95 (0.61–1.48)	1.18 (0.85–1.65)	0.96 (0.65–1.42)
Pack-years	2.03 ^{***} (1.55–2.65)	3.48 ^{***} (1.39–8.74)	1.98 [*] (1.15–3.42)	2.43 ^{***} (1.77–3.31)	2.58 ^{***} (1.54–4.32)	2.80 ^{***} (1.73–4.55)
Ethanol (g/day)	1.05 (0.80–1.38)	0.57 (0.28–1.16)	0.86 (0.68–1.09)	1.18 (0.84–1.64)	0.78 (0.41–1.48)	1.02 (0.79–1.31)
Lipid medications	0.83 (0.19–3.57)	0.75 (0.32–1.78)	1.91 (0.90–4.08)	0.79 (0.12–5.06)	2.36 (0.96–5.80)	2.87 ^{***} (1.29–6.37)

^a ORs were calculated for each standard deviation increase in all continuous variables except age. Abbreviations as in Table 1

* p 0.05

** p<0.01

*** p<0.001

Table 3

Odds ratio (ORs) and 95% confidence interval (CIs) for aortic calcium score (AoCaS) >0 and 100 in bi-racial men populations (2002–2006)

	AoCaS-0				AoCaS 100			
	N	OR (95% CI)	p-value	ROC	OR (95% CI)	p-value	ROC	
Japanese compared to White								
Model-1	611	0.24 (0.17–0.34)	p<0.001	0.71	1.06 (0.70–1.60)	0.797	0.64	
Model-2	611	0.10 (0.06–0.16)	p<0.001	0.75	0.33 (0.19–0.59)	p<0.001	0.76	
Model-3	611	0.13 (0.08–0.23)	p<0.001	0.80	0.31 (0.16–0.62)	p<0.001	0.78	
Model-4	603	0.15 (0.08–0.25)	p<0.001	0.80	0.32 (0.16–0.65)	0.002	0.79	
Japanese compared to Japanese-Americans								
Model-1	602	0.37 (0.26–0.52)	p<0.001	0.68	0.97 (0.64–1.45)	0.866	0.62	
Model-2	602	0.17 (0.11–0.26)	p<0.001	0.74	0.29 (0.16–0.50)	p<0.001	0.76	
Model-3	601	0.20 (0.12–0.33)	p<0.001	0.78	0.26 (0.13–0.50)	p<0.001	0.79	
Model-4	601	0.20 (0.12–0.35)	p<0.001	0.79	0.30 (0.15–0.60)	0.001	0.81	
White compared to Japanese-Americans								
Model-1	593	1.45 (1.03–2.06)	0.035	0.57*	0.89 (0.59–1.34)	0.567	0.61	
Model-2	593	1.50 (1.05–2.14)	0.027	0.64	0.86 (0.56–1.33)	0.492	0.70	
Model-3	592	1.58 (1.06–2.36)	0.024	0.75	1.15 (0.71–1.85)	0.568	0.75	
Model-4	584	1.50 (1.00–2.27)	0.053	0.75	1.27 (0.77–2.09)	0.342	0.77	

Model 1: Adjusted for age

Model 2: Adjusted for age and pack-years

Model 3: Further adjusted for BMI, hypertension, diabetes, LDL, HDL, triglycerides

Model 4: Further adjusted for C-reactive protein, fibrinogen, lipid-lowering medications, and ethanol

ROC, area under the Receiver Operating Characteristic curve estimated using predictive probabilities of logistic regression models in detecting AoCaS at a given cut point. All p-values were <0.001 except one (*) was 0.006