Prevalence and Correlates of Coronary Calcification in Black and White Young Adults

The Coronary Artery Risk Development in Young Adults (CARDIA) Study


Abstract—Whereas cardiovascular risk factor levels are substantially different in black and white Americans, the relative rates of cardiovascular disease in the 2 groups are not always consistent with these differences. To compare the prevalence of coronary calcification, an indicator of coronary atherosclerosis, in young adult blacks and whites, we performed electron-beam computed tomography of the heart in 443 men and women aged 28 to 40 years recruited from a population-based cohort. The presence of calcium, defined as at least 1 focus of at least 2.05 mm² in area and >130 Hounsfield units in density within the coronary arteries, was identified in 16.1% of black men, 11.8% of black women, 17.1% of white men, and 4.6% of white women (P = 0.04 for comparison across groups). Coronary calcium was associated with age and male sex, and after adjustment for age, race, and sex, coronary calcium was positively associated with body mass index, weight, systolic blood pressure, total cholesterol, low density lipoprotein cholesterol, triglycerides, and fasting insulin and negatively associated with education (all P < 0.05). Independent risk factors included male sex, body mass index, and low density lipoprotein cholesterol. Race was not significantly associated with coronary calcium in men or women, before or after adjustment for risk factors. Coronary calcification is associated with increased levels of cardiovascular risk factors in young adults, and its prevalence is not significantly different in blacks and whites. (Arterioscler Thromb Vasc Biol. 2001;21:852-857.)

Key Words: coronary heart disease • risk factors • race • coronary artery calcification

Relative levels of coronary risk factors in blacks and whites suggest that blacks would be at higher risk for coronary heart disease (CHD).1–6 CHD mortality rates appear to reflect higher risk factor levels in blacks,7 but CHD incidence is lower in black men than in white men.8 Clues to possible racial differences in rates of CHD may be found by identifying subclinical disease for which treatment has not been instituted and which is not subject to the biases of disease ascertainment or death certificate coding.9–12 To compare the prevalence of a marker of coronary atherosclerosis in a population-based sample of young adult blacks and whites, to examine risk factor correlates, and to determine whether any racial differences in prevalence might be explained by risk factor differences, we measured coronary calcification by using electron-beam computed tomography (EBCT) of the heart and risk factors in men and women aged 28 to 40 years who have participated in an ongoing epidemiological study of the coronary disease risk factors. Coronary calcium is a specific marker for coronary atherosclerosis13 and can be quantified by EBCT.14–16

Methods

Participants

Participants in the present study were from the Coronary Artery Risk Development in Young Adults (CARDIA) Study. The baseline CARDIA examination took place from 1985 to 1986 and included 5115 women and men from 4 centers (Birmingham, Ala; Chicago, Ill; Minneapolis, Minn; and Oakland, Calif). Participants had been sampled from the total community or from selected census tracts, except for participants in Oakland, for whom a health plan membership was used. Fifty-two percent of participants were black, and 55% were women. Details of the study design have been published previously.17 At the conclusion of a reexamination of the cohort between June 1995 and June 1996 (year 10), at which 78.5% of the surviving cohort participated, 443 individuals from the Chicago and Oakland centers were recruited to participate in a substudy of coronary calcification. Sampling was designed to achieve approximately equal numbers of black and white men and women. Women

Received July 28, 2000; revision accepted January 31, 2001.
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Arterioscler Thromb Vasc Biol is available at http://www.atvbaha.org

852
were scanned during the 2 weeks after the beginning of their menstrual cycles to avoid radiation during pregnancy. Participants who weighed >280 pounds were not included, because the scanning apparatus could not accommodate them. Scans were performed between May 1996 and January 1997. The time between the year-10 examination, during which risk factors were measured, and EBCT scanning was 347±103 days (mean±SD). The protocol was approved by the institutional review boards of both medical centers, and informed consent was obtained from all participants.

Scanning Protocol
EBCT scanners (Imatron C-100) were used to obtain 40 contiguous 3-mm-thick transverse images from the root of the aorta to the apex of the heart. Images were obtained at 80% of the ECG RR interval. An 180° turn was used, a focus was at least 2.05 mm². Lesions of this size have been found to represent blood pressure and obesity, respectively. All models were constructed by using baseline and year-10 risk factor variables. Logistic regression was used to estimate the odds of having coronary calcification in relation to each baseline and year-10 risk factor, with adjustment for age, race, and sex.

Risk Factor Measurements
Risk factor measurements were made at the baseline and year-10 examinations. Years of education and history of smoking were self-reported. Weight and height were measured with subjects in light clothing and without shoes. Body mass index (BMI) was calculated as weight (kilograms) divided by height² (meters squared). Standard methods for measuring blood pressure, fasting total cholesterol, HDL cholesterol, triglycerides, alcohol intake, and physical activity were used, as previously described.17,20–23 LDL cholesterol was calculated using the Friedewald equation.24 Insulin was measured by radioimmunoassay (Linco). Diabetes was defined as having been told by a physician that the participant had diabetes, other than during pregnancy. Smoking history was defined by questionnaire as current, former, or never. Current and former smokers were grouped together as ever smokers. Participants were also asked if they had ever had a heart attack or angina.

Statistical Methods
Distributions of year-10 risk factors and coronary calcium scores and the prevalence of coronary calcification were determined for each race-sex group. ANOVA and χ² contingency table analysis were used to test for differences in risk factors across the 4 race-sex groups. Risk factor variables with marked skewness were logarithmically transformed to normalize their distributions for statistical testing, but untransformed variables are displayed. Logistic regression was used to estimate the odds of having coronary calcification in relation to each baseline and year-10 risk factor, with adjustment for age, race, and sex.

Additional multivariable logistic regression models were constructed to predict calcium presence by first adjusting for all variables with significant age-, race-, and sex-adjusted associations with coronary calcium in the entire sample and by then identifying a set of independent variables with the use of backward stepwise regression. Race was forced into a model with the remaining variables to examine its relation to coronary calcification independent of other risk factors. Systolic blood pressure and BMI were used to represent blood pressure and obesity, respectively. All models were constructed by using baseline and year-10 risk factor variables. Areas under receiver operator characteristic (ROC) curves were estimated to assess the performance of the models. Areas may range from 0.50 (no discrimination between participants with and without coronary calcium by model) to 1.00 (100% discrimination between participants with and without coronary calcium by model).

| TABLE 1. Characteristics of Study Sample at Year 10 |
|-------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age, y                        | (n=118)         | (n=127)         | (n=111)         | (n=87)          | P               |
| 34.5±3.6                      | 34.9±3.9        | 35.2±3.4        | 35.8±3.4        | 0.07            |
| Education, y                  | 13.4±1.9        | 13.6±2.0        | 15.5±2.8        | 15.2±2.6        | <0.0001         |
| Weight, kg                    | 86.9±17.5       | 83.5±21.8       | 83.3±12.2       | 68.0±15.4       | <0.0001         |
| BMI, kg/m²                    | 27.5±5.4        | 30.8±8.1        | 26.2±3.6        | 24.8±5.7        | <0.0001         |
| Systolic blood pressure, mm Hg| 115.9±11.0      | 111.6±13.7      | 112.9±9.8       | 105.4±9.4       | <0.0001         |
| Diastolic blood pressure, mm Hg| 76.5±9.5        | 74.1±11.4       | 74.5±8.4        | 69.6±7.7        | <0.0001         |
| Hypertension, %               | 12.0            | 14.3            | 3.6             | 1.0            | 0.0007          |
| Smoking history, %            | 60.2            | 52.8            | 69.4            | 64.4            | 0.06            |
| Never                         | 39.8            | 47.2            | 30.6            | 35.6            |                 |
| Total cholesterol, IU         | 4.76±1.02       | 4.46±0.82       | 4.71±0.97       | 4.68±0.88       | 0.06            |
| LDL cholesterol, IU           | 2.96±0.88       | 2.62±0.69       | 3.01±0.87       | 2.81±0.79       | 0.0012           |
| HDL cholesterol, IU           | 1.28±0.37       | 1.39±0.38       | 1.16±0.25       | 1.44±0.35       | <0.0001         |
| Triglycerides, IU             | 1.08±1.07       | 0.78±0.45       | 1.17±0.94       | 0.89±0.71       | <0.0001         |
| Insulin, pmol/L               | 87.2±60.0       | 86.3±52.1       | 70.1±28.3       | 64.7±24.9       | 0.006           |
| Alcohol intake, mL/d          | 16.6±21.4       | 8.6±23.0        | 15.2±21.2       | 7.1±12.0        | <0.0001         |
| Diabetes, %                   | 4.3             | 3.1             | 0.9             | 1.2             | 0.32            |
| Physical activity score       | 441±294         | 236±194         | 442±290         | 347±233         | <0.0001         |

Values are mean±SD, except for hypertension, smoking, and diabetes (percentages). P values indicate comparison across the 4 race-sex groups.
There were 443 participants with complete EBCT data. At year 10, 2 participants were excluded from analyses of lipids because they were on lipid-lowering medication; 6 participants were excluded from analyses of blood pressure because they were on antihypertensive medication and their blood pressure was below the 90th percentile for those not on medication; and 35 participants were excluded from analyses of LDL cholesterol, triglycerides, and insulin because they had not fasted for at least 9 hours. Because of missing variables, the sample for multivariable analysis with all covariates included 392 participants. At baseline, the same exclusions resulted in a final sample of 427.

Analyses were performed by using SAS, version 6.10. Statistical significance was set at \( P < 0.05 \) for 2-sided tests.

### Results

Mean age was \( \approx 35 \) years across the race-sex groups (Table 1). Significant differences across the groups were found for all variables except age, smoking, total cholesterol, and diabetes. No participant reported ever having had a heart attack or angina. These characteristics were generally similar to the race-sex group characteristics of the whole CARDIA cohort (data not shown).

The prevalence of coronary calcium was highest (17.1\%) in white men and lowest (4.6\%) in white women (\( P = 0.04 \) for comparison across groups, Table 2). The distributions of calcium scores indicate skewness toward higher values. There were no significant differences by race in either men or women (\( P = 0.84 \) and 0.07, respectively) or by sex group among blacks (\( P = 0.33 \)). However, the prevalence was significantly higher among white men than women (\( P = 0.006 \)).

The presence of calcium was significantly positively associated with age, male sex, BMI, weight, systolic blood pressure, and total and LDL cholesterol at baseline and year 10 (Table 3) and was significantly associated with year-10 fasting triglycerides and fasting insulin. Education was significantly inversely associated with the presence of calcium.

In the model including year-10 risk factors that were associated with calcium, only male sex (odds ratio [OR] 3.94, 95\% CI 1.62 to 9.57; \( P = 0.003 \)) and BMI (OR for a 5-U difference 1.61, 95\% CI 1.16 to 2.25; \( P = 0.005 \)) were significantly associated with coronary calcium prevalence (Table 4, model 1). After backward stepwise regression, male sex (OR 4.06, 95\% CI 1.76 to 9.38; \( P = 0.001 \)), BMI (OR for a 5-U difference 1.68, 95\% CI 1.30 to 2.17; \( P < 0.0001 \)), and LDL cholesterol (OR for a 0.78-IU difference 1.39, 95\% CI 1.12 to 1.70; \( P = 0.0002 \)) were significantly associated with presence of calcium.
1.02 to 1.89; \( P = 0.04 \) were associated with coronary calcium (model 2). When race was reintroduced into the analysis, there was no association between black race and the presence of calcium (OR 0.98, 95% CI 0.49 to 1.99; \( P = 0.96 \)), but male sex, BMI, and LDL cholesterol retained significant associations with the presence of calcium (model 3). Results were similar with the use of baseline risk factors. Among all models in Table 4, areas under the ROC curves ranged from 0.73 to 0.78.

**Discussion**

In this population-based sample of young black and white men and women, coronary calcium was associated with traditional coronary risk factors, as expected. Race was not associated with the presence of coronary calcium before or after adjustment for sex, BMI, and LDL cholesterol.

Pathological studies have found more extensive fatty streaks in the aortas and coronary arteries of blacks than of whites, but similar amounts of raised lesions, which are more likely to include calcium. However, these data are limited because they include individuals of African heritage outside the United States, who may not be representative of blacks in the United States, and because autopsied decedents may not be representative of the living population.

Studies of subclinical cardiovascular disease are important for understanding whether racial differences in clinical disease and mortality have a biological basis or are due to differences in access to care or disease presentation and treatment. Two large studies have found that blacks have thicker common carotid intimal-medial thickness (IMT) than whites, but that black men have thinner internal carotid IMT than white men, with 1 of the studies also finding that black women had thinner internal carotid IMT than white women. A third study found no difference in maximum internal carotid artery plaque thickness between blacks and whites. A fluoroscopic study conducted in persons at high risk for coronary disease identified coronary calcium in only 36% of blacks compared with 60% of whites and Asian Americans. However, the selection of participants and the small number of blacks (n = 87), particularly black women, raises concern about the validity of this finding. Another study from this group of investigators found a lower prevalence of coronary calcium in blacks by use of EBCT, but there were only 2 black women in the study. In a study of persons enrolled in a large health plan, black race, compared with white race, was significantly associated with a 35% higher prevalence of aortic calcification in women, but there was no significant association in men. The present study did not find a significantly greater prevalence of coronary calcium among blacks. However, the inconsistency of findings among different studies suggests that more research is needed on subclinical cardiovascular disease among different racial groups.
In the present study, age, male sex, systolic blood pressure, weight, BMI, total and LDL cholesterol, fasting triglycerides, and fasting insulin were each related to coronary calcium, as expected, given that coronary calcium appears to be an excellent marker of atherosclerosis. Several other studies, including a study in young adults, have found relationships between EBCT-measured coronary calcium and coronary risk factors. Coronary calcium has also been found to predict mortality and CHD events. These findings confirm that coronary calcium is a marker of atherosclerosis and suggest that it is a useful tool in studying the origins of atherosclerotic heart disease. Of additional interest, hostility has been found to be associated with coronary calcification in this population.

Body weight and BMI were relatively strong risk factors in the present study and in the Muscatine Study, which included a similar age group, and were also associated with atherosclerosis in the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study. However, obesity may be associated with more artifacts on EBCT scans, which could lead to false-positive readings, particularly if a sensitive definition for coronary calcium is used. A 3-pixel definition from only 1 scan was used in the Muscatine study, which may be responsible for the particularly high ORs for weight and obesity, ranging from 6.4 to 19.6, comparing the highest with the lower 9 deciles for body size. We found that the lower the pixel level in the definition of a focus, the stronger was the association between BMI and calcium score (data not shown). We believe that the 3-pixel definition may be overly sensitive in younger populations, in whom the amount of coronary calcium is relatively low with respect to the amount of artifacts.

Finally, we examined the association of risk factors measured concurrently with coronary calcium and measured 10 years before coronary calcium measurement and found remarkably similar risk factor–calcium relationships. We chose not to focus on baseline risk factors because we do not know when coronary calcium developed and, thus, cannot imply that risk factors preceded coronary calcification. It is likely that the fibrous lesions into which calcium is incorporated were present many years before the detection of calcium.

There are several limitations to the present study. First, the sample consisted of volunteers from the original cohort, who might have had particular concern about their risks of coronary disease. However, none of the participants provided a history of heart attack or angina. Also, their characteristics were similar to the entire CARDIA cohort at year 10. Second, small amounts of calcium, as found in this cohort, may not be assessed reliably. We chose a more specific definition for coronary calcium to reduce the possibility of false-positive readings. Third, the present study did not have sufficient power to address the relationship between race and coronary calcification in each sex group. A larger study of coronary calcium in this cohort is currently planned; this upcoming study will allow the issue of race-sex interaction to be addressed. Finally, there are undoubtedly other unmeasured factors that are associated with calcium deposition in coronary atherosclerosis, including other risk factors, inflammatory and thrombotic factors, hormonal factors, and genetic factors. Our intent was not to completely explain the presence of coronary calcium but rather to demonstrate its association with known risk factors in young adults.

In conclusion, coronary calcium was associated with male sex and with CHD risk factors, particularly obesity and LDL cholesterol, in these young adults. The prevalence of calcium did not appear to be higher in blacks than in whites before or after adjusting for CHD risk factors.

Acknowledgments

This study was supported by National Heart, Lung, and Blood Institute contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-95005.

References


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doi: 10.1161/01.ATV.21.5.852
Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/21/5/852

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