ELSEVIER

Correlates of Coronary Artery Calcified Plaque in Blacks and Whites with Type 2 Diabetes

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PURPOSE: To examine whether the relationship between cardiovascular disease risk factors and coronary artery calcification (CAC) is modified by race among those with diabetes.
METHODS: Data were pooled data from three studies (Multi-Ethnic Study of Atherosclerosis, Family Heart Study, Diabetes Heart Study) for a total of 835 blacks and 1122 whites with diabetes. CAC was quantified by cardiac computed tomography and risk factors were obtained using standard methods. Regression models examined the relationship between risk factors and presence and quantity of CAC.
RESULTS: The average age of the cohort was 60 years; 57% were women. Presence of CAC was lower in blacks compared to whites (odds ratio = 0.22 for men, 0.57 for women, $p < 0.01$). Hemoglobin A1c, duration of diabetes, low-density lipoprotein, smoking, and body mass index were independently associated with presence of CAC; high-density lipoprotein, triglycerides, and C-reactive protein were not. Race did not modify these associations. Adjustment for multiple risk factors did not explain the race disparity in CAC.
CONCLUSIONS: CAC was reduced in blacks compared to whites in persons with diabetes. This effect was most pronounced in men. The relationship between risk factors and CAC did not differ between races. Racial differences in CAC are likely due to unmeasured risk factors and/or genetic susceptibility.
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KEY WORDS: Coronary Artery Disease, Diabetes Mellitus, Epidemiology, African-Americans, Cohort Studies.

INTRODUCTION

Coronary artery calcification (CAC) is less prevalent in blacks than whites (1–4), although this finding is not universal (5, 6). The underlying cause(s) of racial differences in CAC are not understood. Differences in the frequency of cardiovascular disease (CVD) risk factors or the strength of their relationship with CAC may play a role. These relationships have not been fully examined in persons with type 2 diabetes, in whom atherosclerosis is accelerated.

We previously reported different risk factor relationships between blacks and whites for low-density lipoprotein (LDL), hemoglobin A1c (HbA1c), and sex, with CAC (7). In each case, the strength of the association was greater in whites than in blacks. The present report extends these findings to a larger sample of blacks by pooling three cohorts that include large numbers of blacks in which measurement of CAC was obtained similarly. The cohorts include the Multi-Ethnic Study of Atherosclerosis (MESA), the Family Heart Study (FHS), and the Diabetes Heart Study (DHS). We hypothesize that risk factors for atherosclerosis among adults with diabetes are at least as frequent in blacks as in whites, but their relationship with CAC is weaker.

METHODS

Data were pooled from three cohorts in which CAC was quantified by cardiac computed tomography (CT). Persons with diabetes who were free of clinical CVD were selected for this analysis (835 blacks and 1122 whites). Cross-sectional associations between CVD risk factors and CAC were analyzed and compared between blacks and whites.

MESA

MESA was initiated to investigate the prevalence, correlates, and progression of subclinical CVD (8). The

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Selected Abbreviations and Acronyms

BMI = body mass index
CAC = coronary artery calcification
CRP = C-reactive protein
CT = computed tomography
CVD = cardiovascular disease
DHS = Diabetes Heart Study
FHS = Family Heart Study
GEE1 = generalized estimating equations
HbA1c = hemoglobin A1c
HDL = high-density lipoprotein
LDL = low-density lipoprotein
MESA = Multi-Ethnic Study of Atherosclerosis

cohort of 6814 persons aged 45–84 years was recruited in 2000–2002 from six urban sites using population-based methods with oversampling of blacks, Chinese and Hispanics. Recruitment was restricted to persons free of clinical CVD. The cohort includes participants with both previously diagnosed and newly diagnosed diabetes. All data for this report were collected at the baseline examination with the exception of HbA1c, collected at Exam 2. MESA contributed data for 332 blacks and 158 whites.

FHS

FHS recruited and examined 5381 participants from 1245 families in four sites in 1994–1996 to identify and evaluate genetic and nongenetic determinants of coronary heart disease (CHD) (9). Half of the families were chosen at random and the other half on the basis of a higher than expected risk of CHD. In 2002–2004, a substudy of 3359 FHS participants aged 30–93 years was conducted to obtain cardiac CT scans for the measurement of CAC (10). For this CAC substudy, a fifth site was added in Birmingham, AL, to recruit blacks, who were inadequately represented in the original FHS. This site recruited individuals from the HyperGEN study of hypertensive sibships (11). The cohort includes participants with both previously diagnosed and newly diagnosed diabetes. For this analysis, we excluded persons with clinical CVD defined as myocardial infarction, stroke, and coronary artery bypass graft. FHS contributed data for 120 blacks and 209 whites.

DHS

The Diabetes Heart Study (DHS) is a family study of the genetics and epidemiology of CVD in 1125 siblings concordant for diabetes, conducted at a single site in Forsyth County, NC (7). Participants aged 30–86 years with a history of diabetes were recruited from the community and outpatient clinics and examined in 1999–2005. A companion study (the African-American DHS) was initiated in 2007 and is recruiting 500 additional unrelated blacks to conduct admixture mapping for CAC (12). Participants with clinical CVD defined as myocardial infarction, stroke, and coronary artery bypass graft were excluded. The DHS studies contributed data for 383 blacks and 755 whites.

Variables

We selected only those variables that were obtained using similar techniques. CAC was measured in each study by noncontrast cardiac CT with ECG gating in late diastole based on a previously published protocol (13). Data are presented as Agatston score using 130 CT number threshold. Diabetes was defined either by fasting glucose of at least 7.0 mmol/l (126 mg/dl), self-reported previous physician diagnosis, or use of diabetes medication. The data set is comprised largely of persons with type 2 diabetes, although it likely that there are a small number of persons with type 1 diabetes included. Race and ethnicity were obtained by self-report. Risk factors were obtained using standard methods and include duration of and treatment for diabetes, HbA1c (not available in FHS), LDL, high-density lipoprotein (HDL), triglycerides, body mass index (BMI), C-reactive protein (CRP), smoking status and pack-years, hypertension, and use of lipid-lowering medications.

Statistical Analysis

CAC was analyzed as both a binary variable (presence versus absence) and a continuous variable (quantity). For the continuous variable, the natural log of CAC + 1 was analyzed. To account for the correlations among the observations (FHS and DHS include related individuals), tests of significance were based on generalized estimating equations (GEE1) assuming exchangeable correlation and using the robust estimator of the variance. We used the identity link for quantity of CAC and the logit link for the presence of CAC. To test whether a putative risk factor was related to quantity of CAC, a GEE1 linear model was computed separately for each risk factor. Age, study, race, sex, and race-by-sex interaction (race × sex) were included in all models. The models also included an interaction term between the risk factor and race, to test whether the risk factor's influence on CAC differed by race. To test whether a putative risk factor was related to presence of CAC, a GEE1 model using the logit link was computed separately for each risk factor following the steps outlined above for the linear model. Model 1 minimally adjusted for age, study, race, sex, and race × sex. A full model (Model 2) was fit by including all factors in Model 1 plus all risk factors.

RESULTS

The average age of the pooled cohort was 60 years, 57% were women, and 43% were black (Table 1). Several CVD risk