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Significantly greater progression of intima-media thickness of the carotid artery in Japanese American men than white men—the ERA JUMP Study:

Racial difference in subclinical vascular disease

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Abstract

Background—Although Westernized lifestyle was associated with increased coronary heart disease (CHD) morbidity and mortality in first and second generation Japanese Americans; CHD mortality was reported to be lower in them than whites. Risk profile of CHD for third and fourth generation Japanese Americans is not known. We compared progression of CIMT between third or fourth generation Japanese Americans and whites.

Methods—Population-based samples of 473 men (Japanese Americans=227 and whites=246) aged 40–49 years at baseline and free of clinical cardiovascular disease were examined for CIMT at baseline (2002–06) and follow-up (2007–13). CIMT was read centrally at the University of Pittsburgh. Analysis of covariance was used to compare annualized progression of CIMT between Japanese Americans and whites, adjusting for cardiovascular risk factors and baseline CIMT.

Results—Progression of CIMT was significantly greater in Japanese Americans than whites both before and after adjusting for covariates (mean in $\mu\text{m}/\text{year}$ [95% confidence interval]): 14.4 (12.3,

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16.4) vs 9.8 (7.8, 11.7), $P<0.05$ and 15.1 (13.1, 17.1) vs 9.1 (7.2, 11.0), $P<0.05$, respectively. Age, total cholesterol/high-density lipoprotein-cholesterol, and diabetes in Japanese Americans and age, hypertension, and lipid medication in whites were significantly associated with progression of CIMT.

Conclusions—The significantly greater progression of CIMT in Japanese Americans than whites might suggest a higher burden of CHD in Japanese Americans than whites in the future. The current study identifies Japanese Americans as an important target group for prevention of CHD. Future research assessing carotid plaque in addition to CIMT is warranted.

Introduction

Research has associated incorporation of Western culture (acculturation) with adverse risk factors of coronary heart disease (CHD) and increased CHD morbidity and mortality in Japanese Americans (1, 2). Further, using vital statistic data of the 1950 census, rates of CHD mortality in Japanese Americans were reported to be intermediate between low rates in Japan and high rates in the US (3). The participants in the above mentioned study were either first or second generation Japanese Americans. It is likely that third or fourth generation Japanese Americans have a worse risk profile of CHD than first or second generation Japanese Americans due to adopting Westernized lifestyle since birth.

Although the Framingham Risk Score (FRS) is reported to overestimate the risk of CHD in first and second generation Japanese Americans, estimation of the risk of CHD using the FRS in third or fourth generation Japanese Americans is not known (4). Moreover, the current rates of CHD in third or fourth generation Japanese Americans compared to whites are not known. Therefore, it might be of clinical importance to use subclinical atherosclerosis such as intima-media thickness of the carotid artery (CIMT) as a surrogate marker to estimate the risk of CHD in third or fourth generation Japanese Americans.

From a cross-sectional analysis of the Electron-Beam Computed Tomography and Risk Factor Assessment among Japanese and U.S. Men in the Post World War II Birth Cohort (ERA JUMP) study, we previously reported significantly higher baseline CIMT in third and fourth generation Japanese Americans than whites independent of traditional cardiovascular risk factors (5). In this study, we aim to compare progression of CIMT between Japanese Americans and whites. We also examined which risk factors were associated with progression of CIMT in Japanese Americans and whites so that ethnicity-specific risk factors can be targeted to prevent progression of CIMT.

Materials and methods

We have described the methods for selection of participants previously (6). Briefly, during 2004 to 2007, 613 men were randomly selected: 310 white men from the Allegheny County, Pennsylvania (6) and 303 Japanese American men from a representative sample of offspring of fathers who participated in the Honolulu Heart Program, Honolulu, Hawaii (7, 8). These offspring were third or fourth generation of Japanese Americans without ethnic admixture (7). The participants were without clinical cardiovascular disease, type 1 diabetes, or other severe diseases (6). The current analyses include 473 participants (227 Japanese Americans

and 246 whites) who underwent carotid-ultrasound at baseline and during the follow-up from 2008 to 2013. Informed consent was obtained from all participants. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the Institutional Review Boards of the University of Pittsburgh, Pennsylvania and the Kuakini Medical Center, Honolulu, Hawaii.

All participants underwent a physical examination, lifestyle questionnaire, and laboratory examination as described previously (6, 7). Body weight and height were measured while participants were wearing light clothing without shoes. Body-mass index (BMI) was calculated as weight (kg)/height squared (m^2). Blood pressure was measured in the right arm of the seated participants after they emptied their bladder and sat quietly for five minutes, using an automated sphygmomanometer (BP-8800; Colin Medical Technology, Komaki Japan), and an appropriate sized cuff. The average of two measurements was used in the analyses. Venipuncture was performed early in the clinic visit after a 12 hour fast. Plasma and serum samples were stored at $-80^{\circ}C$, shipped to the University of Pittsburgh, and were assayed for glucose, insulin, and lipids including total cholesterol, triglycerides, low-density lipoprotein-cholesterol, and high-density lipoprotein-cholesterol (HDL-C).

Participants were considered current smokers if they reported current use of cigarettes or having stopped smoking within the last 30 days. Hypertension and diabetes were defined using the criteria by the 7th Report of the Joint National Committee (9) and the 2013 American Diabetes Association guidelines (10).

The scanning procedures have been described in detail elsewhere (6, 11). Briefly, before the study initiated, sonographers were trained for carotid ultrasound scanning provided by the Ultrasound Research Laboratory, University of Pittsburgh. A Toshiba 140A scanner at Pittsburgh and a Siemens Acuson Cypress scanner at Honolulu were used. The right and left common-carotid arteries, carotid-bulbs, and internal-carotid arteries were scanned. A total of 8 segments were scanned: the far and near wall of the common-carotid arteries 1 cm proximal to the carotid-bulbs, the far wall of the carotid-bulbs and the internal-carotid arteries. The scans were recorded on videotape and sent to the Ultrasound Research Laboratory for scoring. Trained readers digitized the best image for scoring and then using semi-automated edge detection software measured the average CINT across all the 8 segments. Continuous quality improvement procedures were employed to assure the accuracy of measurements (12). The same protocol and ultrasound machines were utilized for measuring CINT at repeated scans 4–6 years later. The intra-class correlation coefficients for repeated scans between machines, sonographers, and readers were 0.90, 0.96, and 0.98, respectively.

We calculated mean (median) and standard deviation (interquartile range) for continuous variables and proportions for categorical variables. For comparing continuous and categorical variables between Japanese Americans and whites, we used t-tests or Wilcoxon rank-sum tests and chi-square tests. We defined annual progression of CINT as: (follow-up average CINT – baseline average CINT)/follow-up (years). We performed analysis of covariance (ANCOVA) to compare annual mean progression of CINT between the two races, adjusting for the following covariates from the baseline visit: age (years), BMI (kg/

m²), current smoking (yes or no), hypertension (yes or no), diabetes (yes or no), total cholesterol/HDL-C ratio, and lipid medication (yes or no). We also compared unadjusted and covariate-adjusted segment-specific progression of CIMT in the common-carotid arteries, carotid-bulbs, and internal-carotid arteries in Japanese Americans and whites.

We built race-specific models using multiple linear regressions to examine risk factor associated with progression of CIMT in each racial subgroup, adjusting for baseline age, BMI, current smoking, hypertension, diabetes, total cholesterol/HDL-C ratio, and lipid medication. We log transformed total cholesterol/HDL-C because its distribution was non-normal. Total cholesterol/HDL-C ratio was used because it demonstrated the strongest association with CIMT among lipids in our study and earlier studies (13). Further, we adjusted all models for baseline CIMT because it was significantly and inversely associated with progression of CIMT in the whole sample (-0.26 , $P<0.05$) and each race (Japanese Americans (-0.35 , $P<0.05$) and whites (-0.19 , $P<0.05$)). P -values <0.05 were considered significant. P -values <0.1 were considered significant for testing effect-modification. All P -values were 2-tailed. All statistical analyses were performed using SAS software, version 9.3, Cary, NC, US.

In secondary analyses, in order to assess whether progression of risk factors affected progression of CIMT, we considered annual change in BMI, systolic blood pressure (SBP), total cholesterol/HDL-C ratio, and glucose as covariates in addition to baseline variables (age, BMI, SBP, glucose, total cholesterol/HDL-C ratio, medication for hypertension, lipid medication, and medication for diabetes). Annual change in risk factors were calculated in the same manner as mentioned above for annual change in CIMT, i.e., (follow-up levels – baseline levels)/follow-up (years). For multivariable analyses we used forward selection and selected all risk factors associated with outcome at $P = 0.25$ in univariable analyses. In multivariable analyses, we entered covariates with small P -values followed by covariates with large P -values. Covariates were dropped from the final model with $P = 0.1$. We forced baseline age, baseline CIMT, hypertension medication, and lipid medication in all models.

Results

Table 1 describes the characteristics of the study population at baseline. Japanese Americans were significantly older than whites. Japanese Americans had significantly higher systolic blood pressure, glucose, and prevalence of hypertension, diabetes and lipid medication use than whites. In contrast, Japanese Americans had significantly lower low-density lipoprotein-cholesterol and total cholesterol/HDL-C ratio than whites. In the follow-up, the prevalence of hypertension, use of lipid medication, and diabetes increased in both races but more in Japanese Americans than whites. The baseline characteristics of participants who attended the follow-up ($n=473$) did not differ from the baseline characteristics of the total participants ($n=613$) with respect to any of the biomarkers (Supplemental Table S1).

Table 2 presents the baseline CIMT, follow-up CIMT, and follow-up duration in the study population; all were greater in Japanese Americans than whites. Progression of CIMT was significantly greater in Japanese Americans than whites in the unadjusted analyses, (mean in $\mu\text{m}/\text{year}$ [95% confidence interval]): 14.4 (12.3, 16.4) vs. 9.8 (7.8, 11.7), $P<0.05$,

respectively (Figure 1A). Moreover, progression of CIMT remained significantly greater in Japanese Americans than whites even after adjusting for cardiovascular risk factors, 15.1 (13.1, 17.1) vs. 9.1 (7.2, 11.0), $P < 0.05$, respectively (Figure 1B).

Table 3 shows the risk factors associated with progression of CIMT in Japanese Americans and whites. In Japanese Americans, age and total cholesterol/HDL-C were positively associated and diabetes was negatively associated with progression of CIMT. In whites, age and hypertension were positively associated and lipid medication was negatively associated with progression of CIMT. There was a significant interaction between diabetes and use of lipid medication in Japanese Americans ($b = -0.01$, $P = 0.06$).

In secondary analyses where we considered annual change in risk factors as covariates in addition to baseline risk factors, progression of CIMT was nevertheless greater in Japanese Americans than whites (Supplemental Table S2). Only Japanese American race and medication for diabetes were associated with progression of CIMT in the final model.

Discussion

Progression of CIMT was significantly greater in middle-aged Japanese American men than in white men. The greater progression of CIMT in Japanese Americans than whites was not completely explained by differences in cardiovascular risk factors. Although age was associated with progression of CIMT in both races, associations with other risk factors were different by race, i.e., total cholesterol/HDL-C and diabetes in Japanese Americans and hypertension and lipid medication in whites. These differences in association or risk factors for progression of CIMT between races can be utilized for prevention of ethnic-specific progression of CIMT.

Our finding of greater progression in Japanese Americans than whites is in contrast to recently reported slower progression of CIMT in Chinese and Hispanics than whites in the Multi-Ethnic Study of Atherosclerosis (MESA) (14). The MESA is a population-based prospective cohort study of 6814 participants free of clinical CVD and an average age of 60.3 (9.4) years at baseline with a follow-up of 9.4 (0.5) years. Majority of Chinese and Hispanic participants in the MESA were not born in the US (around 96% Chinese and 70% Hispanic) and therefore less likely to be exposed to the Western culture as opposed to third or fourth generation Japanese Americans in our study (15). The Bogalusa Heart Study and the Atherosclerosis Risk in Communities study also examined racial differences in progression of CIMT between whites and blacks (13, 16, 17); these studies did not find any racial difference in progression of CIMT.

In our study, diabetes was negatively associated with progression of CIMT in Japanese Americans in contrast to previously reported positive association (17). This negative association of diabetes with progression of CIMT in Japanese Americans may be due to widespread use of lipid medications in participants with diabetes (54% of participants with diabetes were on lipid-lowering medications compared to 15% of the participants without diabetes); lipid medications lead to slowed progression of CIMT (18). The negative association between diabetes and progression of CIMT may also be explained by negative

interaction between diabetes and lipid medication indicating that the effect of diabetes on progression of CIMT was not deleterious in participants with diabetes on lipid medication compared to participants with diabetes not on lipid medication. After excluding participants on lipid medications, diabetes was not associated with progression of CIMT in Japanese Americans (data not shown).

Japanese Americans were followed for an average of two more years than whites. Although in our study the outcome was annual progression of CIMT, biologically a non-linear progression in two extra years of follow-up may be suggested as a reason for greater progression in Japanese Americans than whites. The longer period of follow-up may be ruled out as an explanation for greater progression in Japanese Americans than whites in our study by the observation that the distribution of progression of CIMT was normal in both Japanese Americans and whites (Supplemental Figure S1 A and B).

The significantly greater progression of CIMT in Japanese Americans than whites was driven by progression in the carotid-bulb and internal-carotid artery (Supplemental Figure S2 A–F); CIMT in these segments of the carotid artery is associated with risk factors of atherosclerosis (19). Furthermore, progression of CIMT remained greater in Japanese Americans than whites even among participants without diabetes and hypertension (Supplemental Figure S3 A and B). The propensity of significantly greater progression of CIMT in Japanese Americans than whites in the carotid-bulb and internal-carotid artery and greater progression in participants without diabetes and hypertension may suggest that Japanese Americans are more vulnerable than whites to accelerated atherosclerosis.

In the past, CHD was reported to be lower among Japanese Americans than whites (3). Two recent studies reported lower prevalence or mortality of CHD in Japanese Americans than whites (20, 21). However, in these studies, majority of participants were either first or second generation Japanese Americans (3, 22). It is highly likely that first and second generation immigrants had retained a traditional Japanese lifestyle compared to third and fourth generation Japanese Americans in our study who adopted Western lifestyle since birth. In our study, significantly greater progression of IMT in Japanese Americans than whites, therefore, might suggest a higher burden of CHD in these Japanese Americans than whites in the future.

In population-based studies, the association between progression of CIMT and CHD among healthy participants is still under debate. A recent meta-analysis by the PROG-IMT project (individual progression of carotid intima-media thickness as a surrogate of vascular risk) found a significant positive association between mean of two ultrasound measures of CIMT and CHD, but not between progression of CIMT and CHD (23). The baseline CIMT is significantly and positively associated with CHD independent of cardiovascular risk factors (24). However, the association between progression of CIMT and CHD in this meta-analysis may have been underestimated because: slow progression of atherosclerosis and difficulty to detect slow rates of progression in healthy individuals (25), introduction of survivor selection bias because the participants with previous cardiovascular events or death due to cardiovascular disease were excluded, and calculating mean reduces error while the

difference or change compounds it. The use of progression of CIMT in predicting CHD requires further validation.

The strengths of our study are that it is a population-based study with a high follow-up rate, CIMT and other cardiovascular risk factors were assessed in a standardized manner and It provides a unique opportunity to examine risk profile of CHD in third and fourth generation Japanese Americans. Progression of CIMT remained greater in Japanese Americans than whites after accounting for education, a surrogate marker of socio-economic status (data not shown). Progression of CIMT was greater in Japanese Americans than whites even without adjusting for the baseline CIMT (data not shown) that may rule out the potential of measurement error. This study must be interpreted in the context of its known limitations as well. The sample only included men, thus the results cannot be generalized to women. Unfortunately, our study does not have information on follow-up plaque, a stronger predictor of CHD than CIMT (26, 27).

In conclusion, we found a greater progression of CIMT in third and fourth generation Japanese American men than white men independent of cardiovascular risk factors. The current study identifies Japanese Americans as an important target group for prevention of CHD. Future research assessing carotid plaque in addition to CIMT is warranted especially in context of overestimation of risk of CHD by the FRS in Japanese Americans.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Marmot MG, Syme SL. Acculturation and coronary heart disease in Japanese-Americans. *American journal of epidemiology*. 1976 Sep; 104(3):225–47. [PubMed: 961690]
2. Watanabe H, Yamane K, Egusa G, Kohno N. Influence of westernization of lifestyle on the progression of IMT in Japanese. *Journal of atherosclerosis and thrombosis*. 2004; 11(6):330–4. [PubMed: 15644586]
3. Gordon T. Mortality experience among the Japanese in the United States, Hawaii, and Japan. *Public health reports*. 1957 Jun; 72(6):543–53. [PubMed: 13432134]
4. D'Agostino RB Sr, Grundy S, Sullivan LM, Wilson P. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. *JAMA : the journal of the American Medical Association*. 2001 Jul 11; 286(2):180–7. [PubMed: 11448281]
5. Sekikawa A, Curb JD, Ueshima H, El-Saed A, Kadowaki T, Abbott RD, et al. Marine-derived n-3 fatty acids and atherosclerosis in Japanese, Japanese-American, and white men: a cross-sectional study. *Journal of the American College of Cardiology*. 2008 Aug 5; 52(6):417–24. [PubMed: 18672160]
6. Sekikawa A, Ueshima H, Kadowaki T, El-Saed A, Okamura T, Takamiya T, et al. Less subclinical atherosclerosis in Japanese men in Japan than in White men in the United States in the post-World War II birth cohort. *American journal of epidemiology*. 2007 Mar 15; 165(6):617–24. [PubMed: 17244636]

7. Abbott RD, Ueshima H, Rodriguez BL, Kadowaki T, Masaki KH, Willcox BJ, et al. Coronary artery calcification in Japanese men in Japan and Hawaii. *American journal of epidemiology*. 2007 Dec 1; 166(11):1280–7. [PubMed: 17728270]
8. Kagan A, Harris BR, Winkelstein W Jr, Johnson KG, Kato H, Syme SL, et al. Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: demographic, physical, dietary and biochemical characteristics. *Journal of chronic diseases*. 1974 Sep; 27(7–8):345–64. [PubMed: 4436426]
9. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA : the journal of the American Medical Association*. 2003 May 21; 289(19):2560–72. [PubMed: 12748199]
10. Standards of medical care in diabetes--2013. *Diabetes care*. 2013 Jan; 36(Suppl 1):S11–66. [PubMed: 23264422]
11. Matthews KA, Kuller LH, Sutton-Tyrrell K, Chang YF. Changes in cardiovascular risk factors during the perimenopause and postmenopause and carotid artery atherosclerosis in healthy women. *Stroke; a journal of cerebral circulation*. 2001 May; 32(5):1104–11.
12. Thompson T, Sutton-Tyrrell K, Wildman R. Continuous quality assessment programs can improve carotid duplex scan quality. *The journal of Vascular Technology*. 2001 Jan; 25(1):33–9.
13. Johnson HM, Douglas PS, Srinivasan SR, Bond MG, Tang R, Li S, et al. Predictors of carotid intima-media thickness progression in young adults: the Bogalusa Heart Study. *Stroke; a journal of cerebral circulation*. 2007 Mar; 38(3):900–5.
14. Tattersall MC, Gassett A, Korcarz CE, Gepner AD, Kaufman JD, Liu KJ, et al. Predictors of carotid thickness and plaque progression during a decade: the Multi-Ethnic Study of Atherosclerosis. *Stroke; a journal of cerebral circulation*. 2014 Nov; 45(11):3257–62.
15. Lutsey PL, Diez Roux AV, Jacobs DR Jr, Burke GL, Harman J, Shea S, et al. Associations of acculturation and socioeconomic status with subclinical cardiovascular disease in the multi-ethnic study of atherosclerosis. *American journal of public health*. 2008 Nov; 98(11):1963–70. [PubMed: 18511718]
16. Nguyen QM, Toprak A, Xu JH, Srinivasan SR, Chen W, Berenson GS. Progression of segment-specific carotid artery intima-media thickness in young adults (from the Bogalusa Heart Study). *The American journal of cardiology*. 2011 Jan; 107(1):114–9. [PubMed: 21146698]
17. Chambless LE, Folsom AR, Davis V, Sharrett R, Heiss G, Sorlie P, et al. Risk factors for progression of common carotid atherosclerosis: the Atherosclerosis Risk in Communities Study, 1987–1998. *American journal of epidemiology*. 2002 Jan 1; 155(1):38–47. [PubMed: 11772783]
18. Amarencu P, Labreuche J, Lavalley P, Touboul PJ. Statins in stroke prevention and carotid atherosclerosis: systematic review and up-to-date meta-analysis. *Stroke; a journal of cerebral circulation*. 2004 Dec; 35(12):2902–9.
19. Polak JF, Person SD, Wei GS, Godreau A, Jacobs DR Jr, Harrington A, et al. Segment-specific associations of carotid intima-media thickness with cardiovascular risk factors: the Coronary Artery Risk Development in Young Adults (CARDIA) study. *Stroke; a journal of cerebral circulation*. 2010 Jan; 41(1):9–15.
20. Palaniappan L, Wang Y, Fortmann SP. Coronary heart disease mortality for six ethnic groups in California, 1990–2000. *Annals of epidemiology*. 2004 Aug; 14(7):499–506. [PubMed: 15310526]
21. Holland AT, Wong EC, Lauderdale DS, Palaniappan LP. Spectrum of cardiovascular diseases in Asian-American racial/ethnic subgroups. *Annals of epidemiology*. 2011 Aug; 21(8):608–14. [PubMed: 21737048]
22. Palaniappan LP, Araneta MR, Assimes TL, Barrett-Connor EL, Carnethon MR, Criqui MH, et al. Call to action: cardiovascular disease in Asian Americans: a science advisory from the American Heart Association. *Circulation*. 2010 Sep 21; 122(12):1242–52. [PubMed: 20733105]
23. Lorenz MW, Polak JF, Kavousi M, Mathiesen EB, Volzke H, Tuomainen TP, et al. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. *Lancet*. 2012 Jun 2; 379(9831):2053–62. [PubMed: 22541275]

24. van den Oord SC, Sijbrands EJ, ten Kate GL, van Klaveren D, van Domburg RT, van der Steen AF, et al. Carotid intima-media thickness for cardiovascular risk assessment: systematic review and meta-analysis. *Atherosclerosis*. 2013 May; 228(1):1–11. [PubMed: 23395523]
25. Stary HC, Chandler AB, Glagov S, Guyton JR, Insull W Jr, Rosenfeld ME, et al. A definition of initial, fatty streak, and intermediate lesions of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Circulation*. 1994 May; 89(5):2462–78. [PubMed: 8181179]
26. Duivenvoorden R, Stroes ES, Hovingh GK. The value of screening for carotid plaque in patients referred for echocardiography. *The Canadian journal of cardiology*. 2014 Oct; 30(10):1148–9. [PubMed: 25154805]
27. Inaba Y, Chen JA, Bergmann SR. Carotid plaque, compared with carotid intima-media thickness, more accurately predicts coronary artery disease events: a meta-analysis. *Atherosclerosis*. 2012 Jan; 220(1):128–33. [PubMed: 21764060]

Figure 1. Annual progression (mean [95% confidence interval]) of average intima-media thickness of the carotid artery (CIMT) in Japanese American men and white men in the ERA JUMP Study unadjusted (A) and adjusted (B)

Table 1

Baseline and follow-up characteristics of participants in the ERA JUMP study

	Baseline		Follow-up	
	Japanese American men (n=303)	White men (n=310)	Japanese American men (n=227)	White men (n=246)
Age (years)	46.3 (2.8)	45.0 (2.9) *	-	-
BMI (kg/m ²)	27.7 (4.5)	27.9 (4.2)	28.1 (4.8)	28.7 (4.5)
Current Smokers (%) [†]	11.9	6.9	8.8	6.1
SBP (mmHg)	126.4 (11.7)	122.6 (10.9) *	124.2 (12.7)	125.7 (13.0)
Hypertension (%) [§]	29.1	13.8 *	39.7	25.2 *
LDL-C (mmol/L)	3.1 (0.80)	3.5 (0.82) *	3.1 (0.99)	3.4 (0.86) *
Total Cholesterol/HDL-C	4.0 (3.4, 5.0)	4.7 (3.9, 5.5) *	3.9	4.5 *
Lipid Medication (%)	24.2	13.1 *	38.3	22.0 *
Glucose (mmol/L)	5.9 (5.6, 6.3)	5.6 (5.2, 5.9) *	6.2 (5.4, 6.3)	6.0 (5.5, 6.2) *
Diabetes (%) ^{//}	13.2	3.7 *	16.4	9.4 *

Categorical variables are expressed as (%) and continuous variables as mean (standard deviation) or median (interquartile range)

BMI, body-mass index; SBP, systolic blood pressure; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol

* Significant at $P < 0.05$
[†] Current smokers were considered if participants reported current use of cigarettes or having stopped smoking within the last 30 days

[§] Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or use of antihypertensive medications

^{//} Diabetes was defined as fasting serum glucose level ≥ 126 mg/dl or use of medications for type 2 diabetes

Table 2

Baseline CIMT, follow-up CIMT, and follow-up duration in the ERA JUMP Study

	Japanese American men (n=227)	White men (n=246)	P Value
Baseline Average CIMT (µm)	724.0 (122.2)	676.6 (103.7)	<0.05
Follow-up Average CIMT (µm)	820.3 (131.7)	722.4 (114.0)	<0.05
Follow-up time (years)	6.5 (0.50)	4.6 (0.21)	<0.05

mean (standard deviation) are presented

CIMT, intima-media thickness of the carotid artery

Table 3

Regression coefficients of progression of CIMT on cardiovascular risk factors (adjusted for baseline CIMT)

	Japanese Americans (n=226)		Whites (n=245)	
	b (95% CI)	P	b (95% CI)	P
Age	0.001 (0.0001, 0.002)	<0.05	0.001 (0.001, 0.002)	<0.05
BMI	0.001 (0.00001, 0.001)	0.05	0.00005 (−0.0005, 0.0005)	0.86
Log-total Cholesterol/HDL-C	0.009 (0.001, 0.017)	<0.05	−0.002 (−0.010, 0.005)	0.09
Current Smoking [*]	0.0003 (−0.006, 0.006)	0.92	0.006 (−0.001, 0.013)	0.09
Hypertension [†]	0.002 (−0.003, 0.007)	0.40	0.006 (0.001, 0.011)	<0.05
Diabetes [§]	−0.008 (−0.014, −0.001)	<0.05	−0.005 (−0.015, 0.005)	0.34
Lipid medication	−0.002 (−0.007, 0.004)	0.51	−0.006 (0.011, 0.001)	<0.05

CIMT, carotid-intima media thickness, CI, confidence interval, BMI, body-mass index; HDL-C, high-density lipoprotein-cholesterol

^{*} Current smokers were considered if participants reported current use of cigarettes or having stopped smoking within the last 30 days

[†] Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or use of antihypertensive medications

[§] Diabetes was defined as fasting serum glucose level ≥126 mg/dl or use of medications for type 2 diabetes