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Intima-media thickness of the carotid artery and the distribution of lipoprotein subclasses in men aged 40–49 between whites in the U.S. and the Japanese in Japan for the ERA JUMP Study

Akira Sekikawa, MD, **Hirotsugu Ueshima, MD**, **Kim Sutton-Tyrrell, DrPH**, **Takashi Kadowaki, MD**, **Aiman El-Saed, MD**, **Tomonori Okamura, MD**, **Tomoko Takamiya, MD**, **Yoshiki Ueno, MD**, **Rhobert W. Evans, PhD**, **Yasuyuki Nakamura, MD**, **Daniel Edmundowicz, MD**, **Atsunori Kashiwagi, MD**, **Hiroshi Maegawa, MD**, and **Lewis H. Kuller, MD**
From the Department of Epidemiology, Graduate School of Pubic Health (A.S., K.T., A.E., T.T., R.W.E., and L.H.K.), Cardiovascular Institute (D.E.), University of Pittsburgh, Pittsburgh, USA, the Department of Health Science (H.U., T.K., T.O.), the Department of Internal Medicine: Endocrinology and Metabolism (A.K., H.M.), and the Department of Internal Medicine: Cardiology (Y.U., Y.N.), Shiga University of Medical Science, Otsu, Japan

Abstract

In men in the post World War II birth cohort, *i.e*., men aged 40–49, whites in the United States (U.S.) had significantly higher levels of intima-media thickness of the carotid arteries (IMT) than the Japanese in Japan. The difference remained after adjusting for traditional risk factors. Primary genetic effects are unlikely, given the degree to which IMT is increased in the Japanese who migrated to the U.S. We investigated whether the differences in the distributions of lipoprotein subclasses explain the difference in IMT between the two populations. We examined population-based samples of 466 randomly-selected men aged 40–49 (215 whites from Allegheny County, U.S., and 241 Japanese from Kusatsu, Japan). Lipoprotein subclasses were determined by nuclear magnetic resonance (NMR) spectroscopy. The whites had significantly higher levels of large very-low-density-lipoprotein particles and significantly lower levels of large high-density-lipoprotein particles than the Japanese, whereas the two populations had similar levels of small low-density-lipoprotein particles. The two populations had similar associations of IMT with NMR lipoproteins. Adjusting for NMR lipoproteins did not attenuate the significant difference in IMT between the two populations (0.671 ± 0.006 for the whites and 0.618 ± 0.006 mm for the Japanese, P=0.01, mean (standard error)). Differences in the distributions of NMR lipoproteins between the two populations did not explain the higher IMT in the whites.

Introduction

We have recently reported that among men aged 40–49, whites in the United States (U.S.). had significantly higher levels of intima-media thickness of the carotid arteries (carotid IMT) than the Japanese in Japan.(1) The difference remained after adjusting for traditional and other risk factors including fasting insulin, fibrinogen, and C-reactive protein (CRP).(1) This is despite the fact that levels of total cholesterol and blood pressure have been similar throughout their lifetime between the populations.(1) Moreover, rates of smoking in this birth cohort have been

Correspondence: Akira Sekikawa, MD, PhD, Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, 130 North Bellefield Avenue, Suite 546, Pittsburgh PA, 15213, USA, Tel:412-624-3225, Fax:412-383-1956, E-mail: akira@pitt.edu.

much lower in whites.(1) Primary genetic effects are unlikely, given the degree to which carotid IMT is increased in the Japanese who migrated to the U.S.(2,3)

Small low-density-lipoprotein (LDL) and LDL particle size are associated with carotid IMT independent of total cholesterol or LDL cholesterol (LDL-C).(4–6) It is possible that levels of small LDL are higher in whites in the U.S. than in the Japanese in Japan although levels of LDL-C were similar between the two populations. No previous study has, however, compared levels of lipoprotein subclasses and their associations with carotid IMT between whites in the U.S. and the Japanese in Japan.

In this study, we examined whether the difference in the distribution of lipoprotein subclasses between white men in the U.S. and Japanese men in Japan explains the difference in carotid IMT between the two populations.

Participants and Methods

Detailed descriptions of subjects and methods were published elsewhere except for lipoprotein subclass measurements. Participants were population-based samples of 493 randomly-selected men aged 40–49 examined in 2002 to 2005, without clinical cardiovascular disease: 243 white men from Allegheny County, Pennsylvania, U.S and 250 Japanese men from Kusatsu City, Shiga, Japan. In this study, we excluded those taking lipid lowering medications for the analyses, resulting in 215 whites and 241 Japanese. Informed consent was obtained from all participants. The study was approved by the Institutional Review Boards of University of Pittsburgh, Pittsburgh, Pennsylvania, U.S. and Shiga University of Medical Science, Otsu, Shiga, Japan.

Body weight and height were measured while the participant was wearing light clothing without shoes. Body-mass index was calculated as weight divided by the square of the height. Blood pressure was measured with an automated sphygmomanometer (BP-8800, Colin Medical Technology, Komaki, Japan). The average of two measurements was used.

Venipuncture was performed early in the clinic visit after a 12-hour fast. The samples were stored at −80C° and shipped on dry ice to the Heinz Laboratory, University of Pittsburgh. Serum lipids were determined using CDC-standardized methods. Serum glucose was determined using an enzymatic assay, serum insulin using a radio-immuno assay (Linco Research Inc., St. Charles, U.S.), CRP using an immuno-sorbent assay, and fibrinogen using an automated-clot-rate assay (Diagnostica Stago, Parsippany, U.S.).

A self-administered questionnaire was used to obtain information on demography, smoking habits, alcohol drinking, and other factors. Alcohol drinkers were defined as those who drink alcohol two days per week or more. 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 mmol/L (126 mg/dL) or use of anti-diabetic medications.

A Toshiba 140A scanner equipped with a 7.5 MHz-linear-array imaging probe was used for carotid scanning at both centers. We used the mean of eight measurements of the average IMT across 1-cm segments: near and far walls of the common carotid artery (CCA) and the far wall of the carotid bulb and internal carotid artery (ICA) on both sides. The scans were recorded on videotape, and sent to the Ultrasound Research Laboratory in Pittsburgh for scoring. We applied continuous quality-assessment programs developed by the laboratory to assure the scanning quality,(7) which included standardized protocols, centralized training of technicians, and continuous evaluation of scan quality and protocol adherence by the Ultrasound Research Laboratory. The evaluation of scan quality and protocol adherence was excellent. Under continuous quality-assessment programs, correlation coefficients between sonographers and between readers for average IMT were 0.96 and 0.99, respectively.(7)

Lipoprotein subclass measurements

Lipoprotein subclass particle concentrations and average very-low-density lipoprotein (VLDL), LDL, and high-density-lipoprotein (HDL) particle diameters were determined by nuclear magnetic resonance (NMR) spectroscopy at LipoScience, Inc. (Raleigh, U.S.) on serum samples stored at −80C°.(8) Briefly, the NMR method uses the characteristic signals broadcast by lipoprotein subclasses of different size as the basis of their quantification. Particle concentrations of the following lipoprotein species were determined: 3 VLDL subclasses (large: >60 nm, medium: 35 to 60 nm, and small: 27 to 35 nm), 3 LDL subclasses (intermediate-density lipoprotein (IDL): 23 to 27 nm, large: 21.3 to 23 nm, small: 18.3 to 21.2 nm), and 3 HDL subclasses (large: 8.8 to 13 nm, medium: 8.2 to 8.8 nm, and small: 7.3 to 8.2 nm).(9) Weighted average particle sizes of VLDL, LDL, and HDL were calculated from the subclass levels.

Statistical analyses

To compare risk factors between the populations, a t-test for continuous variables except for triglycerides and CRP, the Mann-Whitney U test for triglycerides and CRP, and chi-square test for categorical variables were used. Spearmen correlations of carotid IMT with continuous risk factors were calculated for each population. To compare carotid IMT between the populations, general-linear-model analyses were performed to calculate multivariate-adjusted carotid IMT. All P-values were two-tailed. P-value <0.05 was considered as significant. SPSS software (release 13.0, SPSS Inc., Chicago, U.S.) was used for all statistical analyses.

Results

The whites had lower levels of blood pressure, triglycerides, and glucose, and lower rates of cigarette smoking and hypertension than the Japanese. The two populations had similar levels of total cholesterol and LDL-C. Meanwhile the whites were more obese, had higher levels of insulin, fibrinogen, and CRP, and lower levels of HDL cholesterol (HDL-C) (Table 1).

The two populations had similar levels of small LDL particles. The whites had significantly higher levels of large VLDL, total LDL, and IDL particles. Additionally, the whites had significantly lower levels of total, large, and medium HDL particles (Table 2).

The two populations had similar associations of carotid IMT with NMR lipoproteins. Both populations had positive associations of carotid IMT with total LDL, IDL, and small LDL particles and negative associations of carotid IMT with LDL size, large HDL particles, and HDL size. Although only the whites had significant associations of carotid IMT with large VLDL particles and VLDL size (Table 3), there was no significant interaction between the two populations and each of VLDL particles and VLDL size in predicting carotid IMT. Similarly, although only the whites had significant associations of carotid IMT with total cholesterol and triglycerides and only the Japanese had a significant association of carotid IMT with HDL-C (Table 3), there was no significant interaction between the two populations and each of total cholesterol, triglycerides, and HDL-C in predicting carotid IMT.

Generally, the whites had significant associations of carotid IMT with NMR lipoproteins independent of standard lipids. The associations with total LDL, small LDL particles and LDL size were independent of LDL-C (p=0.01, 0.02, and 0.02 respectively). The association with large HDL and HDL size were independent of HDL-C (p=0.01 and <0.01, respectively). Meanwhile the associations with large VLDL particles and VLDL size were not independent of triglycerides. In contrast, the Japanese did not have significant associations of carotid IMT with NMR lipoproteins independent of standard lipids.

The whites had a significantly higher carotid IMT than the Japanese after adjusting for age, blood pressure, and current smoking; the difference remained after further adjusting for NMR lipoproteins (Model II in Table 4). The significant difference remained after further adjusting for other factors (Models III and IV in Table 4). Further adjusting for standard lipids did not change the result.

Discussion

This population-based study in men aged 40–49 has shown that whites in the U.S. had significantly higher large VLDL particles and significantly lower large HDL particles than the Japanese in Japan, and that the difference in the lipoprotein distribution lipoprotein between the two populations did not explain the difference in carotid IMT. Additionally, the study has shown that the associations of NMR lipoproteins with carotid IMT were similar between the two populations and that the distributions of LDL particles were similar between the two populations. This is the first population-based study comparing the association of carotid IMT with NMR lipoproteins between whites in the U.S. and the Japanese in Japan.

Carotid IMT is considered to be a surrogate marker of generalized atherosclerosis.[10] Increased carotid IMT and its progression are associated with cardiovascular risk factors in Americans and the Japanese.[11–14] Carotid IMT is an independent risk factor for cardiovascular disease in Americans and the Japanese.(15,16)

Reported ethnic differences in carotid IMT are congruent with ethnic differences in mortality from coronary heart disease (CHD),(17–19) which is consistent with the result of our study and CHD mortality statistics.(20) No previous study has, however, examined whether the ethnic difference in the distribution of lipoprotein subclasses explains the ethnic difference in carotid IMT. Some studies showed that ethnic difference in IMT of ICA but not CCA becomes insignificant after adjusting for risk factors.(17,19) In our study, however, the significant differences in both ICA and CCA remained after adjusting for NMR lipoproteins (data not shown).

Differences in genetic factors or lifetime exposures to traditional risk factors do not appear to explain the difference in carotid IMT. As for genetic factors, a study of Japanese migrants to the U.S. showed that Japanese Americans had significantly greater carotid IMT than the Japanese in Japan.(2,3) Japanese Americans appear to have greater carotid IMT than whites in the U.S. in the same age group.(21) As to lifetime exposure to traditional risk factors, available data from national or population-based surveys in this birth cohort, *i.e*., those aged 40–49, show that white men in the U.S. and Japanese men in Japan have had very similar levels of total cholesterol and blood pressure from childhood (22–25) to adulthood.(26,27) Furthermore, white men have had much lower rates of cigarette smoking than Japanese men.(26,27)

Other potential explanations may be differences in levels of insulin resistance and fish consumption. Insulin resistance is associated with carotid IMT in both whites and the Japanese independent of traditional risk factors.(28,29) Because the whites were significantly more obese than the Japanese, the whites are expected to be more insulin resistant. Significantly higher large VLDL and lower large HDL particles in whites than in the Japanese support this hypothesis.(30) Although we adjusted for fasting insulin, levels of fasting insulin alone do not necessarily represent insulin resistance.(31) The difference in prevalence of metabolic syndrome by the criteria of the International Diabetes Federation(32) did not explain the difference in IMT between the two populations, either (data not shown). A cross-sectional study in Japan reported that fish consumption is significantly and inversely associated with carotid IMT.(33) Because whites in the U.S. eat much less fish than the Japanese,(26) this may be associated with higher carotid IMT in the whites. Further investigations are needed.

Our observation that the whites had a significant association of carotid IMT with small LDL independent of LDL-C is in accordance with previous reports.(4–6) Additionally, we found that the whites had significant associations of carotid IMT with large HDL particles independent of HDL-C. Reasons why we did not observe these independent associations in the Japanese remain unexplained.

The study has several limitations. The study is cross sectional in design and we can not establish any causality. The study examined men aged 40–49 only. We focused on this specific sex- and age-group because population levels of total cholesterol and blood pressure have been similar between the Japanese and whites throughout their lifetime. Levels of total cholesterol have been higher in whites than the Japanese in older age groups. A profile of traditional risk factors in women has been less favorable in U.S. whites than in the Japanese.(1) The fact that the population levels of total cholesterol and blood pressure have been similar throughout their lifetime does not necessarily mean that the men in these two populations had similar trajectory of these risk factors. Based on CHD mortality statistics in men aged 35–44 in examined areas, however, populations examined in this study are unlikely to deviate largely from nation representing samples.(34,35) Based on the rate of cigarette smoking, the whites in this study may be healthier than the general white population. This does not, however, change our results that the whites had higher carotid IMT than the Japanese. Although there was no interaction between populations and each of NMR lipoproteins and standard lipids in predicting the IMT, this may be due to the small sample size. Although we excluded those without lipid-lowering medications, the conclusion remains the same when we included all participants.

In conclusion, the study shows that in men aged 40–49 whites in the U.S. had significantly higher VLDL particles and significantly lower HDL particles than the Japanese in Japan, but the differences in the lipoprotein distributions between whites in the U.S. and the Japanese in Japan did not explain the higher carotid IMT in the whites.

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References

1. 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. Am J Epidemiol 2007 Mar 15;165(6):617–24. [PubMed: 17244636]
2. Watanabe H, Yamane K, Fujikawa R, Okubo M, Egusa G, Kohno N. Westernization of lifestyle markedly increases carotid intima-media wall thickness (IMT) in Japanese people. Atherosclerosis 2003;166(1):67–72. [PubMed: 12482552]
3. Kadowaki T, Curb DJ, Abbott RD, Sekikawa A, Shin C, Okamura T, et al. Intima-media thickness of the carotid artery and associated risk factors in Japanese men in Japan and Hawaii. Circulation 2007 Feb;115(8):E286-E.
4. Skoglund-Andersson C, Tang R, Bond MG, de Faire U, Hamsten A, Karpe F. LDL particle size distribution is associated with carotid intima-media thickness in healthy 50-year-old men. Arterioscler Thromb Vasc Biol 1999;19(10):2422–30. [PubMed: 10521372]
5. Liu ML, Ylitalo K, Nuotio I, Salonen R, Salonen JT, Taskinen MR. Association between carotid intima-media thickness and low-density lipoprotein size and susceptibility of low-density lipoprotein to oxidation in asymptomatic members of familial combined hyperlipidemia families. Stroke 2002;33 (5):1255–60. [PubMed: 11988600]

6. Mora S, Szklo M, Otvos JD, Greenland P, Psaty BM, Goff DC Jr, et al. LDL particle subclasses, LDL particle size, and carotid atherosclerosis in the Multi-Ethnic Study of Atherosclerosis (MESA). Atherosclerosis. in press. (e-release date June 9, 2006)
7. Thompson T, Sutton-Tyrrell K, Wildman R. Continuous quality assessment programs can improve carotid duplex scan quality. Journal of Vascular Technology 2001;25:33–9.
8. Otvos JD. Measurement of lipoprotein subclass profiles by nuclear magnetic resonance spectroscopy. Clin Lab 2002;48(3–4):171–80. [PubMed: 11934219]
9. Freedman DS, Otvos JD, Jeyarajah EJ, Shalaurova I, Cupples LA, Parise H, et al. Sex and Age Differences in Lipoprotein Subclasses Measured by Nuclear Magnetic Resonance Spectroscopy: The Framingham Study. Clin Chem 2004 July 1;2004 50(7):1189–200.
10. Grobbee DE, Bots ML. Carotid artery intima-media thickness as an indicator of generalized atherosclerosis. J Intern Med 1994 Nov;236(5):567–73. [PubMed: 7964435]
11. Ahna C, Lee H, Park S, Song Y, Huh KSJO, et al. Decrease in carotid intima media thickness after 1 year of cilostazol treatment in patients with type 2 diabetes mellitus. Diabetes Research and Clinical Practice 2001;52(1):45–53. [PubMed: 11182215]
12. Kitamura A, Iso H, Imano H, Ohira T, Okada T, Sato S, et al. Carotid Intima-Media Thickness and Plaque Characteristics as a Risk Factor for Stroke in Japanese Elderly Men. Stroke 2004;35(12): 2788–94. [PubMed: 15528460]
13. Mannami T, Konishi M, Baba S, Nishi N, Terao A. Prevalence of Asymptomatic Carotid Atherosclerotic Lesions Detected by High-Resolution Ultrasonography and Its Relation to Cardiovascular Risk Factors in the General Population of a Japanese City: The Suita Study. Stroke 1997 March 1;1997 28(3):518–25.
14. Salonen R, Salonen J. Progression of carotid atherosclerosis and its determinations: a population-based ultrasonography study. Atherosclerosis 1990;81:33–40. [PubMed: 2407252]
15. Chambless L, Folsom A, Clegg L, Sharrett A, Shahar E, Nieto F, et al. Carotid wall thickness is predictive of incident clinical stroke: the Atherosclerosis Risk in Communities (ARIC) study. Am J Epidemiol 2000;151(5):478–87. [PubMed: 10707916]
16. Kitamura A, Iso H, Imano H, Ohira T, Sato S, Naito Y, et al. Prevalence and correlates of carotid atherosclerosis among elderly Japanese men. Atherosclerosis 2004;172(2):353–9. [PubMed: 15019546]
17. Urbina EM, Srinivasan SR, Tang R, Bond MG, Kieltyka L, Berenson GS. Impact of multiple coronary risk factors on the intima-media thickness of different segments of carotid artery in healthy young adults (The Bogalusa Heart Study). Am J Cardiol 2002;90(9):953–8. [PubMed: 12398961]
18. Ranjit N, Diez-Roux AV, Chambless L, Jacobs DR Jr, Nieto FJ, Szklo M. Socioeconomic Differences in Progression of Carotid Intima-Media Thickness in the Atherosclerosis Risk in Communities Study. Arterioscler Thromb Vasc Biol 2006;26(2):411–6. [PubMed: 16322533]
19. D'Agostino RB Jr, Burke G, O'Leary D, Rewers M, Selby J, Savage PJ, et al. Ethnic differences in carotid wall thickness. The Insulin Resistance Atherosclerosis Study. Stroke 1996;27(10):1744–9. [PubMed: 8841322]
20. Sekikawa A, Horiuchi BY, Edmundowicz D, Ueshima H, Curb JD, Sutton-Tyrrell K, et al. A "natural experiment" in cardiovascular epidemiology in the early 21st century. Heart 2003;89(3):255–7. [PubMed: 12591821]
21. Howard G, Sharrett A, Heiss G, Evans G, Chambless L, Riley W, et al. Carotid artery intimal-medial thickness distribution in general populations as evaluated by B-mode ultrasound. Stroke 1993;24(9): 1297–304. [PubMed: 8362421]
22. Morrison JA, deGroot I, Edwards BK, Kelly KA, Rauh JL, Mellies M, et al. Plasma cholesterol and triglyceride levels in 6,775 school children, ages 6--17. Metabolism 1977;26(11):1199–211. [PubMed: 909396]
23. Frerichs RR, Srinivasan SR, Webber LS, Berenson GR. Serum cholesterol and triglyceride levels in 3,446 children from a biracial community: the Bogalusa Heart Study. Circulation 1976;54(2):302–9. [PubMed: 939028]
24. Ueshima H, Kitada M, Iida M, Tanigaki M, Shimamoto T, Konishi M, et al. Serum total cholesterol, triglyceride level, and dietary intake in Japanese students aged 15 years. Am J Epidemiol 1982 Aug; 116(2):343–52. [PubMed: 7114043]

25. Yano, A.; Ueshima, H.; Iida, K.; Yamazaki, S.; Kohima, S.; Tanaka, H., et al. Primary prevention of cardiovascular disease in youth (in Japanese). In: Komachi, Y., editor. Trands in cardiovasucular disease. Tokyo: Hoken Dojin Sha; 1987. p. 326-46.
26. Ministry of Health and Welfare. National Nutrition Survey 1998. Tokyo: Daiichi Shuppan Publisher; 2000.
27. National Center for Health Statistics. Health, United States, 2004 With Chartbook on Trends in the Health of Americans. Hyattsville, Maryland: U.S. Department of Health and Human Services; 2004.
28. Howard G, O'Leary DH, Zaccaro D, Haffner S, Rewers M, Hamman R, et al. Insulin Sensitivity and Atherosclerosis. Circulation 1996;93(10):1809–17. [PubMed: 8635260]
29. Suzuki M, Shinozaki K, Kanazawa A, Hara Y, Hattori Y, Tsushima M, et al. Insulin Resistance as an Independent Risk Factor for Carotid Wall Thickening. Hypertension 1996;28(4):593–8. [PubMed: 8843883]
30. Goff, DC., Jr; D'Agostino, RB., Jr; Haffner, SM.; Otvos, JD. Metabolism. 54. 2005 Feb. Insulin resistance and adiposity influence lipoprotein size and subclass concentrations. Results from the Insulin Resistance Atherosclerosis Study; p. 264-70.
31. Kim SH, Abbasi F, Reaven GM. Impact of Degree of Obesity on Surrogate Estimates of Insulin Resistance. Diabetes Care 2004;27(8):1998–2002. [PubMed: 15277430]
32. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005 Oct 25;112(17):2735–52. [PubMed: 16157765]
33. Hino A, Adachi H, Toyomasu K, Yoshida N, Enomoto M, Hiratsuka A, et al. Very long chain N-3 fatty acids intake and carotid atherosclerosis: An epidemiological study evaluated by ultrasonography. Atherosclerosis 2004;176(1):145–9. [PubMed: 15306187]
34. Sekikawa A, Kuller LH, Ueshima H, Park JE, Suh I, Jee SH, et al. Coronary heart disease mortality trends in men in the post World War II birth cohorts aged 35–44 in Japan, South Korea and Taiwan compared with the United States. Int J Epidemiol 1999 Dec;28(6):1044–9. [PubMed: 10661646]
35. Sekikawa A, Satoh T, Hayakawa T, Ueshima H, Kuller LH. Coronary heart disease mortality among men aged 35–44 years by prefecture in Japan in 1995–1999 compared with that among white men aged 35–44 by state in the United States in 1995–1998: vital statistics data in recent birth cohort. Jpn Circ J 2001 Oct;65(10):887–92. [PubMed: 11665793]

Table 1

Characteristics of white men in Allegheny County, Pennsylvania, U.S. and Japanese men in Kusatsu, Shiga, Japan in 2002–2005

	White (n = 215)	Japanese (n = 241)	P
Age (years)	45.0 ± 2.9	45.1 ± 2.8	0.64
Body-mass index (kg/m^2)	27.5 ± 3.9	23.8 ± 3.1	<0.01
Systolic blood pressure (mmHg)	122.8 ± 11.5	124.8 ± 16.1	0.13
Diastolic blood pressure (mmHg)	73.5 ± 8.8	76.3 ± 11.9	<0.01
Total cholesterol (mmol/L)	5.53 ± 0.98	5.64 ± 0.92	0.24
LDL-C (mmol/L)	3.54 ± 0.88	3.46 ± 0.92	0.33
HDL-C (mmol/L)	1.24 ± 0.33	1.39 ± 0.34	<0.01
Triglycerides (mmol/L)	1.38 (1.01, 2.10)	1.53 (1.16, 2.02)	0.08
Glucose (mmol/L)	5.53 ± 0.64	5.87 ± 0.87	<0.01
Insulin (pmol/L)	100.9 ± 52.4	72.0 ± 31.8	<0.01
Fibrinogen (umol/L)	8.60 ± 2.06	7.38 ± 1.91	<0.01
C-reactive protein (mg/L)	0.85 (0.45, 1.83)	0.31 (0.15–0.67)	<0.01
Smoker (%)	5.6	49.8	<0.01
Drinker (%)	47.0	66.4	<0.01
Hypertension (%)	13.5	26.1	<0.01
Diabetes (%)	2.3	4.6	0.21

LDL-C: low-density-lipoprotein cholesterol, HDL-C: high-density-lipoprotein cholesterol, Smoker was defined as current smoker, drinker as those who drank alcohol ≥two days a week, hypertension as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or use of anti-hypertensive medications, and diabetes as fasting glucose level ≥7 mmol/L (126 mg/dL) or use of anti-diabetic medications.

Values are expressed as mean (SD) or median (inter-quartile range) for continuous variables.

Table 2

Comparison of lipoprotein subclasses among men aged 40–49 between whites in Allegheny County, Pennsylvania, U.S. and the Japanese in Kusatsu, Shiga, Japan in 2002–2005

	Whites (n = 215)	Japanese (n = 241)	P
Lipoprotein particle concentration			
VLDL particles (nmol/L)			
Total	91.7 ± 43.5	91.8 ± 45.2	0.80
Large	1.46 (0.59, 6.22)	0.50 (0.10, 2.75)	<0.01
Medium	34.1 (17.5, 55.5)	40.3 (18.7, 58.8)	0.14
Small	46.3 ± 21.3	44.0 ± 24.7	0.28
LDL particles (nmol/L)			
Total	1491.9 ± 415.8	1410.6 ± 443.1	<0.05
IDL	40.8 (10.2, 80.3)	18.0 (0.0, 53.5)	<0.01
Large	524.9 ± 283.8	514.8 ± 224.1	0.67
Small	915.1 ± 523.9	861.6 ± 511.1	0.27
HDL particles (μmol/L)			
Total	31.5 ± 5.7	35.0 ± 6.1	<0.01
Large	5.2 ± 3.2	8.4 ± 3.8	<0.01
Medium	0.06 (0.00, 1.22)	1.10 (0.00, 3.30)	<0.01
Small	25.2 ± 25.2	23.9 ± 23.9	<0.01
Lipoprotein particle size (nm)			
VLDL	49.6 ± 7.9	44.0 ± 7.0	<0.01
LDL	20.9 ± 0.9	21.1 ± 0.8	0.15
HDL	8.6 ± 0.5	9.1 ± 0.4	<0.01

VLDL: very low density lipoprotein, LDL: low-density lipoprotein, IDL: intermediate-density lipoprotein, HDL: high-density lipoprotein

Values are expressed as mean (± standard deviation) or median (inter-quartile range) for continuous variables.

Table 3

Spearman correlations of lipoprotein subclasses with carotid intima-media thickness among white men aged 40–49 in Allegheny County, Pennsylvania, U.S. and among Japanese men aged 40–49 in Kusatsu, Shiga, Japan in 2002–2005

Lipoprotein subclasses	Whites (n = 215) Rho	P	Japanese (n = 241) Rho	P
Lipoprotein particle concentration				
VLDL particles				
Total	0.08	0.23	−0.03	0.61
Large	0.13	0.05	0.01	0.78
Medium	0.03	0.72	−0.05	0.48
Small	0.08	0.25	0.01	0.83
LDL particles				
Total	0.24	<0.01	0.12	0.06
IDL	0.12	0.09	0.11	0.08
Large	0.00	0.95	−0.06	0.37
Small	0.19	0.01	0.12	0.05
HDL particles				
Total	−0.01	0.86	−0.09	0.16
Large	−0.18	0.01	−0.16	0.01
Medium	−0.02	0.74	0.03	0.68
Small	0.06	0.37	0.05	0.42
Lipoprotein particle size				
VLDL	0.13	0.06	−0.03	0.68
LDL	−0.13	0.06	−0.12	0.07
HDL	−0.19	0.01	−0.14	0.03
Standard lipids				
Total cholesterol	0.23	<0.01	0.09	0.16
LDL-C	0.22	<0.01	0.13	0.04
HDL-C	−0.09	0.21	−0.19	<0.01
Triglycerides	0.14	0.04	0.03	0.65

Refer to tables 1 and 2 for abbreviation.

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Table 4

Comparison of multivariate-adjusted carotid intima-media thickness (mm) among men aged 40–49 between whites in Allegheny County, Pennsylvania, U.S. and the Japanese in Kusatsu, Shiga, Japan in 2002–2005

	Whites (n = 215)	Japanese (n = 241)	P
Model I	0.676 ± 0.006	0.613 ± 0.006	<0.01
Model II	0.671 ± 0.006	0.618 ± 0.006	<0.01
Model III	0.666 ± 0.007	0.622 ± 0.006	<0.01
Model IV	0.666 ± 0.007	0.622 ± 0.006	<0.01

Model I: Adjusted for age, systolic blood pressure, and current smoking.

Model II: Further adjusted for large VLDL, total LDL, and large HDL particles.

Model III: Further adjusted for BMI, glucose, and insulin.

Model IV: Further adjusted for fibrinogen, CRP, and alcohol.

Refer to tables 1 and 2 for abbreviation.

Values are expressed as mean (± standard error).