Original Contribution

Sex Differences in Subclinical Atherosclerosis by Race/Ethnicity in the Multi-Ethnic Study of Atherosclerosis

Catherine Kim*, Ana V. Diez-Roux, Jennifer A. Nettleton, Joseph F. Polak, Wendy S. Post, David S. Siscovick, Karol E. Watson, and Anjel M. Vahratian

* Correspondence to Dr. Catherine Kim, 300 North Ingalls, Room 7C13, Mailstop 5429, Ann Arbor, MI 48109 (e-mail: cathkim@umich.edu).

Sex differences in cardiovascular disease mortality are more pronounced among non-Hispanic whites than other racial/ethnic groups, but it is unknown whether this variation is present in the earlier subclinical stages of disease. The authors examined racial/ethnic variation in sex differences in coronary artery calcification (CAC) and carotid intimal media thickness at baseline in 2000–2002 among participants ($n = 6,726$) in the Multi-Ethnic Study of Atherosclerosis using binomial and linear regression. Models adjusted for risk factors in several stages: age, traditional cardiovascular disease risk factors, behavioral risk factors, psychosocial factors, and adult socioeconomic position. Women had a lower prevalence of any CAC and smaller amounts of CAC when present than men in all racial/ethnic groups. Sex differences in the prevalence of CAC were more pronounced in non-Hispanic whites than in African Americans and Chinese Americans after adjustment for traditional cardiovascular disease risk factors, and further adjustment for behavioral factors, psychosocial factors, and socioeconomic position did not modify these results (for race/sex, $P_{interaction} = 0.047$). Similar patterns were observed for amount of CAC among adults with CAC. Racial/ethnic variation in sex differences for carotid intimal media thickness was less pronounced. In conclusion, coronary artery calcification is differentially patterned by sex across racial/ethnic groups.

calcification, physiologic; continental population groups; coronary vessels; sex; social class

Abbreviations: CAC, coronary artery calcification; cIMT, carotid intimal media thickness; CVD, cardiovascular disease; MESA, Multi-Ethnic Study of Atherosclerosis.

Women have a lower prevalence and incidence of age-adjusted cardiovascular disease (CVD) and CVD mortality than men (1). The magnitude of this sex difference varies substantially across countries (1), as well as by race/ethnicity within the United States (2). The reasons for these racial/ethnic variations in sex differences have not been determined.

Previous studies examining sex differences by race/ethnicity have focused largely on CVD mortality (2–4) rather than on subclinical measures of atherosclerosis. Examination of subclinical markers of CVD, as opposed to CVD mortality, would help to determine whether racial variation in sex differences in CVD occurs during the early stages of atherosclerosis development and is, therefore, not completely attributable to racial and sex differences in CVD diagnosis (5), referral for treatment (6), and responses to therapy (7). In addition, if sex differences are observed, it is important to investigate the contributions of a range of factors, but most previous studies of sex variations in CVD mortality by race/ethnicity have not accounted for a range of traditional and nontraditional CVD risk factors.

We used cross-sectional data from the Multi-Ethic Study of Atherosclerosis (MESA) to examine variation in sex differences in subclinical atherosclerosis by race/ethnicity. In order to determine whether any variations in sex differences were due to differential sex patterning of CVD risk factors by race/ethnicity, we examined racial/ethnic variation in sex differences before and after adjustment for age and traditional CVD risk factors, as well as behavioral factors such as diet and physical activity, psychosocial factors, and socioeconomic position.

MATERIALS AND METHODS

MESA is a longitudinal cohort study that has been described previously (8). The MESA cohort includes 6,814 men and women aged 45–84 years at baseline recruited at 6 field centers: Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles, California; New York, New York; and St. Paul, Minnesota. Only persons free of clinical CVD at baseline were eligible. The baseline visit for the cohort (on which these analyses are based) took place between July 2000 and September 2002. The study was approved by institutional review boards at each site, and all participants gave written, informed consent.

Coronary artery calcification (CAC) was assessed by chest computed tomography that used either a cardiac-gated electron-beam computed tomography scanner (9, 10) or a multidetector computed tomography system (9). Scans were read blindly with respect to scan pairs and to other participant data by using a computer interactive scoring system similar to that described by Yaghoubi et al. (11). The average Agatston score (12) for the 2 scans was used in all analyses. Kappa statistics for intra- and interreader reproducibility of CAC prevalence were both 0.92. Intraclass correlation coefficients for intra- and interreader reproducibility of CAC scores exceeded 0.99.

Trained technicians in each field center performed B-mode ultrasonography of the right and left near and far walls of the internal carotid and common carotid arteries (13). An ultrasound-reading center measured maximal carotid intimal media thickness (cIMT) of the internal and common carotid sites as the mean of the maximum cIMT of the near and far walls of the right and left sides. Intraclass correlation coefficients for intrareader reproducibility of common and internal cIMT both exceeded 0.98 and, for interreader reproducibility, were 0.87 and 0.94, respectively.

Questionnaires administered as part of the baseline visit in English, Spanish, or Chinese were used to obtain information on sociodemographic indicators. Race and ethnicity were characterized on the basis of participants' responses to the ethnicity and race questions modeled on the year 2000 US Census. All participants who reported their ethnicity as Hispanic were classified as Hispanic in these analyses. All others were classified into 3 groups (non-Hispanic whites, African Americans, and Chinese Americans) by their responses to the race question. Centrally trained clinical teams collected information on CVD risk factors during the baseline examination. Hypertension was defined as a systolic blood pressure of ≥140 mm Hg, diastolic blood pressure of ≥90 mm Hg, or use of medication prescribed for hypertension. A central laboratory measured total and high density lipoprotein cholesterol and glucose levels from blood samples obtained after a 12-hour fast. Low density lipoprotein cholesterol was calculated with the Friedewald (14) equation. Diabetes was defined as a fasting glucose level of ≥126 mg/dL or use of hypoglycemic medication, and impaired fasting glucose was defined as a fasting glucose level of ≥110 mg/dL. Body mass index was calculated as weight (kg)/height (m)^2.

Usual dietary intake over the preceding year was quantified by a 120-item food frequency questionnaire at baseline (15). Dietary patterns were empirically derived by using principal components analysis with orthogonal (varimax) rotation, creating uncorrelated dietary patterns (mean = 0, standard deviation = 1) (15). Four dietary patterns were retained and named according to the food groups loading highest on the respective dietary patterns in Table 1. A higher score indicated greater conformity with the pattern being calculated. Physical activity was measured by an activity questionnaire adapted from the Cross-Cultural Activity Participation Study (16). The physical activity measure investigated was intentional activity measured in metabolic equivalent hours/day.

Psychosocial factors were assessed by using standardized questionnaires written in English, Spanish, or Chinese. Depression was assessed by the Center for Epidemiology Studies Depression (CES-D) Scale (17), anger and anxiety were assessed by use of the Spielberger trait anger and the Spielberger trait anxiety scales (18), and chronic psychologic stress was assessed by using the chronic burden scale (19). Scores were analyzed as continuous variables.

As part of the baseline examination, participants were asked to select their total gross family income in the past 12 months from 13 categories. Income was collapsed into 4 categories (<$25,000, $25,000–$39,999, $40,000–$74,999, or ≥$75,000) for these analyses. Participants also reported the highest educational level completed. Education was categorized into 4 categories (completed high school or less, some college but no degree/technical school certificate, associate or bachelor's degree, or graduate/professional degree) for these analyses. The 4 wealth variables were as follows: 1) whether the participant, or his/her family, had investments such as stocks, bonds, mutual funds, retirement investments, or other investments (yes/no); 2) whether the participant owned his/her home (yes/no); 3) whether the participant owned a car (yes/no); and 4) whether the participant owned land or another property that was not his/her primary residence (yes/no). A summary adult socioeconomic position score was created by summing scores for income (0–3, from lowest to highest category) and education (0–3 from lowest to highest) and adding 1 point for each wealth indicator present (20). Adult socioeconomic position was characterized as being low, medium, or high.

CAC scores were classified as a dichotomous variable (0 = absence; 1 = presence if the calcium score > 0). The absolute risk or probability of having any CAC was modeled by using the GENMOD procedure in SAS software (SAS Institute, Inc., Cary, North Carolina); these generalized linear models use maximum likelihood estimation for β, where β is interpreted as the risk difference for each unit change in the predictor variable (21). Models were fit in several stages, in order to determine whether any observed heterogeneity in sex differences by race/ethnicity was accounted for by different sets of factors. The first set of models adjusted for age (continuous). The second set of models also adjusted for traditional CVD risk factors, including diabetes (no diabetes, impaired fasting glucose, diabetes), cigarette smoking (never, former, current), presence of hypertension, low density lipoprotein cholesterol levels (continuous), high density lipoprotein cholesterol levels (continuous), and triglycerides (continuous). The third set of models also adjusted for behavioral factors, specifically, dietary patterns (all 4

Table 1. Characteristics of the Study Population, Stratified by Race/Ethnicity and Sex, Multi-Ethnic Study of Atherosclerosis, 2000–2002

Characteristics	Non-Hispanic White				African American				Hispanic				Chinese			
	Men (n = 1,247)		Women (n = 1,349)		Men (n = 825)		Women (n = 1,026)		Men (n = 713)		Women (n = 767)		Men (n = 388)		Women (n = 411)	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%
Age, years	63 (10)		63 (10)		62 (10)		62 (10)		61 (10)		61 (10)		62 (10)		62 (10)	
Body mass index, kg/m^2	28 (4)		28 (6)		29 (5)		31 (6)		29 (4)		30 (6)		24 (3)		24 (3)	
Hypertension		39		38		56		61		38		45		35		39
Diabetes status																
Impaired fasting glucose		14		9		17		13		18		14		21		13
Untreated diabetes		3		1		4		3		3		3		4		2
Treated diabetes		5		4		15		13		16		13		10		10
Total cholesterol, mg/dL	189 (35)		202 (34)		182 (34)		196 (37)		193 (37)		202 (38)		189 (31)		195 (32)	
LDL cholesterol, mg/dL	117 (30)		117 (31)		114 (32)		119 (34)		119 (33)		120 (33)		116 (29)		114 (29)	
HDL cholesterol, mg/dL	45 (12)		59 (16)		47 (13)		57 (16)		43 (10)		52 (14)		46 (11)		53 (13)	
Triglycerides, mg/dL	135 (102)		131 (78)		109 (69)		102 (69)		164 (106)		151 (96)		142 (86)		144 (84)	
Systolic blood pressure, mm Hg	124 (19)		123 (22)		130 (19)		133 (23)		126 (20)		127 (24)		124 (19)		125 (24)	
Diastolic blood pressure, mm Hg	74 (9)		67 (10)		77 (10)		73 (10)		75 (10)		68 (10)		75 (9)		69 (11)	
Cigarette smoking																
Never		40		49		37		52		40		68		53		96
Former		49		39		43		32		44		22		37		2
Current		11		12		20		16		16		11		10		2
Physical activity, hours/day	12.1 (4.8)		13.3 (5.1)		13.8 (7.1)		14.7 (6.8)		11.4 (5.7)		11.8 (5.9)		10.0 (4.4)		10.0 (4.2)	
Dietary scores																
Fats and processed meats	0.38 (0.97)		0.02 (0.87)		0.44 (1.16)		0.18 (1.11)		−0.16 (0.89)		−0.45 (0.85)		−0.56 (0.51)		−0.78 (0.45)	
Vegetables and fish	−0.28 (0.70)		−0.22 (0.72)		0.001 (0.85)		0.09 (0.91)		−0.39 (0.74)		−0.31 (0.73)		1.32 (1.34)		1.21 (1.30)	
Beans, tomatoes, and refined grains	−0.12 (0.64)		−0.22 (0.61)		−0.28 (0.84)		−0.39 (0.58)		1.00 (1.46)		0.84 (1.40)		−0.29 (0.46)		−0.40 (0.42)	
Whole grains and fruit	0.27 (0.95)		−0.41 (0.95)		−0.16 (0.96)		0.14 (0.96)		−0.30 (0.95)		−0.06 (0.94)		−0.85 (0.74)		−0.72 (0.72)	
Spielberger anger	14.8 (3.3)		14.9 (3.5)		14.0 (3.3)		14.3 (3.4)		14.8 (4.3)		15.1 (4.2)		15.5 (3.8)		15.3 (3.7)	
Spielberger anxiety	15.4 (4.2)		16.8 (4.7)		14.5 (4.0)		15.7 (4.3)		15.6 (4.8)		16.6 (4.7)		15.9 (4.1)		16.7 (4.7)	
Chronic burden	0.9 (1.1)		1.3 (1.2)		1.0 (1.1)		1.3 (1.2)		1.0 (1.1)		1.2 (1.2)		0.6 (0.9)		0.7 (1.1)	
CES-D Scale score	6.1 (6.3)		7.9 (7.6)		6.0 (6.1)		8.3 (7.9)		7.9 (7.7)		11.1 (9.7)		5.3 (5.6)		7.1 (7.2)	
Socioeconomic position																
Low		15		30		37		49		69		81		58		67
Medium		40		39		39		33		24		17		26		20
High		45		31		24		18		7		2		26		14

Abbreviations: CES-D, Center for Epidemiologic Studies Depression; HDL, high density lipoprotein; LDL, low density lipoprotein; SD, standard deviation.

patterns, each score modeled as a continuous variable) and physical activity level (continuous). The fourth set of models also adjusted for psychosocial factors (continuous), and the fifth set of models adjusted for all types of risk factors including adult socioeconomic position.

In addition, we also examined associations of sex with amount of calcium among persons with calcium by modeling the ln(Agatston score) as a function of covariates using linear regression. Exponentiated coefficients derived from these models can be interpreted as relative differences in the amount of calcium in women compared with men. For example, a relative difference of 1.5 represents a 50% difference in the Agatston score. A similar modeling approach was used for common and internal cIMT. As with CAC Agatston scores, we log transformed cIMT values. Models were fit in stages as described for CAC.

To determine if there were significant differences in associations of sex with subclinical measures by race/ethnicity, we tested interactions by including a race/ethnicity × sex interaction term (in addition to the main effects of race and sex) in models pooling across racial/ethnic groups. We also examined interaction terms between each race/ethnicity dummy and sex in order to compare associations of sex with the outcome in each racial/ethnic group to the sex association observed in whites as the reference category. To determine if associations were different among women likely to be postmenopausal, we examined the subset of participants aged greater than 50 years but found similar patterns (results not shown). All statistical analyses were calculated with SAS, version 9.1, software (SAS Institute, Inc.). Probability values correspond to 2-tailed tests.

RESULTS

Table 1 shows the distribution of risk factors by sex and race/ethnicity. Although men and women were of similar ages across groups, the magnitude and pattern of sex differences in risk factors varied by race/ethnicity. The most marked racial/ethnic variations in sex differences were present in hypertension; that is, non-Hispanic white men and women had similar prevalences of hypertension, but hypertension was more common in women among African Americans, Hispanics, and Chinese Americans. The prevalence of smoking was much lower in Chinese-American women compared with Chinese-American men, but sex differences were much smaller in other racial/ethnic groups. Although men had a higher socioeconomic position than women in all racial/ethnic groups, the prevalence of low socioeconomic position was slightly lower in Chinese-American women compared with Chinese-American men than in women versus men in other ethnic groups. Across all racial/ethnic groups, women had a lower prevalence of CAC and lower CAC scores than men (Table 2), although the sex difference varied substantially by race/ethnicity, with the largest sex difference observed in non-Hispanic whites and the smallest sex difference observed in African Americans. Women also had thinner common and internal cIMT than men (Table 2), but variation in sex differences by race/ethnicity was less pronounced.

Table 3 shows the absolute differences in the probability of having any CAC in women versus men, before and after

Table 2. Outcomes of Interest, Stratified by Race/Ethnicity and Sex, Multi-Ethnic Study of Atherosclerosis, 2000–2002

	Non-Hispanic White				Non-Hispanic African American				Hispanic				Chinese			
	Men (n = 1,247)		Women (n = 1,349)		Men (n = 825)		Women (n = 1,026)		Men (n = 713)		Women (n = 767)		Men (n = 388)		Women (n = 411)	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%
Coronary artery calcification																
Yes		70.3		44.6		52.1		36.5		56.4		35.1		59.0		42.1
No		29.7		55.4		47.9		63.5		43.6		64.9		41.0		57.9
Agatston score[a]	419.4 (677.6)		209.6 (339.0)		328.9 (660.2)		215.3 (447.7)		370.5 (695.3)		147.4 (260.6)		213.4 (397.8)		155.6 (284.2)	
Common carotid intimal media thickness, mm	0.89 (0.21)		0.84 (0.18)		0.93 (0.20)		0.88 (0.19)		0.87 (0.20)		0.84 (0.17)		0.84 (0.17)		0.81 (0.18)	
Internal carotid intimal media thickness, mm	1.21 (0.64)		1.06 (0.60)		1.15 (0.61)		1.07 (0.61)		1.13 (0.64)		0.95 (0.52)		0.93 (0.49)		0.82 (0.44)	

Abbreviation: SD, standard deviation.
[a] Among those who had recorded coronary artery calcification at baseline.

Table 3.   Absolute Risk Difference for the Presence of Any Coronary Artery Calcification in Women Versus Men, by Race/Ethnicity and Men as Reference Group, Multi-Ethnic Study of Atherosclerosis, 2000–2002

	Non-Hispanic White		African American		Hispanic		Chinese		$P_{interaction}$ for Race and Sex
	Difference	95% CI	Difference	95% CI	Difference	95% CI	Difference	95% CI	
Unadjusted	−0.25	−0.29, −0.22	−0.16	−0.20, −0.11	−0.21	−0.26, −0.16	−0.17	−0.24, −0.10	0.035
Model 1 (adjusted for age)	−0.25	−0.28, −0.22	−0.15	−0.20, −0.11	−0.22	−0.26, −0.17	−0.17	−0.23, −0.10	0.048
Model 2 (adjusted for age and traditional risk factors)[a]	−0.20	−0.25, −0.16	−0.16	−0.21, −0.11	−0.21	−0.26, −0.15	−0.19	−0.27, −0.11	0.095
Model 3 (adjusted for factors in models 1 and 2, physical activity, and diet)	−0.21	−0.26, −0.17	−0.16	−0.21, −0.10	−0.19	−0.25, −0.13	−0.20	−0.29, −0.12	0.022
Model 4 (adjusted for factors 1–3 and psychosocial factors)[b]	−0.21	−0.25, −0.17	−0.16	−0.21, −0.10	−0.19	−0.25, −0.13	−0.20	−0.29, −0.12	0.031
Model 5 (adjusted for factors in models 1–4 and socioeconomic position)	−0.21	−0.25, −0.16	−0.15	−0.21, −0.09	−0.19	−0.25, −0.13	−0.20	−0.29, −0.11	0.047

Abbreviation: CI, confidence interval.

[a] Smoking, hypertension, diabetes, low density lipoprotein cholesterol, high density lipoprotein cholesterol, triglycerides, cholesterol, and body mass index.

[b] Anxiety, anger, depression, and chronic burden.

adjustment for covariates. Women had a lower probability of any CAC than men, but the magnitude of sex differences varied by race/ethnicity (for race/sex, $P_{interaction} = 0.047$ for the fully adjusted model). In this model (Model 5), the sex difference was smallest in African Americans compared with other racial/ethnic groups (for African Americans × sex, $P_{interaction} = 0.03$). Differences in the sex patterning were largest when African Americans were compared with whites ($P = 0.002$) and when Chinese Americans were compared with whites ($P = 0.004$), but Hispanic versus non-Hispanic white comparisons were only of borderline statistical significance ($P = 0.18$). Among the subset of adults with any CAC, there was a similar pattern for the extent of CAC (Table 4).

Women tended to have thinner common cIMT than men in all models, before and after adjustment for risk factors (Table 5). However, racial/ethnic variation in sex differences was not statistically significant in any of the models. There was some evidence that sex differences in internal cIMT were smaller in African Americans compared with other racial/ethnic groups ($P = 0.09$) and in African Americans compared with whites ($P = 0.10$), but these differences were not statistically significant.

DISCUSSION

Although it is well recognized that women have a lower burden of age-adjusted CVD than men, and that these sex differences may vary by race/ethnicity, previous studies of sex differences have focused primarily on CVD mortality (2). Thus, it is not known if previous racial/ethnic variation in sex differences was attributable to differences in diagnosis and treatment or in the development of atherosclerosis. Using a large population-based multiethnic study of subclinical atherosclerosis, we found that women consistently had less CAC than men across racial/ethnic groups. There was also significant racial/ethnic variation in sex differences

in CAC. Sex differences were most pronounced in non-Hispanic whites, with white men having the highest prevalence of CAC, and were less pronounced in African Americans and Chinese Americans. African Americans also had smaller differences in internal cIMT than whites, although these differences were not statistically significant.

Previous studies documenting racial/ethnic variation in cardiac mortality have also found that sex differences were more pronounced in non-Hispanic whites than in African Americans, particularly for cardiac events (2). As with CAC prevalence and amount, cardiac mortality was higher in men. In a pooled analysis of several prospective cohort studies, African-American men had approximately twice the cardiac disease mortality of African-American women, whereas non-Hispanic white men had 6 times the cardiac disease mortality of non-Hispanic white women (2). Racial/ethnic variation in sex differences tends to be less pronounced in older populations, although sex differences remain strongest in non-Hispanic whites even in the older age groups. In a 1980s' study using death certificate data from California, the male:female cardiac mortality rate ratio of 2.1 was higher in non-Hispanic whites than that of 1.8 in African Americans (3). Similarly, in an analysis of Cardiovascular Health Study participants who were aged ≥65 years at enrollment, the coronary disease hazard in men versus women was approximately 1.8 in non-Hispanic whites and 1.4 in African Americans (4). Our study suggests there are also differences in subclinical atherosclerosis. Such differences may be present before middle age; a report by Bild et al. (22) in adults aged 28–40 years found greater sex differences in CAC prevalence in non-Hispanic whites compared with African Americans. To our knowledge, previous studies have not examined sex differences in CVD events in Chinese-American samples.

Prior studies have found less pronounced sex differences in stroke and less pronounced racial/ethnic variation in gender differences in stroke than in cardiac mortality (4). In the

Table 4. Adjusted Relative Differences in the Amount of Coronary Calcium (Agatston Score) When Any Coronary Calcium Is Present, for Women Compared With Men and Stratified by Race/Ethnicity, Multi-Ethnic Study of Atherosclerosis, 2000–2002

	Non-Hispanic White		African American		Hispanic		Chinese		$P_{interaction}$ for Race and Sex
	Difference	95% CI	Difference	95% CI	Difference	95% CI	Difference	95% CI	
Unadjusted	0.50	0.41, 0.60	0.70	0.55, 0.91	0.49	0.37, 0.64	0.73	0.52, 1.01	0.049
Model 1 (adjusted for age)	0.41	0.34, 0.49	0.64	0.50, 0.81	0.43	0.33, 0.56	0.65	0.47, 0.90	0.011
Model 2 (adjusted for age and traditional risk factors)[a]	0.43	0.35, 0.54	0.59	0.44, 0.78	0.35	0.25, 0.49	0.63	0.41, 0.97	0.008
Model 3 (adjusted for factors in models 1 and 2, physical activity, and diet)	0.41	0.33, 0.52	0.59	0.43, 0.81	0.35	0.24, 0.50	0.62	0.40, 0.98	0.015
Model 4 (adjusted for factors in models 1–3 and psychosocial factors)[b]	0.43	0.34, 0.54	0.58	0.42, 0.80	0.36	0.25, 0.52	0.66	0.42, 1.03	0.012
Model 5 (adjusted for factors in models 1–4 and socioeconomic position)	0.43	0.33, 0.54	0.57	0.41, 0.80	0.36	0.24, 0.52	0.66	0.41, 1.04	0.022

Abbreviation: CI, confidence interval.
[a] Smoking, hypertension, diabetes, low density lipoprotein cholesterol, high density lipoprotein cholesterol, triglycerides, cholesterol, and body mass index.
[b] Anxiety, anger, depression, and chronic burden.

Table 5. Adjusted Relative Differences in Carotid Intimal Media Thickness for Women Compared With Men, Stratified by Race/Ethnicity, Multi-Ethnic Study of Atherosclerosis, 2000–2002

	Non-Hispanic White		African American		Hispanic		Chinese		$P_{interaction}$ for Race and Sex
	Difference	95% CI	Difference	95% CI	Difference	95% CI	Difference	95% CI	
Common carotid intimal media thickness									
Unadjusted	0.95	0.93, 0.96	0.95	0.93, 0.96	0.96	0.94, 0.98	0.95	0.93, 0.98	0.73
Model 1 (adjusted for age)	0.95	0.93, 0.96	0.95	0.93, 0.96	0.96	0.94, 0.97	0.96	0.93, 0.98	0.83
Model 2 (adjusted for age and traditional risk factors)[a]	0.95	0.93, 0.96	0.93	0.91, 0.95	0.95	0.93, 0.98	0.95	0.92, 0.98	0.20
Model 3 (adjusted for factors in models 1 and 2, physical activity, and diet)	0.95	0.93, 0.97	0.92	0.90, 0.95	0.96	0.93, 0.98	0.95	0.92, 0.98	0.07
Model 4 (adjusted for factors in models 1–3 and psychosocial factors)[b]	0.95	0.93, 0.97	0.93	0.91, 0.95	0.96	0.93, 0.98	0.95	0.92, 0.98	0.12
Model 5 (adjusted for factors in models 1–4 and socioeconomic position)	0.95	0.93, 0.97	0.93	0.91, 0.95	0.96	0.93, 0.98	0.95	0.91, 0.98	0.16
Internal carotid intimal media thickness									
Unadjusted	0.87	0.84, 0.90	0.93	0.89, 0.97	0.86	0.82, 0.90	0.88	0.83, 0.93	0.07
Model 1 (adjusted for age)	0.88	0.85, 0.91	0.93	0.89, 0.97	0.85	0.82, 0.89	0.88	0.83, 0.93	0.04
Model 2 (adjusted for age and traditional risk factors)[a]	0.87	0.84, 0.91	0.90	0.86, 0.95	0.84	0.79, 0.89	0.84	0.78, 0.91	0.10
Model 3 (adjusted for factors in models 1 and 2, physical activity, and diet)	0.88	0.84, 0.92	0.91	0.86, 0.96	0.84	0.79, 0.89	0.83	0.77, 0.90	0.10
Model 4 (adjusted for factors in models 1–3 and psychosocial factors)[b]	0.88	0.84, 0.92	0.90	0.85, 0.95	0.84	0.79, 0.89	0.84	0.78, 0.91	0.12
Model 5 (adjusted for factors in models 1–4 and socioeconomic position)	0.87	0.84, 0.91	0.90	0.85, 0.96	0.84	0.71, 0.89	0.83	0.77, 0.90	0.13

Abbreviation: CI, confidence interval.
[a] Smoking, hypertension, diabetes, low density lipoprotein cholesterol, high density lipoprotein cholesterol, triglycerides, cholesterol, and body mass index.
[b] Anxiety, anger, depression, and chronic burden.

Cardiovascular Health Study, minimal racial/ethnic variations in sex differences in stroke were seen (4). In the death certificate study, sex differences in stroke were modest, generally not exceeding 1.4 for any racial/ethnic group (3). The presence of relatively small racial/ethnic variations in sex differences in stroke incidence and mortality is compatible with our findings of smaller or null racial/ethnic variation in sex differences in cIMT. In MESA, previous studies have found that CAC was more strongly associated with incident coronary events than cIMT and that CAC was a better predictor of all subsequent CVD events than cIMT (23), although the number of strokes compared with coronary events was small. It is also possible that both CAC and cIMT have additive effects on stroke risk (23). In general, our findings of greater racial/ethnic variation in sex differences in CAC than in cIMT are consistent with other work showing greater racial/ethnic variations in sex differences in coronary disease than in stroke (2).

Explanations for the racial/ethnic variation in CAC sex differences remain speculative, particularly for the Chinese Americans who have been relatively understudied. In the Framingham Study, bone density was inversely related to vascular calcification (24), and in at least one cohort study, Chinese-American women tend to have lower bone density than African-American women (25). This racial/ethnic difference in bone density could potentially reflect larger sex differences in bone density in Chinese Americans compared with African Americans, but this comparison has not been reported. Adipocytokines may contribute to the observed sex differences. For example, in a recent analysis of adiponectin single-nucleotide polymorphisms in MESA, particular single-nucleotide polymorphisms were associated with increased prevalence of CAC in African Americans but not in Chinese Americans or non-Hispanic whites, potentially reflecting various sex differences in adipocytokines in African Americans versus other races/ethnicities, although comparisons by sex were not reported. Vitamin D polymorphisms have also been found to be associated with CAC levels (26), and the magnitude of vitamin D sex differences varies by race/ethnicity (27), suggesting that vitamin D may be a possible mediator of racial/ethnic variation in CAC sex differences. Finally, women's estradiol levels, either endogenous (28) or exogenous (29), may be associated with CAC, and levels can also vary by race/ethnicity (30), suggesting that estradiol could play a role in the observed CAC variations.

Strengths of this analysis include its population-based sampling and measurement of both CAC and cIMT, as well as our ability to adjust for an extensive list of traditional and nontraditional factors that previously have been found to vary by sex and race/ethnicity. Limitations include the fact that we adjusted for potential confounders using single cross-sectional measures, which may not fully capture the full confounding effects of life-course exposures to these factors. In addition, MESA has a relatively smaller number of Chinese-American participants.

We conclude that racial/ethnic variation in sex differences is significant for CAC and persists after adjustment for traditional, behavioral, and psychosocial risk factors, with the most pronounced sex differences occurring in non-Hispanic whites and smaller differences occurring in African Americans and Chinese. This suggests that differential patterning of CVD risk factors by sex across racial/ethnic groups does not explain racial/ethnic variation in sex differences. Of note, although the magnitude of sex difference varied by race, men consistently have CAC more often and in greater amounts than women. In contrast, racial/ethnic differences in sex effects on cIMT were not statistically significant. Further investigation of the factors contributing to this racial/ethnic heterogeneity could yield important insights into sex differences in CVD generally.

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