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The Prevalence and Severity of Coronary Artery Calcification on Coronary Artery Computed Tomography in Black and White Subjects

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OBJECTIVES We studied the relationship between coronary artery calcium (CAC) and race in asymptomatic, active-duty personnel in the Prospective Army Coronary Calcium (PACC) project.

BACKGROUND Valid cardiovascular risk assessments in black Americans using coronary artery computed tomography (coronary CT) require the generalizability of population-based CAC score distributions derived from primarily white patient populations.

METHODS Among 1,000 consecutive participants (mean age, 42 ± 2 years; range, 40 to 45 years), 999 participants underwent coronary CT and indicated a specific racial affiliation. This included white, non-Hispanic in 699 (69.9%) participants and black, non-Hispanic in 194 (19.4%) participants. Univariate associations between race and cardiovascular risk variables were entered into a logistic regression model for CAC that also controlled for socioeconomic status and education.

RESULTS Coronary artery calcium was nearly twice as prevalent in white (19.2%) than in black participants (10.3%) ($p = 0.004$). Black individuals had a threefold greater prevalence of hypertension, left ventricular hypertrophy, ST-T-wave abnormalities, and current cigarette smoking. Black subjects also had significantly greater blood pressure, high-density lipoprotein cholesterol, glycosylated hemoglobin, lipoprotein(a) and fibrinogen levels, and lower triglyceride levels and waist girth than white subjects. After adjustment for these differences, and socioeconomic adjusters, black individuals were 39% as likely to have any CAC present (odds ratio, 0.39; 95% confidence interval, 0.20 to 0.78; $p = 0.007$).

CONCLUSIONS Despite a worse cardiovascular risk profile, black Americans have significantly less CAC than white Americans. The use of coronary CT as an accurate risk prediction tool in black Americans will require ethnic-specific data on the presence and severity of CAC. (J Am Coll Cardiol 2003;41:39–44) © 2003 by the American College of Cardiology Foundation

The presence of extensive age- and gender-adjusted coronary artery calcium (CAC) on coronary artery computed tomography (coronary CT) indicates a higher than expected atherosclerotic burden and greater absolute and relative risk for the development of incident coronary heart disease (1–4). Thus, this test is increasingly applied as a tool to measure cardiovascular risk. However, coronary CT-based risk assessments utilize age- and gender-specific CAC

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distributions derived from predominately white, male, and well-educated patients (5,6). The generalizability of coronary CT as a risk-screening tool to other ethnic groups, for example, black individuals, is critically dependent on cross-ethnic stability in these CAC distributions. Major interracial differences in cardiovascular risk factors associated with CAC, such as hypertension and hyperlipidemia, and in calcium and bone metabolism (7–9) provide the rationale for validating the assumption that coronary CT scores have cross-ethnic validity.

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Previous studies on race and CAC have yielded discrepant results. In a study using digital fluoroscopy, Doherty et al. (10) found a significantly lower prevalence of CAC yet higher cardiovascular event rates in black individuals. More recently, the Coronary Artery Risk Development in Young Adults study (CARDIA) reported an absence of racial differences in the prevalence and severity of coronary artery calcification using coronary CT (11). Thus, additional data are needed to clarify the relationship between race and CAC.

The Prospective Army Coronary Calcium (PACC) project is an ongoing, prospective study evaluating the utility of coronary CT as a screening tool for coronary heart disease risk in active-duty U.S. Army men and women between the ages of 40 to 45 years. This analysis evaluates the relationships between CAC and race in this narrow-age ranged, demographically diverse population. We hypothesized that black and white study participants would have a similar prevalence and severity of CAC.

METHODS

The Walter Reed Army Medical Center Department of Clinical Investigation Human Use Committee approved this study, for which the methods (12) and some prelimi-

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Abbreviations and Acronyms

BMI	= body mass index
CAC	= coronary artery calcium
CARDIA	= Coronary Artery Risk Development In young Adults study
coronary CT	= coronary artery computed tomography
PACC	= Prospective Army Coronary Calcium project

nary results have been previously described. Briefly, the PACC cohort consists of active duty U.S. Army personnel between the ages of 40 to 45 years who voluntarily participated in the research study under informed consent at the time of mandatory, periodic Army physical evaluation. The study procedures included a health risk appraisal and other validated questionnaires, serologic testing of cardiovascular risks factors, and a coronary CT scan. All subjects were asymptomatic and free of known cardiovascular disease at the time of enrollment. Between October 1998 and August 2000, among 1,000 consecutive participants, 999 indicated a specific racial affiliation and had a coronary CT scan. This included white, non-Hispanic in 699 (69.9%) participants and black, non-Hispanic in 194 (19.4%) participants.

Each participant provided details of their medical history, including known diagnoses of hypertension, diabetes mellitus, and hypercholesterolemia. Smoking was self-reported as current, recent (within 6 months), or remote (>6 months) cigarette use. A family history of coronary heart disease included a history of sudden death, myocardial infarction, or coronary revascularization in a first degree relative before the age of 55 years (males) or 65 years (females). Height and weight were measured, and body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Waist girth was measured to the nearest centimeter using a tape on exposed skin at the level of the umbilicus in the standing position with the arms and shoulders relaxed. Resting blood pressure was measured using an automated sphygmomanometer, and was recorded as the average of three seated measurements taken 5 min apart. Hypertension was defined as either a systolic blood pressure of >135 mm Hg, a diastolic blood pressure of >85 mm Hg (13), or a history of hypertension (treated or untreated). Fasting blood was collected for the measurement of serum glucose, glycosylated hemoglobin, insulin, homocysteine, lipoprotein(a), and fibrinogen. Low-density lipoprotein cholesterol was measured using a direct assay. Standard 12-lead electrocardiograms were evaluated by an investigator without knowledge of the CAC score or other cardiovascular risk factors. Left ventricular hypertrophy was classified according to the methods of the Framingham study (14). The metabolic syndrome was classified according to the recommendations of the National Cholesterol Education Program (15).

Coronary CT scanning and analysis. Coronary CT was performed using an Imatron C-150LXP electron beam CT scanner (Imatron Inc., San Bruno, California). Images were obtained using a 40- to 50-slice (3-mm thickness) protocol with image acquisition gated to 70% to 80% of the electrocardiographic RR interval while respirations were held. Scans were interpreted in a blinded manner by an experienced radiologist (I. M. F.) using the Agatston scoring method (16). A focus of coronary calcium was defined as the presence of four or more contiguous pixels with >130 Hounsfield U (field of view, 350 mm). A total CAC score was determined from the sum of individual scores of the four major epicardial coronary arteries. A scan was considered positive for CAC when the total CAC score was >0 (17).

Statistical analysis. Cardiovascular risk factor differences between white and black subjects were explored. Risk factor comparisons between groups of patients with and without CAC using a threshold value of any detectable coronary calcium (CAC score = 0) were performed. Continuous variables were compared using a *t* test for independent groups. For comparison of CAC scores between groups, data were log-transformed using the formula: log (CAC + 1). Categorical variables were compared using the chi-squared test. The relationship between multiple cardiovascular risk factors and the presence of CAC was assessed using stepwise logistic regression analysis. Risk factor variables with a univariate relationship ($p \leq 0.05$) to CAC were entered into the model. Race, categorically defined as white or black, socioeconomic status (military rank was used as a surrogate), and education level (highest level attained) were also entered into the model. All analyses were performed using SPSS for Windows (version 10.05, SPSS Inc., Chicago, Illinois). Data are presented as mean ± SD. A two-tailed p value of ≤0.05 was considered statistically significant.

RESULTS

Table 1 displays the baseline demographics and cardiovascular risk variables of the black and white study participants. Overall, black individuals were significantly more likely to be current smokers, and have hypertension. White patients were more likely to have the metabolic syndrome. Among measured variables, black individuals more commonly had left ventricular hypertrophy and electrocardiographic ST-T-wave abnormalities. They also had significantly higher mean values for BMI, systolic and diastolic blood pressure, and levels of high-density lipoprotein cholesterol, hemoglobin A1C, and lipoprotein(a) than white participants. In comparison, white subjects had statistically higher serum triglyceride levels.

Overall, the prevalence of CAC was 17.3%, and was associated with BMI, waist girth, diastolic blood pressure, high-density lipoprotein cholesterol, triglyceride level, hemoglobin A1C, lipoprotein(a), and fibrinogen. White sub-

Table 1. Cardiovascular Risk Variables Among White and Black Patients Studied With Coronary CT

	White N = 699	Black N = 194	p Value
Coronary CT			
Any CAC present (%)	134 (19.2)	20 (10.3)	0.004
Mean CAC score (%)	15 ± 93	7 ± 58	0.003
Hypertension (%)	44 (6.3)	32 (16.5)	< 0.001
ECG LVH present (%)	30 (4.3)	26 (13.4)	< 0.001
ST-T-wave abnormalities (%)	25 (3.6)	34 (18.1)	< 0.001
Cigarette smoking, current (%)	33 (4.7)	31 (16.1)	< 0.001
Cigarette smoking, former (%)	134 (19.2)	50 (25.8)	< 0.001
Metabolic syndrome (%)	70 (10.0)	8 (4.1)	0.01
Family history of coronary heart disease (%)	136 (19.5)	32 (16.5)	0.43
Current statin medication use (%)	21 (3.0)	8 (4.1)	0.40
Body mass index (kg/m^2)	27.2 ± 3.1	28.2 ± 3.6	0.03
Waist girth (cm)	93.0 ± 9.8	91.0 ± 9.7	0.97
Blood pressure, systolic (mm Hg)	122 ± 12	124 ± 15	<0.001
Blood pressure, diastolic (mm Hg)	76 ± 9	78 ± 10	0.001
Total cholesterol (mg/dl)	202 ± 36	202 ± 37	0.90
LDL cholesterol (mg/dl)	131 ± 33	129 ± 35	0.33
HDL cholesterol (mg/dl)	51 ± 13	57 ± 16	0.003
Trigylcerides (mg/dl)	130 ± 91	99 ± 57	0.001
Hemoglobin AIC (%)	5.5 ± 0.6	5.7 ± 0.6	0.017
Fasting glucose (mg/dl)	91 ± 11	90 ± 10	0.90
Lipoprotein(a) (mg/dl)	27 ± 33	58 ± 45	0.000
Homocysteine (μmol/l)	9.5 ± 2.6	9.6 ± 2.7	0.34
Fibrinogen (mg/dl)	307 ± 58	324 ± 61	0.69
Insulin (μU/ml)	8.2 ± 7.2	9.3 ± 6.6	0.96
C-reactive protein (mg/dl)	0.26 ± 0.89	0.26 ± 0.42	0.79

CAC = coronary artery calcium; CT = computed tomography; ECG = electrocardiogram; HDL = high-density lipoprotein; LDL = low-density lipoprotein; LVH = left ventricular hypertrophy.

jects had nearly twice the prevalence of CAC as black subjects (19.2% vs. 10.3%, p = 0.004). The CAC prevalence and coronary CT scores for gender and racial subgroups are shown in Table 2. Coronary artery calcium was more common in both white men (trend: p = 0.06) and white women (p = 0.02). Overall, the mean CAC score was also significantly higher for white than for black subjects. No black woman had detectable CAC, and the mean CAC score was significantly higher in white women (p = 0.03).

Univariate associations between race and cardiovascular risk variables were entered into a logistic regression model for CAC, controlling for race and socioeconomic status. After adjustment for these factors, race, BMI, and the serum levels of triglycerides and lipoprotein(a) remained statistically significant predictors of CAC (p < 0.05). The odds ratio for CAC in black individuals, after controlling for these factors, was 0.39 (95% confidence interval, 0.20 to 0.78, p = 0.007) (Table 3).

DISCUSSION

In this age-narrow screening population, the prevalence of CAC was nearly 50% lower in black than in white individuals. Furthermore, this difference widened after adjustment for socioeconomic status, educational level, and the expected race-related differences in the cardiovascular risk factor profile. These data have important implications for the generalizability of coronary CT score distributions of the presence and severity of CAC within ethnic subgroups for the purpose of cardiovascular risk determinations.

The biologic basis for differences between black and white subjects in the presence of preclinical atherosclerosis is partly founded in major interracial differences in cardiovascular risk factors. Whereas hypertension, diabetes, and obesity are more prevalent in black individuals, lipid profile abnormalities (particularly lower high-density lipoprotein cholesterol and higher triglyceride levels) are more prevalent

Table 2. Coronary Calcium Scores and Prevalence in Black and White Subjects

	Overall		Men			Women		
	CAC Score	Prevalence	n	CAC Score	Prevalence	n	CAC Score	Prevalence
Black	7 ± 58	20/194 (10.3%)	145	9 ± 67	20/145 (13.8%)	49	0	0/49 (0%)
White	15 ± 93	134/698 (19.2%)	597	16 ± 100	124/597 (20.8%)	97	4 ± 27	10/97 (10.3%)
p Value	0.003	0.004		0.053	0.057		0.020	0.017

CAC = coronary artery calcium.

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Table 3. Logistic Regression Coefficients and Confidence Intervals for a Multivariate Model Evaluating Associations With Coronary Artery Calcium

Variables	Odds Ratio	95% CI for Odds Ratio		p Value
		Lower	Upper	
Body mass index (per kg/m^2)	1.113	1.039	1.193	0.002
Black race	0.394	0.200	0.776	0.007
Triglycerides (per mg/dl)	1.003	1.001	1.006	0.011
Lipoprotein(a) (per mg/dl)	1.008	1.003	1.013	0.003
Systolic blood pressure (per mm Hg)	1.008	0.987	1.030	0.456
HDL-C (per mg/dl)	1.005	0.988	1.023	0.547
Left ventricular hypertrophy	0.758	0.325	1.771	0.523
ST-T-abnormalities	1.190	0.508	2.791	0.688
Former smoker	0.815	0.313	2.122	0.675
Military rank (pay grade)	1.022	0.917	1.139	0.691
Highest education level	1.201	0.861	1.676	0.280
Hemoglobin AIC (per 0.1%)	1.038	0.750	1.436	0.822
Fibrinogen (per mg/dl)	1.000	0.996	1.003	0.894

CI = confidence interval; HDL-C = high-density lipoprotein cholesterol.

in whites. However, current evidence from pathology studies of early atherosclerosis (18,19) and ultrasound studies of carotid intima-media thickness in asymptomatic individuals (20–22) indicate that, after controlling for differences in risk factors and socioeconomic status, race does not have an independent relationship to atherosclerosis.

Extending this assumption to the process of atherosclerosis calcification may be a mistake. Indeed, the use of coronary CT-derived CAC scores as a surrogate for atherosclerosis burden in different racial groups assumes that the process of coronary calcification occurs as a race-independent phenomenon. Doherty et al. (10) showed a CAC prevalence of 36% in black individuals, versus 60% in whites, using digital fluoroscopy in a middle-aged to elderly, primarily male and higher-risk population from the South Bay Heart Watch study. Furthermore, these differences remained after adjustment for cardiovascular risk factors. A recent study (23) of the very elderly also found that black individuals were less likely to have CAC, a difference that persisted after adjustment for age differences between racial groups. Our findings in middle-aged, asymptomatic white and black subjects are in agreement with these investigators, and extend the lower prevalence of coronary calcium in black patients in the South Bay Heart Watch cohort to include both men and women.

These data differ from the published findings of the CARDIA study, which reported a similar prevalence of CAC in blacks and whites using coronary CT in the year 10 examination (11). These results from the CARDIA study are particularly notable because, similar to the current study, CARDIA was also a screening study of younger individuals. In general, we recommend that caution must be used in interpreting data on subclinical calcified atherosclerosis from cohorts of racially and geographically over-sampled participants that could be biased by genetic clustering. However, the discrepancy with the CARDIA study appears to be most likely a result of false positive studies from obesity-related CT scan artifacts (personal communication, Robert Detrano, MD, PhD, January 2002). This is supported by a recently presented analysis (24) of CARDIA year 15 coronary CT scans that refutes the original CARDIA publication (11) by showing a lower prevalence of CAC in black individuals, although this finding was restricted to men. Thus, the current evidence favors the conclusion that black individuals are substantially less likely to have CAC.

Despite the lower prevalence of CAC in black individuals within the South Bay Heart Watch, the associated cardiovascular event rate was over twofold higher than in whites (10). Consistent with the established greater cardiovascular event burden in ethnic minorities, in part due to a shift from atherosclerotic to hypertensive vascular disease as a cause of death (25,26), these race-related differences in CAC, and the altered relationship to cardiovascular events, suggest that the application of race-nonspecific CAC distributions to black individuals and conceivably other ethnic groups will lead to inaccurate atherosclerosis burden assessments and inherent inaccuracy in the cardiovascular risk assessment. Although the present study did not have sufficient power to definitively address the relationship between gender, race, and coronary calcification, this study appears to support that this limitation would extend to both black men and women. In comparison, assessments of noncalcified atherosclerosis using technologies, such as B-mode carotid ultrasound, have not demonstrated a consistent pattern of major interracial differences in atherosclerosis burden (20,21). Thus, in minorities, atherosclerosis burden testing using methods other than coronary CT is most appropriate until data on race-specific CAC distributions and its prognostic relationships are known.

There is no definitive causal mechanism linking ethnicity with coronary calcification; however, racial differences in osteoporosis (8,27) and its complications (28) establish a precedence for interracial variability in the regulation of tissue calcification. Atherosclerosis calcification is an active, regulated process similar to osteogenesis that is partially

influenced by hormonal factors. For example, higher levels of 1,25 dihydroxy vitamin D predict lower coronary calcium mass, regardless of race (7,9), although there is controversy on this subject (29). Genetic factors may also contribute to race-related differences in CAC and concomitant atherosclerosis. Although specific genetic associations have not yet been identified, chief among these is matrix gla protein polymorphisms (30), which may provide a relative protection from atherosclerosis tissue calcification (31). The increasing frequency of interracial marriages and racial admixtures will create an opportunity to test these genetic hypotheses as the racial constructs of black and white, or Hispanic and Asian, become increasingly blurred (32).

CONCLUSIONS

Cardiovascular risk assessments incorporating CAC assume that population-based CAC distributions can be evenly generalized to all racial groups. Currently available data in populations ranging in age from middle-aged to the elderly support that this assumption is incorrect, based upon the substantially lower prevalence of CAC, but not necessarily lower rates of incident cardiovascular events, in blacks compared with whites. Thus, the cross-ethnic generalization of current population-based CAC distributions and cardiovascular risk assessments is premature until the relationships between race, CAC, and cardiovascular outcomes are specifically established in ethnic minorities.

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