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Type 2 diabetes does not attenuate racial differences in coronary calcification

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Abstract

Aims—Coronary artery calcification (CAC) is a strong predictor of atherosclerotic cardiovascular disease (CVD). Whites appear to have a higher prevalence of CAC than African-Americans (AAs), but it is unknown if type 2 diabetes, a major cardiovascular risk factor, attenuates this difference. We investigated the relationship of race and CAC in a sample of patients with type 2 diabetes without clinical CVD.

Methods—Multivariable analyses of self-reported ethnicity and CAC scores, stratified by gender, in 861 subjects [32% AA, 66.9% male] with type 2 diabetes.

Results—AA race was associated with lower CAC scores in age-adjusted models in males [Tobit ratio for AAs vs. Whites 0.14 (95% CI 0.08–0.24, $p < 0.001$)] and females [Tobit ratio 0.26 (95% CI 0.09–0.77, $p = 0.015$)]. This persisted in men after adjustment for traditional, metabolic and inflammatory risk factors, but adjustment for plasma triglycerides [0.48 (95% CI 0.15–1.49, $p = 0.201$)] and HOMA-IR [0.28 (95% CI 0.08–1.03, $p = 0.055$)] partially attenuated the association in women.

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Conclusions—Relative to African-Americans, White race is a strong predictor of CAC, even in the presence of type 2 diabetes. The relationship in women appears less robust possibly due to gender differences in metabolic risk factors.

Keywords

Race; Coronary artery calcification; Atherosclerosis; Type 2 diabetes

1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality in patients with type 2 diabetes and accounts for over 34% of the mortality disparity between African-Americans (AA) and Whites in the United States [1]. Coronary artery calcification (CAC) is a useful marker of subclinical atherosclerosis in both of these populations. In addition to associations with traditional CVD risk factors [2], CAC correlates with the atherosclerotic burden at autopsy [3] and at angiography in patients without clinical CVD [4] and in diabetic patients with symptomatic cardiac disease [5]. It is also predictive of cardiovascular events across a spectrum of CVD risk, including in AAs and in patients with type 2 diabetes [6–8].

Several large epidemiologic studies have demonstrated greater CAC in White compared to AA men of similar age [9–11]. The data in women are less consistent with some studies demonstrating no association between race and CAC [12,13] and one study suggesting higher odds of CAC in AA women [10]. In both men and women, type 2 diabetes mellitus is an independent risk factor for CAC and is associated with greater prevalence and severity of CAC [10,14]. Notably, type 2 diabetes was associated with a greater increase in CAC scores in AAs compared to Whites [9,10]. In fact, type 2 diabetes has been shown to attenuate age differences in calcium scores [14]. Because type 2 diabetes is a strong independent CVD risk factor which is more common in AAs, we hypothesized that type 2 diabetes may attenuate the racial differences in CAC.

The influence of type 2 diabetes on racial differences in CAC is poorly understood because studies have been limited by two factors: large multi-ethnic studies of CAC have included only small numbers of subjects with type 2 diabetes and, similarly, studies of CAC in patients with type 2 diabetes have not recruited significant numbers of AA patients [8,9,13,15]. We conducted a study in a racially diverse population with type 2 DM to examine its influence on the relationship between African-American race and CAC.

2. Subjects

2.1. Study participants

The Penn Diabetes Heart Study (PDHS) has been described in detail previously [16,17]. In brief, it is an ongoing, single-center, community-based, cross-sectional study of novel risk factors for coronary atherosclerosis in patients with type 2 diabetes mellitus but without clinical cardiovascular disease (defined by history of myocardial infarction, previously documented angiographic disease, positive stress test, coronary or peripheral arterial revascularization, stroke or transient ischemic attack). Participants were eligible if they were between 35 and 75 years, had been previously diagnosed with type 2 diabetes (defined by a fasting plasma glucose ≥126 mg/dl, 2-h post-prandial glucose ≥200 mg/dl or use of oral hypoglycemic agents or insulin in subjects older than 40 years) and a negative pregnancy test, if applicable. Exclusion criteria were the presence of clinical cardiovascular disease, type 1 diabetes mellitus (defined pragmatically by insulin use prior to age 35), serum creatinine above 2.5 mg/dl, active infection or malignancy and weight in excess of the 300 pound electron beam tomography (EBT) scanner limit. The study was approved by the

University of Pennsylvania Institutional Review Board and informed consent was obtained from all study participants.

3. Materials and methods

3.1. Evaluated parameters

Eligible subjects were evaluated at the Clinical and Translational Research Center (CTRC) after a 12-h overnight fast. A questionnaire detailing demographic data, including self-reported ethnicity, medical, family and social history, medication use and cardiac history was completed. Complete blood count, routine chemistries, including glucose and hemoglobin A_{1c} (HbA_{1c}) assays, and microalbuminuria assays were performed at the clinical laboratories at the Hospital of the University of Pennsylvania. Plasma total and low-density lipoprotein (LDL), high-density lipoprotein (HDL), very low-density lipoprotein (VLDL) cholesterol and triglycerides (TG) as well as apolipoprotein B, apolipoprotein A-I and apolipoprotein A-II were measured enzymatically (Hitachi 912, Roche Diagnostic Systems Inc., NJ, USA) in lipoprotein fractions after ultracentrifugation (β-quantification technique) [17] in Penn's Center for Disease Control-certified lipid laboratory. Plasma C reactive protein (CRP) levels were batch-assayed using a high-sensitivity latex turbidimetric immunoassay (Wako Ltd., Osaka Japan) on the Hitachi 912 [17]. Plasma levels of adiponectin, leptin and insulin (Linco, St Charles MO), as well as IL-6 (R+D Systems, Minneapolis) were measured by enzyme-linked immunosorbant assay. The intra- and inter-assay coefficients of variation for pooled human plasma were 5.65% and 9.9% for adiponectin; 5.5% and 12.4% for leptin; 4.1% and 11.6% for insulin; 8.7% and 10.9% for IL-6; and 8.0% and 8.3% for CRP respectively. In 697 patients who were not being treated with insulin, the homeostasis model assessment of insulin resistance (HOMA2-IR) was calculated [18].

Clinical parameters, including blood pressure and waist circumference, were assessed as previously reported [16,17] and laboratory test results were generated by personnel blinded to the clinical characteristics and CAC scores of research subjects. Framingham risk scores (FRS) were determined as described by Wilson et al. [19]. Participants were classified as having the metabolic syndrome using the revised National Cholesterol Education Program (NCEP) definition (glucose cut-point 100 mg/dl); all PDHS subjects were designated as meeting metabolic syndrome glucose criteria. Global CAC scores were determined as previously reported [16,17] using the method of Agatston et al. from 40 continuous 3 mm-thick computed tomograms collected on an EBT scanner using customized software (Imatron, San Francisco, CA).

3.2. Statistical analysis

Data are reported as medians and interquartile ranges for continuous variables and proportions for categorical variables. The Mann–Whitney U test was used to compare medians and chi-square test to compare proportions between ethnicities within gender-stratified groups. Tobit conditional regression of the natural log (CAC+1) was used in multivariable analyses of CAC scores. Tobit conditional regression takes into account both the presence of CAC and its extent, combining both logistic and linear regression approaches. It is therefore appropriate for analysis of CAC data in which there are many zero scores but also a significant right skew when CAC is present [20]. The association between race and CAC scores was explored in age-adjusted models (including age and age^2 terms) which were further adjusted for potentially confounding CVD risk factors both individually and grouped according to atherosclerotic risk factors, 10 year Framingham risk score (FRS) and metabolic syndrome composite variables, markers of insulin resistance and inflammatory markers. Tobit ratios are presented for AAs compared to Whites in models

stratified by gender as well as in the full sample. Gender interaction was assessed in multivariable models using the likelihood ratio test. Statistical analyses were performed using Stata version 11.0 software (Stata Corp, College Station, TX, USA)

4. Results

4.1. Study sample characteristics

The characteristics of the study sample are presented in Table 1. Of 861 participants, 32% were AAs (26.2% of males and 43.5% of females). Whites tended to be older, have higher TG and VLDL levels, use more lipid lowering medications and have less cigarette smoking history. Despite lower TG and higher HDL with roughly similar BMI and waist circumference, AA men and women had significantly lower plasma adiponectin levels and tended to have higher CRP and IL-6. More AAs were on insulin therapy, perhaps reflecting their higher HbA1c concentrations and slightly longer duration of diabetes. Associations between increasing age, male gender, smoking history and history of hypertension were broadly similar across races (Supplementary Table 1), but the study was likely underpowered to detect racial differences in risk factors.

4.2. CAC scores are lower in African-Americans

Median CAC scores were higher in Whites than AAs in both genders, with a greater proportion of Whites having detectable CAC. In analysis stratified by age group (Table 2), this pattern persisted. There was a statistically significant higher score across all age groups in men, with the exception of the youngest age group in which there was very little CAC in either race. Age trends were similar in women but less striking.

4.3. Race is an independent predictor of CAC in type 2 diabetes

Despite a trend toward stronger inverse association with CAC in AA men compared to women, there was no statistically significant gender-difference in the CAC association (gender interaction p values from 0.08 to 0.30 across all models). Results are presented, therefore, for each gender separately as well as in the combined sample. In age-adjusted Tobit regression, race was a significant predictor of CAC in men and women with AA men having ~85% less CAC ($p < 0.001$) and AA women having ~75% less CAC ($p = 0.015$) than Whites (Table 3). In the combined sample, AA had ~83% less CAC than Whites ($p < 0.001$).

In Tobit models adjusted further for individual traditional and novel CVD risk factors one at a time, there was no attenuation of the relationship between race and CAC in men by any individual factor (Table 3, left column). In women (Table 3, middle column), there was modest, but notable, attenuation of the CAC association after adjusting for triglycerides (Tobit ratio of 0.48, 95% CI 0.15–1.49, $p = 0.20$ compared to 0.26, 95% CI 0.09–0.77, $p = 0.015$ for age-adjusted model; gender interaction p of 0.08). A similar, but weaker, trend was apparent with adjustment for VLDL in women (Table 3). Notably, adjustment for menopause and use of hormone replacement therapy (Tobit ratio of 0.21, 95% CI 0.07–0.60, $p = 0.004$) did not attenuate the association of race with CAC in women. In gender-combined analysis, race was consistently associated with CAC regardless of adjustment for any individual risk factor (Table 3, right column).

4.4. Traditional, metabolic and inflammatory risk factors do not account for racial difference in CAC scores in type 2 diabetes

Because we noted a trend toward weakened association of race and CAC in women after adjusting for plasma TG and VLDL levels, we performed incremental adjustment for combinations of traditional lipoprotein, metabolic, adipose and insulin resistance, and

inflammatory risk factors in order to further elucidate whether the association of race with CAC was driven by particular domains of CVD risk that share common pathophysiologies (Table 4). Race remained a significant predictor of CAC in men after adjustment for all groupings of risk factors (Table 4, left column). However, in women, combinations of metabolic factors [e.g., waist circumference, HOMA-IR, leptin and adiponectin; Tobit ratio of 0.48 (95% CI 0.12–1.94)] attenuated of the association of race with CAC (Table 4, middle column). In gender-combined analysis, however, race was significantly associated with CAC regardless of adjustment for any grouping of risk factors (Table 4, right column). Notably, adjustment for the inflammatory factors CRP and IL-6 had no impact on race-CAC association in either men or women.

5. Discussion

Our study demonstrates that differences in CAC scores between AAs and Whites reported in the general population persist in patients with type 2 diabetes. The difference was more striking in men than women, in whom adjustment for metabolic factors, particularly TG, tended to attenuate the racial difference. Overall, in this type 2 diabetes sample, CAC scores were ~80% lower in AA compared to Whites. Thus, there was no evidence that the type 2 diabetes state attenuated racial differences in CAC scores.

Our findings in type 2 diabetes confirm work in population-based epidemiologic studies of ethnic differences in coronary calcification. The Multi-Ethnic Study of Atherosclerosis (MESA), the largest population-based study to date of CAC in different ethnic groups, reported higher CAC scores in Whites (N = 2619) compared to African-Americans (N = 1898) in both genders [9]. Similar findings were reported by Lee et al. who described an almost two-fold increase in CAC in Whites of both genders in a relatively young sample aged 40–45 years [11] and Hatwalkar et al. in an asymptomatic, physician-referred minority population which was age- and gender-matched with a control White population [21].

In contrast, the Dallas Heart Study [13] and Coronary Artery Risk Development in Young Adults (CARDIA) [15] study reported no racial differences in CAC. The Dallas Heart Study was a population-based study in which AAs were oversampled (N = 761) to achieve 50% representation. Type 2 diabetes was present in 13.7% of the sample (17.3% AA and 7.4% White). No differences in the prevalence or severity of CAC were found. CARDIA also failed to detect any significant racial differences in CAC, although this analysis was conducted in a relatively young population (mean age 35 years) with low prevalent CAC. Notably, in our analysis of patients with type 2 diabetes, significant racial differences were not apparent in subjects aged less than 45, it will be interesting to see if racial differences emerge in later CARDIA study visits.

There are very little published data on the relationship between race and CAC in patients with type 2 diabetes. The PREDICT study, one of the largest studies evaluating CAC in patients with type 2 diabetes recruited only White and Asian subjects and excluded Afro–Caribbean patients due to the low CHD event rate in this population in the United Kingdom [8]. We demonstrate that differences between AAs and Whites in CAC persist, despite the strong independent and potential race-differential effect of type 2 diabetes on CAC and its progression [2]. Notably, patients in our study had well controlled type 2 diabetes with median HbA_{1c} of 6.7–7.0%. This contrasts with other studies of CAC in patients with type 2 diabetes without clinical cardiovascular disease in which mean HbA_{1c} ranged between 8.1 and 8.2% [22,23]. It is possible that the racial difference may be less marked in patients with worse glycemic control, if the effect of diabetes is indeed more significant in AAs than in Whites.

The association between lower CAC scores and AA race tended to be less robust in women than in men, although not statistically different. Furthermore, the association in women, but not men, was partially attenuated by adjustment for traditional and metabolic-adipose risk factors. Other studies have suggested no differences in CAC scores between AA and White women [12,13] and even increased odds of CAC in AA women [10]. The reasons for potential gender differences are not clear but could simply relate to sample size and power. However, our findings raise the possibility that metabolic factors might be more important contributors to CAC development in women than in men, at least in type 2 diabetes. However, larger population studies in the general population as well as in type 2 diabetes will be required to address this hypothesis.

The etiology of racial heterogeneity in CAC remains unclear. Traditional and novel risk factors do not appear, for the most part, to account for the differences [10]. Race heterogeneity is true also for extracoronary vascular calcification [24], suggesting a systemic difference in its regulation across race. Vascular calcification is a complex, highly-regulated process determined, in part, by interaction between bone and vasculature [25]. Animal models have demonstrated a role for osteoprotegerin (OPG), a decoy receptor for receptor activator for nuclear factor κB ligand (RANKL), in inhibiting vascular calcification. In humans, serum OPG was associated with CAD in patients with and without diabetes [26]. Other factors such as the calcium inhibitors matrix Gla proteins, osteopontin and fetuin-A and phosphorus have also been associated with CAC. However, racial differences have been demonstrated only for OPG, in a study of peripheral arterial disease [27]. A relationship between bone and vascular calcification is further supported by the inverse relationship between 25-hydroxyvitamin D and incident CAC [28]. In fact, racial differences in this hormone might contribute to racial heterogeneity in vascular calcification and bone diseases. Larger studies incorporating epidemiologic and genetic data are necessary to elucidate the factors influencing CAC and how they differ between AAs and Whites.

Remarkably, despite lower prevalence of CAC, AAs have higher rates of fatal CVD events. While disparities in treatment and access to care may account for some of the difference, there may also be underlying biological factors. Increased CAC in Whites might represent an increase in total burden of atherosclerosis, but could alternatively reflect greater calcification of similar or even lesser degrees of atherosclerosis relative to that found in AAs. While CAC serves as a surrogate for the extent of atherosclerotic plaque and predicts CVD events in AAs and Whites, it provides no information about the stability of the plaque. Non-calcified lipid plaque, which is more prone to rupture, might be more frequent in AA patients, thus, accounting for higher rates of CVD despite lower CAC scores. Alternatively, increased hypertension in AAs may lead to increased vascular stiffness and diastolic dysfunction with clinical CVD complications unrelated to atherosclerosis or coronary calcification. These hypotheses require further investigation.

Our study is the first conducted exclusively in a sample with type 2 diabetes with significant representation of both Whites and AAs. It does, however, have several limitations. It is a cross-sectional study and therefore, conclusions about causality cannot be made. CAC is also a surrogate measure of CVD, although its clinical predictive value and correlation with angiographic data have been well documented. We did not investigate the racial differences in CAC in a comparison group without diabetes. Although we did not measure novel biomarkers and genetic variation that might account for differences in rates of vascular calcification, our study did provide information on multiple lipoprotein, metabolic, adipose and inflammatory CVD risk markers and their influence on racial differences in CAC.

We report that racial differences in CAC observed in the general population are also strikingly present in patients with type 2 diabetes. The protective relationship in African-

Americans tended to be more robust in men than in women. Further research is required to elucidate what factors account for this difference and why lower CAC scores do not translate into better CVD outcomes in AAs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of study sample

Variable	Males *n* = 576		Females *n* = 285	
	White *n* = 425	African-American *n* = 151	White *n* = 161	African-American *n* = 124
Age (years)	62 (55–69)	58 (53–66)[a]	58 (54–66)	57 (50–64)
Duration of diabetes (years)	5 (2–10)	6 (3–12)[a]	5 (2–10)	5.5 (1–10)
HbA1c (%)	6.7 (6.2–7.4)	7.0 (6.2–8.3)[a]	6.9 (6.2–7.7)	6.9 (6.3–7.7)
Smoking history (%)	34 (8.0)	30 (20.0)[b]	14 (8.7)	13 (10.5)
Systolic blood pressure (mmHg)	132 (122–141)	133 (121–145)	129 (118–136)	132 (123–140.5)[a]
Diastolic blood pressure (mmHg)	76 (70–83)	80 (73–85)[a]	73 (68–78)	74.5 (70–80)[a]
Total cholesterol (mg/dl)	172 (151–198)	175 (153–201)	180 (156–209)	186.5 (163.5–214.5)
LDL cholesterol (mg/dl)	97 (78–119)	101 (83–125)	97 (81–120)	111 (90–128)[a]
HDL cholesterol (mg/dl)	43 (36–50)	44 (37–53)[a]	51 (42–62)	56 (47–65)[a]
Triglycerides (mg/dl)	138 (92–209)	104 (73–145)[b]	129 (95–183)	91.5 (66–115)[b]
VLDL cholesterol (mg/dl)	29 (19–44)	22.0 (16–33)[b]	26 (18–37)	19 (12–28.5)[b]
Apolipoprotein A-I (mg/dl)	120 (110–132)	124 (113–135)[a]	134 (123–152)	137 (122.5–149)
Apolipoprotein A-II (mg/dl)	32 (30–35)	33 (30–36)	32.0 (29.0–36.0)	34 (30–38)
Apolipoprotein B (mg/dl)	83 (71–95)	82 (74–95)	81.0 (70.0–95)	83 (70.5–96)
10 year Framingham risk (%)	16 (10–20)	13 (10–25)	11 (7–15)	10 (7–13)
BMI (kg/m2)	31.3 (28.3–34.8)	30.9 (28.4–34.0)	33.5 (29.0–37.6)	33.6 (28.6–38.3)
Waist circumference (cm)	106.7 (99.1–116.8)	104.1 (96.5–113.0)[a]	104.1 (95.2–119.4)	104.1 (93.3–116.8)
Metabolic syndrome (%)	323 (76.0)	105 (69.5)	130 (80.8)	100 (80.6)
Leptin (ng/ml)	8.89 (5.58–14.57)	8.91 (5.1–12.8)	24.6 (16.0–33.8)	29.6 (19.0–42.5)[a]
Adiponectin (μg/ml)	8.38 (5.70–12.5)	5.94 (4.27–9.43)[b]	12.0 (8.26–17.7)	8.98 (6.10–14.3)[b]
CRP (mg/dl)	1.36 (0.77–2.69)	1.71 (0.80–3.14)	2.74 (1.43–5.53)	3.26 (1.65–7.89)
IL-6 (pg/ml)[c]	1.28 (0.87–2.04)	1.31 (1.05–2.36)	1.42 (0.78–2.24)	1.88 (1.17–3.08)[b]
HOMA2-IR [d]	1.90 (1.40–2.80)	1.80 (1.30–2.70)	2.10 (1.50–2.80)	1.90 (1.45–2.90)
Alcohol use (%)	256 (60.2)	68 (45.0)[a]	82 (50.9)	42 (33.9) [a]
Exercise (%)	280 (65.9)	100 (66.2)	111 (68.9)	76 (61.3)
Post-menopausal (%)			141 (87.6)	104 (83.9)
HRT use (%)			16 (9.9)	8 (6.4)
Metformin use (%)	260 (61.2)	84 (55.6)	103 (64.0)	65 (52.4)[a]
Sulfonylurea use (%)	186 (43.8)	69 (45.7)	42 (26.1)	38 (30.6)
TZD use (%)	122 (28.7)	25 (16.6)[a]	32 (19.9)	27 (21.8)
Insulin use (%)	54 (12.7)	45 (29.8) [b]	30 (18.6)	32 (25.8)
Meglitinide use (%)	28 (6.6)	5 (3.3)	11 (6.8)	5 (4.0)
Statin use (%)	252 (59.3)	70 (46.4)[a]	80 (49.7)	45 (36.3)[a]
Niacin use (%)	32 (7.5)	5 (3.3)	2 (1.2)	0 (0)

Variable	Males *n* = 576		Females *n* = 285	
	White *n* = 425	African-American *n* = 151	White *n* = 161	African-American *n* = 124
Ezetimibe use (%)	22 (5.2)	4 (2.6)	9 (5.6)	4 (3.2)
Fibrate use (%)	54 (12.7)	4 (2.6) [b]	7 (4.4)	0 (0.0)[a]
Aspirin use (%)	207 (48.7)	58 (38.4)[a]	71 (44.1)	44 (35.5)
ACE-I use (%)	268 (63.1)	91 (60.3)	80 (49.7)	76 (61.3)
Beta-blocker use (%)	56 (13.2)	29 (19.2)	19 (11.8)	17 (13.7)
Calcium channel blocker use (%)	71 (16.7)	41 (27.2)[a]	24 (14.9)	34 (27.4)[a]
CAC score	183 (21–676)	9 (0–214)[b]	11 (0–103)	0 (0–26.5)[a]
CAC score > 0 (%)	354 (83.3)	89 (58.9)[b]	91 (56.5)	47 (37.9)[a]

[a] $p < 0.05$.

[b] $p < 0.001$.

[c] IL-6 was available in 690 subjects (319 White men, 102 AA men, 147 White women, 122 AA women).

[d] HOMA2-IR was available in 697 subjects (369 White men, 105 AA men, 131 White women, 92 AA women) HRT-hormone replacement therapy, TZD- thiazolidinedione.

Table 2
Median coronary artery calcification score stratified by age-category, gender and race

Age group	Median (IQR)(*n*)			
	Male		Female	
	White	African-American	White	African-American
35–45	0 (0–22) (30)	0 (0–0) (10)	0 (0–0) (8)	0 (0–0) (20)
46–55	47 (0–183) (90)	0 (0–31) (46)[b]	0 (0–0.5) (44)	0 (0–31) (37)
56–65	180 (28–768) (145)	22 (0–176) (51)[b]	35.5 (0–111.5) (68)	0 (0–15) (43)[b]
>65	421 (159.5–986.5) (160)	189 (16–570) (44)[a]	75 (9–323) (41)	49.5 (0–282.5) (24)

[a] $p < 0.05$.

[b] $p < 0.001$.

Table 3

Association of African-American race with coronary artery calcification adjusted for age and individual risk factors

Variable adjusted for	Males *n* = 576	Females *n* = 285	All[a] *n* = 861
Age	0.14 (0.08–0.24) ($p < 0.001$)	0.26 (0.09–0.77) ($p = 0.015$)	0.17 (0.11–0.28) ($p < 0.001$)
Duration of diabetes	0.13 (0.07–0.22) ($p < 0.001$)	0.25 (0.09–0.73) ($p = 0.011$)	0.16 (0.10–0.27) ($p < 0.001$)
HbA1c	0.14 (0.08–0.24) ($p < 0.001$)	0.26 (0.09–0.76) ($p = 0.014$)	0.17 (0.10–0.28) ($p < 0.001$)
Smoking history	0.12 (0.07–0.22) ($p < 0.001$)	0.26 (0.09–0.74) ($p = 0.012$)	0.16 (0.10–0.26) ($p < 0.001$)
Systolic blood pressure	0.13 (0.07–0.23) ($p < 0.001$)	0.29 (0.10–0.85) ($p = 0.025$)	0.17 (0.10–0.28) ($p < 0.001$)
Diastolic blood pressure	0.14 (0.08–0.24) ($p < 0.001$)	0.27 (0.09–0.80) ($p = 0.018$)	0.18 (0.11–0.29) ($p < 0.001$)
Total cholesterol	0.14 (0.08–0.24) ($p < 0.001$)	0.26 (0.09–0.76) ($p = 0.014$)	0.17 (0.11–0.28) ($p < 0.001$)
LDL cholesterol	0.14 (0.08–0.24) ($p < 0.001$)	0.26 (0.09–0.75) ($p = 0.013$)	0.18 (0.11–0.29) ($p < 0.001$)
HDL cholesterol	0.14 (0.08–0.25) ($p < 0.001$)	0.31 (0.11–0.93) ($p = 0.036$)	0.19 (0.12–0.31) ($p < 0.001$)
Triglycerides	0.15 (0.08–0.26) ($p < 0.001$)	0.48 (0.15–1.49) ($p = 0.201$)	0.20 (0.12–0.34) ($p < 0.001$)
VLDL cholesterol	0.14 (0.08–0.25) ($p < 0.001$)	0.37 (0.12–1.08) ($p = 0.068$)	0.20 (0.12–0.32) ($p < 0.001$)
Apolipoprotein A-I	0.14 (0.08–0.24) ($p < 0.001$)	0.27 (0.09–0.78) ($p = 0.016$)	0.18 (0.11–0.29) ($p < 0.001$)
Apolipoprotein A-II	0.13 (0.08–0.24) ($p < 0.001$)	0.27 (0.09–0.79) ($p = 0.017$)	0.17 (0.11–028) ($p < 0.001$)
Apolipoprotein B	0.14 (0.08–0.24) ($p < 0.001$)	0.27 (0.09–0.80) ($p = 0.018$)	0.17 (0.11–0.28) ($p < 0.001$)
Framingham risk score	0.13 (0.08–0.24) ($p < 0.001$)	0.26 (0.09–0.76) ($p = 0.014$)	0.17 (0.10–0.28) ($p < 0.001$)
BMI	0.14 (0.08–0.24) ($p < 0.001$)	0.27 (0.09–0.78) ($p = 0.016$)	0.17 (0.11–0.28) ($p < 0.001$)
Waist circumference	0.15 (0.09–0.26) ($p < 0.001$)	0.27 (0.09–0.80) ($p = 0.018$)	0.19 (0.11–0.30) ($p < 0.001$)
Metabolic syndrome	0.14 (0.08–0.25) ($p < 0.001$)	0.26 (0.09–0.76) ($p = 0.014$)	0.18 (0.11–0.30) ($p < 0.001$)
Leptin	0.14 (0.08–0.24) ($p < 0.001$)	0.27 (0.09–0.81) ($p = 0.020$)	0.17 (0.10–0.28) ($p < 0.001$)
Adiponectin	0.14 (0.08–0.25) ($p < 0.001$)	0.30 (0.10–0.88) ($p = 0.028$)	0.19 (0.11–0.31) ($p < 0.001$)
CRP	0.14 (0.08–0.24) ($p < 0.001$)	0.24 (0.08–0.69) ($p = 0.008$)	0.17 (0.10–0.28) ($p < 0.001$)
IL-6	0.15 (0.08–0.30) ($p < 0.001$)	0.21 (0.07–0.66) ($p = 0.008$)	0.18 (0.10–0.33) ($p < 0.001$)
HOMA2-IR	0.16 (0.09–0.30) ($p < 0.001$)	0.28 (0.08–1.03) ($p = 0.055$)	0.20 (0.11–0.35) ($p < 0.001$)
Alcohol use	0.14 (0.08–0.24) ($p < 0.001$)	0.33 (0.11–0.97) ($p = 0.044$)	0.19 (0.11–0.31) ($p < 0.001$)
Exercise	0.14 (0.08–0.24) ($p < 0.001$)	0.28 (0.10–0.82) ($p = 0.020$)	0.17 (0.11–0.28) ($p < 0.001$)
Post-menopausal		0.25 (0.08–0.73) ($p = 0.012$)	

Results are presented as age-adjusted Tobit ratios (95% confidence intervals) of increase in CAC scores of AA vs. Whites.

[a] Adjusted for age and gender.

Table 4

Association of African-American race with coronary artery calcification in multivariable tobit models

	Males *n* = 576	Females *n* = 285	All[a] *n* = 861
Model 1	0.14 (0.08–0.25) ($p < 0.001$)	0.25 (0.09–0.75) ($p = 0.013$)	0.18 (0.11–0.30) ($p < 0.001$)
Model 2	0.15 (0.08–0.25) ($p < 0.001$)	0.26 (0.09–0.76) ($p = 0.014$)	0.18 (0.11–0.29) ($p < 0.001$)
Model 3	0.14 (0.08–0.25) ($p < 0.001$)	0.43 (0.13–1.44) ($p = 0.171$)	0.19 (0.11–0.32) ($p < 0.001$)
Model 4[b]	0.17 (0.09–0.32) ($p < 0.001$)	0.48 (0.12–1.94) ($p = 0.300$)	0.22 (0.12–0.39) ($p < 0.001$)
Model 5[c]	0.15 (0.08–0.31) ($p < 0.001$)	0.22 (0.07–0.68) ($p = 0.009$)	0.18 (0.10–0.33) ($p < 0.001$)

Model 1: Race, age, age^2, [a]gender, exercise, family history of coronary artery disease, smoking, alcohol, medications, HbA1c, duration of diabetes.

Model 2: Race, age, age^2, [a]gender, FRS, metabolic syndrome.

Model 3: Race, age, age^2, [a]gender, total cholesterol, HDL, smoker, systolic blood pressure, waist circumference, triglycerides, diastolic blood pressure, fasting glucose, LDL.

Model 4: Race, age, age^2, [a]gender, HOMA2-IR, waist circumference, leptin, adiponectin.

Model 5: Race, age, age^2, [a]gender, CRP, IL-6.

Estimates are Tobit ratios for change in CAC+1 for AAs vs. Whites.

Medications included angiotension converting enzyme inhibitors, alpha-glucosidase inhibitors, aspirin, beta-blockers, calcium-channel blockers, fibrates, insulin, sitagliptin, meglitinides, metformin, niacin, statins, sulfonylureas, thiazolidinediones and ezetimibe.

[b]Model 4 was constructed using 697 subjects (males 474, females 223).

[c]Model 5 was constructed using 690 subjects (males 421, females 269).