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The impact of ethnicity and sex on subclinical cardiovascular disease: the Diabetes Heart Study

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Abstract *Aims/hypothesis:* African Americans with type 2 diabetes and access to adequate healthcare are at lower risk of clinical coronary artery disease than are white diabetic patients. We evaluated whether ethnic differences in subclinical cardiovascular disease, coronary and carotid artery calcified plaque and carotid artery intima–medial thickness (IMT) were present in members of The Diabetes Heart Study families. *Subjects and Methods:* In a bi–racial cohort of 1,180 individuals from families enriched for members with type 2 diabetes, we calculated coronary and carotid artery calcified plaque using fast-gated helical computed tomography, and measured carotid artery IMT and clinical risk factor profiles. Generalised estimating equations were used to test for an association between measures of subclinical cardiovascular disease and ethnicity and sex. *Results:* After adjustment for age, ethnicity and kidney function, African Americans had significantly lower amounts of coronary artery calcified plaque (mean±SE) (866±158 vs 1,915±135, respectively; p=0.0466) and carotid artery calcified plaque (179±51 vs 355±27, respectively; p=0.0240) relative to whites, despite having increased carotid IMT (0.71±0.01 vs 0.67±0.004 cm, respectively; p=0.0007), and higher blood pressure, albuminuria and HbA_1c. Sex-specific analyses revealed that African American men had significantly lower coronary and carotid artery calcified atheroma than white men. In women, ethnic differences in calcified carotid artery plaque, but not coronary artery plaque, were observed. *Conclusions/interpretation:* In families enriched for members with type 2 diabetes, African American men had markedly lower levels of coronary and carotid artery calcified plaque than white men, despite increased carotid artery IMT and conventional risk factors. These findings suggest that susceptibility to subclinical cardiovascular disease differs markedly according to ethnicity and sex.

Keywords African American · Carotid intima–medial thickness · Coronary artery calcium · Ethnicity · Gender · Sex · Type 2 diabetes mellitus

Abbreviations ACR: albumin : creatinine ratio · CABG: coronary artery bypass graft · CCA: common carotid artery · CT: computed tomography · CVD: cardiovascular disease · DHS: Diabetes Heart Study · GEE: generalised estimating equation · IMT: intima–medial thickness · MESA: Multi-Ethnic Study of Atherosclerosis · NHANES: National Health and Nutrition Examination Survey · VA: Veterans' Administration · WFUSM: Wake Forest University School of Medicine

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Introduction

Diabetes mellitus is an independent risk factor for the development of atherosclerotic cardiovascular disease (CVD) and nephropathy [1–5]. In the overall population, diabetic African Americans disproportionately suffer from myocardial infarction, stroke and end-stage renal disease relative to

white diabetic patients [6–8]. Ethnic differences in access to preventive healthcare, medications, coronary artery bypass surgery and catheter-based coronary interventions clearly contribute to this disparity [9–14], although recent reports suggest that control of diabetes and related risk factors is suboptimal in many African American, white and Hispanic–American diabetics [15, 16].

Paradoxically, when insurance status and access to healthcare are equivalent, African Americans have significantly lower rates of clinical coronary artery disease than whites. Karter et al. [17] evaluated 62, 432 diabetic individuals insured by Kaiser Permanente to assess whether access to healthcare was associated with ethnic disparities in diabetes complications. Although there were no statistically significant differences between African Americans relative to whites in overall risk of stroke, congestive heart failure or lower extremity amputation, the adjusted African American:white hazard ratio was 0.56 for myocardial infarction. Young et al. [18] performed a longitudinal cohort study in 429,918 diabetic veterans cared for in a national healthcare system (Veterans' Administration [VA]). A 27–49% lower rate of CVD was observed in ethnic minorities vs whites. A marked survival advantage is also observed among African Americans receiving renal replacement therapy, an effect that is independent from the delivered dose of dialysis [19–23]. Diabetic subjects having renal replacement therapy have access to Medicare insurance coverage; thus the effect of prior healthcare disparities may be minimised. These data suggest that African Americans may be less susceptible than whites to hyperglycaemia–induced macrovascular disease.

The prevalence and incidence rate of CHD increases with increasing coronary calcium score [24, 25]. Despite markedly higher rates of CHD risk factors among African Americans relative to whites, there is a growing body of evidence that hypertensive African Americans have lower levels of coronary artery calcified plaque [26–31]. Prior reports have not evaluated interactions between ethnicity and calcified vascular plaque among type 2 diabetic subjects with preserved renal function. This study was performed to detect and quantify ethnic differences in calcified atheromatous plaque in the coronary and carotid arteries of subjects with type 2 diabetes mellitus enrolled in The Diabetes Heart Study (DHS) [32–34].

Subjects and methods

Study population The DHS evaluated a bi-racial cohort of families, each containing at least two siblings concordant for type 2 diabetes. When possible, one non-diabetic sibling from each family was recruited. Families were identified through community advertising or subjects treated in local general internal medicine and endocrinology clinics in northwestern North Carolina. Entry criteria have been reported previously [32–34]. In brief, index cases having diabetes diagnosed after the age of 34 years (in the absence of historical evidence of diabetic ketoacidosis) and at least one additional type 2 diabetic sibling were recruited. The study was approved by the Institutional Review Board at the Wake Forest University School of Medicine (WFUSM) and all participants gave written informed consent.

Examinations were conducted in the General Clinical Research Center of the WFUSM and included interviews for medical history, current medications and health behaviours, measurements of body size, resting blood pressure, 12-lead electrocardiogram, fasting blood draw and spot urine collection. Laboratory assays included urinary albumin and creatinine (to calculate an albumin : creatinine ratio [ACR]), total cholesterol, LDL, HDL, triglycerides, HbA_1c, highly sensitive C-reactive protein, fasting serum glucose, blood urea nitrogen, serum creatinine and albumin concentrations. GFR were computed according to Modification of Diet in Renal Disease recommendations [35]. History of CVD was provided by participant self-report. Hypertension was considered present if the participant was previously diagnosed, took anti–hypertensive medications, or had a blood pressure >140/90 mmHg at the study visit. We excluded subjects with an elevated serum creatinine concentration (≥141 mmol/l in men, ≥124 mmol/l in women) and those reporting prior coronary artery bypass surgery or carotid endarterectomy, due to the marked effects these procedures would have on vascular calcium score.

Vascular imaging Estimates of coronary and carotid artery calcified plaque were made using fast-gated helical computed tomography (CT) [34]. Scans were performed in duplicate after 3-min rest periods. Cardiac CT examinations were performed on a single-slice subsecond helical CT or a four-channel multidetector CT both with cardiac gating and capable of 500 ms temporal resolution (Hi-Speed LX and LightSpeed QXi with the SmartScore Cardiac scan package; General Electric Medical Systems, Waukesha, WI, USA). Scan parameters were 3-mm slice thickness, 26-cm display field-of-view, retrospective cardiac gating, 120 kV, 240 mA and CT scan pitch adjusted to heart rate for the single-slice system and 2.5-mm slice thickness in 4-slice mode, 26-cm display field-of-view, prospective cardiac gating at 50% of the RR interval, 120 kV, 240 mA for the multidetector CT.

For the carotid examination an un–enhanced CT scan was performed through the neck after instructing the participant to swallow [32]. The start and end locations were the C2–3 and C6–7 disc levels. A helical acquisition using a 3-mm (single-slice) or 2.5-mm (multidetector) slice columniation, a 120 kV, 280 mA, 0.8-s gantry rotation, 360° scan reconstruction and standard reconstruction kernel was performed. The display field of view was 18 cm resulting in pixel dimensions of 0.35×0.35 mm.

CT examinations in both vascular beds were analysed on a GE Advantage Windows Workstation using the research version SmartScores software package (General Electric), which allows calculation of a calcium mass score of the amount of calcified plaque. The reproducibility estimates

of the coronary and carotid calcified plaque scores obtained from the duplicate scans were both 0.98. Two trained readers blinded to the clinical characteristics of the participants analysed the CT images. As previously reported, helical CT scans yield comparable vascular calcium measurements to electron beam CT [36]. The cardiac CT methods that we used in the DHS replicate those employed in the Multi-Ethnic Study of Atherosclerosis (MESA) and Coronary Artery Risk Development In Young Adults studies [37].

Common carotid artery (CCA) intima–medial thickness (IMT) was measured using B-mode ultrasound, as reported previously [33]. Briefly, high-resolution B-mode carotid ultrasonography was performed using a 7.5-MHz transducer and a Biosound Esaote (AU5) machine. Scans were performed of the near and far walls of the distal 10-mm portion of the CCA at five predefined interrogation angles on each side. The mean value of up to 20 CCA IMT values is reported here.

Statistical methods The sample means, SD and medians were computed for the continuous characteristics and the measures of subclinical CVD (coronary and carotid artery calcified plaque and carotid IMT). For the discrete demo-

Table 1 The impact of ethnicity and sex on CVD risk factors in DHS participants[a]

	White (*n*=1000)		African American (*n*=180)		*p*–value	
	Female (*n*=529)	Male (*n*=471)	Female (*n*=122)	Male (*n*=58)	Ethnicity[b]	Sex[c]
Age (years)	61.4 (9.4) 60.8	61.9 (9.3) 62.6	58.5 (9.4) 57.6	58.9 (8.6) 58.7	0.0013	0.9031
T2DM duration (years)	10.1 (6.8) 8	10.8 (7.5) 9	10.3 (7.6) 8	11.3 (8.4) 9	0.4259	0.4269
T2DM (%)	80	86	88.5	91.4	0.0178	0.0469
T2DM treatment						
Insulin (%)	24	20	39.3	32.8	0.0011	0.1222
Oral hypoglycaemic (%)	59	69.4	59	62.1	0.6644	0.0025
Lipid-lowering medication (%)	39	47.1	35.2	31	0.1124	0.0271
BMI (kg/m^2)	32.6 (7.5) 31.1	30.9 (5.5) 30.1	35 (7.3) 34.5	30.9 (6.4) 30.5	0.1275	<0.0001
Systolic blood pressure (mmHg)	139.8 (19.6) 138	137.8 (18.6) 137	143.9 (21.5) 142.5	140 (18.8) 139.8	0.0041	0.0182
Diastolic blood pressure (mmHg)	72.2 (9.8) 71.3	73.8 (10.8) 73.5	76.2 (12.1) 75.5	77.3 (10.4) 78	0.0009	0.0200
Laboratory						
Total cholesterol (mmol/l)	5.10 (1.11) 5.00	4.63 (1.03) 4.56	5.09 (0.99) 5.08	4.63 (0.88) 4.51	0.6892	<0.0001
HDL (mmol/l)	1.24 (0.35) 1.19	0.99 (0.25) 0.96	1.39 (0.41) 1.37	1.15 (0.31) 1.11	0.0001	<0.0001
LDL (mmol/l)	2.82 (0.84) 2.75	2.65 (0.82) 2.59	3.04 (0.92) 2.99	2.81 (0.79) 2.72	0.0198	0.0008
Triglycerides (mmol/l)	2.38 (1.57) 2.02	2.26 (1.49) 1.90	1.50 (0.89) 1.24	1.54 (1.29) 1.13	<0.0001	0.0332
HbA_1c (proportion)	0.073 (0.019) 0.07	0.073 (0.017) 0.071	0.087 (0.03) 0.077	0.084 (0.021) 0.08	<0.0001	0.7566
Fasting glucose (mmol/l)	7.86 (3.33) 6.99	7.77 (3.06) 7.16	8.39 (3.93) 7.55	8.86 (5.23) 8.05	0.2302	0.7273
Serum creatinine (mmol/l)	88.4 (26.5) 88.4	106.1 (26.5) 106.1	97.2 (35.4) 88.4	114.9 (44.2) 114.9	0.0015	0.5031
Urine ACR (mg/mmol)	13.8 (71.9) 1.3	12.1 (42.5) 1.5	29.3 (93.7) 1.9	35.2 (83.2) 2.1	0.0015	0.5031
GFR (ml/s)	1.10 (0.29) 1.05	1.18 (0.31) 1.15	1.23 (0.40) 1.24	1.26 (0.34) 1.29	0.0008	<0.0001
C-reactive protein (μmol/l)	0.06 (0.08) 0.03	0.04 (0.08) 0.02	0.06 (0.06) 0.04	0.05 (0.06) 0.03	0.7028	<0.0001
Smoking						
Current (%)	16	17.6	17.2	43.1	0.0292	0.0141
Past (%)	56.3	23.1	50.8	10.3	0.7436	<0.0001
Never (%)	27.2	59	30.3	46.6		
Pack-years (current)	29.2 (25.8) 25	40.1 (30.4) 36	16.5 (17) 10.5	25.6 (25.5) 21	0.0004	<0.0001
Prevalent cardiovascular conditions, procedures						
Hypertension (%)[d]	68	62.2	73.8	65.5	0.2149	0.0006
Angina (%)	14	20.1	17.2	8.6	0.6752	0.0697
Stroke (%)	7.9	11.3	5.7	6.9	0.3540	0.1153
Heart attack (%)	10.6	29.5	9	6.9	0.0196	<0.0001
CABG (%)	5.5	24	5.7	5.2	0.0409	<0.0001
Coronary angioplasty (%)	10.4	20.4	9.8	1.7	0.0228	<0.0001
Carotid endarterectomy (%)	1.3	3.4	0.8	0	0.2630	0.0666

[a]Variables reported as mean (SD) median
[b] *p* values for ethnicity are from the GEE model, after adjusting for age and sex
[c] *p* values for sex are from the GEE model, after adjusting for ethnicity and age
[d]Hypertension as defined in the text
T2DM type 2 diabetes mellitus

Table 2 The impact of ethnicity, sex and GFR on subclinical CVD in DHS participants[a]

	White (*n*=1000)		African American (*n*=180)		*p*–value		
	Female (*n*=529)	Male (*n*=471)	Female (*n*=122)	Male (*n*=58)	Ethnicity[b]	Sex[c]	GFR[d]
Coronary artery calcium	828 (1151) 110	2988 (4355) 1336	687 (1502) 48	1233 (2583) 166	0.0466	<0.0001	0.0205
Carotid artery calcium	244 (609) 25	465 (763) 36	186 (624) 10.5	195 (585) 14.5	0.0007	<0.0001	0.0747
Carotid IMT (mm)	0.64 (0.10) 0.62	0.71 (0.14) 0.68	0.66 (0.11) 0.64	0.74 (0.13) 0.72	0.0240	<0.0001	0.0169

[a]Variables reported as mean (SD) median
[b]*p* values for ethnicity are from the GEE model, after adjusting for age, sex and GFR
[c]*p* values for sex are from the GEE model, after adjusting for age, ethnicity and GFR
[d]*p* values for GFR are from the GEE model, after adjusting for age, sex and ethnicity

graphic characteristics, the proportions were calculated. A series of generalised estimating equations (GEE) assuming exchangeable correlation and using the empirical estimate of the variance to adjust for familial correlation was computed to test for the relationships between ethnicity, sex and measures of subclinical CVD [38]. To better approximate the distributional assumptions of conditional normality and homogeneity of variance, the natural log (ln) of (coronary calcium score +1) and ln (carotid calcium score +1) were analysed. Standard regression diagnostics for collinearity and influence were computed for each model. All statistical analyses were considered significant at $p<0.05$.

Results

Demographic characteristics of the DHS study population are listed in Table 1. There were 1,000 white participants from 369 families and 180 African American participants from 74 families included in this report. The DHS recruited predominantly white families in order to have adequate statistical power to detect genes underlying susceptibility to subclinical CVD. Among white subjects, 828 were diabetic (423 female and 405 male) and among African American subjects, 161 were diabetic (108 female and 53 male). The African American subjects averaged approximately 3 years younger than the white subjects in this sample. Although younger, a greater percentage of African American participants were taking insulin injections and had diabetes (reflecting the increased recruitment of a non-diabetic sibling in white families). Relative to whites, African American subjects had higher systolic and diastolic blood pressures, HbA_1c, LDL-cholesterol, albuminuria, per cent of current smokers and GFR. Whites had a higher self-reported rate of myocardial infarctions, angina and coronary artery bypass graft (CABG). Sex-related differences were also observed in many clinical and laboratory parameters (Table 1).

Despite the unfavourable risk factor profiles in African Americans and their significantly increased carotid artery IMT, calcified plaque in the coronary and carotid arteries was markedly lower than in whites (Table 2). Marked sex differences in the presence of subclinical CVD were also observed. After adjusting for age, sex and GFR, African American participants had significantly lower coronary artery and carotid artery calcified plaque and increased carotid artery IMT, compared with white subjects. After adjusting for age, sex and ethnicity, GFR was inversely associated with coronary artery calcified plaque and carotid artery IMT, with a trend towards an inverse association with carotid artery calcified plaque (Table 2).

GEE analyses were performed to test whether Ethnicity × Gender interactions were present in subclinical CVD among the 868 DHS participants who had coronary artery CT scans, 859 with carotid CT scans and 785 with carotid artery IMT who denied prior coronary artery bypass surgery or carotid endarterectomy. Table 3 reveals that despite the absence of Ethnicity × Gender interactions in carotid IMT, there were significant Ethnicity × Gender interactions in ln (coronary artery calcified plaque) and ln (carotid artery calcified plaque). Thus, the ethnicity effects for coronary artery and carotid artery calcified plaque were different in men and women. We further studied the sex-specific ethnicity effects in Table 4.

Table 4 reveals sex-specific ethnicity differences in measures of subclinical CVD. Lower coronary artery and carotid artery calcified plaque burden was observed in African American men. In African American women a trend towards reduction in carotid artery calcified plaque was observed in the fully adjusted model ($p=0.06$). In contrast, African American women had significantly increased carotid IMT relative to white women. Similar differences in carotid IMT were observed between African

Table 3 Generalised estimating equations for Ethnicity × Sex interaction[a]

Variable[b]	Ethnicity × Sex interaction term *p* value
ln (coronary artery calcium)	<0.0001
ln (carotid artery calcium)	0.0186
Carotid IMT	0.8509

[a]Analyses include 712 white and 156 African American participants who had not had prior carotid endarterectomy or coronary artery bypass surgery, with no more than ten values missing for any given analysis/ethnicity subset
[b]With adjustment for age, sex, ethnicity and GFR

Table 4 Sex specific ethnicity effects on subclinical CVD[a]

Subclinical CVD measure	Covariates in the sex-specific model	Estimate (SE) and *p* value for African Americans vs white	
		Male	Female
ln (coronary artery calcium)	Age, ethnicity, GFR	−1.23 (0.32), *p*=0.0001	−0.02 (0.26), *p*=0.9497
	Age, ethnicity, BMI, hypertension, smoking, ACR, diabetes, CVD, GFR	−0.95 (0.33), *p*=0.0037	−0.26 (0.26), *p*=0.3146
	Age, ethnicity, BMI, hypertension, smoking, ACR, diabetes, CVD, GFR, triglyceride, HDL, LDL	−1.02 (0.34), *p*=0.0029	−0.22 (0.27), *p*=0.4017
ln (carotid artery calcium)	Age, ethnicity, GFR	−0.99 (0.40), *p*=0.0136	−0.14 (0.20), *p*=0.4923
	Age, ethnicity, BMI, hypertension, smoking, ACR, diabetes, CVD, GFR	−1.02 (0.40) *p*=0.0119	−0.41 (0.21), *p*=0.0482
	Age, ethnicity, BMI, hypertension, smoking, ACR, diabetes, CVD, GFR, triglyceride, HDL, LDL	−0.97 (0.42), *p*=0.0203	−0.42 (0.22), *p*=0.0613
Carotid IMT (mm)	Age, ethnicity, GFR	0.03 (0.02), *p*=0.0909	0.04 (0.01), *p*=0.0035
	Age, ethnicity, BMI, hypertension, smoking, ACR, diabetes, CVD, GFR	0.03 (0.02), *p*=0.1809	0.03 (0.01), *p*=0.0111
	Age, ethnicity, BMI, hypertension, smoking, ACR, diabetes, CVD, GFR, triglyceride, HDL, LDL	0.04 (0.02), *p*=0.0507	0.04 (0.01), *p*=0.0019

[a]Sample sizes are 340 males and 528 females who denied prior carotid endarterectomy or coronary artery bypass surgery, with no more than 28 male or 32 female participants missing in any model

American and white men; however, the *p*-value attained statistical significance only in the fully adjusted model.

Discussion

This report is the first to examine a large bi-racial cohort of individuals with type 2 diabetes for the presence of ethnic and sex-related differences in subclinical CVD. We identified significantly lower calcified atheromatous plaque burden in the coronary and carotid arteries of diabetic African Americans than whites. Sex-specific effects analysis revealed that African American men had significantly lower coronary artery and carotid artery calcified atheroma than white men, and African American women had lower carotid artery calcified atheroma than white women after adjustment for age, BMI, hypertension, smoking, ACR, presence of diabetes, GFR and CVD. Racial differences in calcified coronary artery plaque were not observed in women. These findings, observed despite poorer glycaemic control, generally adverse CVD risk factor profiles and increased carotid artery IMT in African Americans, support the hypothesis that the pathological significance of calcified atherosclerotic plaque varies according to ethnicities and sex. Our results replicate those observed in prior reports measuring calcified atherosclerotic plaque using fluoroscopy and electron-beam CT in predominantly non-diabetic cohorts [26–31]. The MESA results in 2,619 white participants (7.8% were diabetic) and 1,898 African American participants (20.6% were diabetic) revealed that 70.4% of white men and 52.1% of African American men had detectable coronary calcium ($p<0.001$), with median calcium scores of 48 in white men and 3 in African American men ($p<0.001$). We observed higher calcium scores than MESA since the DHS evaluated a population with long-standing and poorly controlled diabetes mellitus.

A recent prospective study demonstrated that calcified coronary artery plaque adds significantly to the prediction of myocardial infarction and CVD death, even in individuals classified as ‘low risk’ by the Framingham Risk Index/National Cholesterol Education Program Adult Treatment Panel III, the standard metric of traditional CVD risk factors [39]. Although vulnerable plaque is not clearly defined in the American Heart Association histological classification of advanced atherosclerotic lesions [40], it reflects a potentially thin-walled fibrous cap overlying a lipid core. DHS CT scans measure the calcified component of coronary plaque (American Heart Association Vb type). However, recent intra-coronary ultrasound data indicate that ‘spotty calcifications’ are indicative of the culprit lesion in individuals with acute myocardial infarction or unstable angina [41]. Biomechanical studies of the vessel wall indicate that the shoulders of calcified plaques may in fact be the ‘vulnerable’ regions. Thus, calcified plaque may play an important role in predicting acute CVD events.

It is estimated that 14.9% of African Americans have either diagnosed or undiagnosed diabetes mellitus, and an additional 6.3% have IGT [42]. On average, an African American individual is twice as likely to have diabetes as is his/her white peer [43] and the prevalence of diabetes among African Americans aged 40–74 years has doubled

from 8.9% in 1976–1989 to 18.2% in 1988–1994 [44]. Diabetic African Americans have markedly higher overall rates of renal failure and CVD-related mortality compared with white diabetics [7, 8, 45]. Lower socioeconomic status and poorer access to healthcare are presumed to contribute to the adverse outcomes in minority populations [7]. However, reports based on the third National Health and Nutrition Examination Survey I (NHANES) and the Insulin Resistance Atherosclerosis Study suggest that the magnitude of racial differences in healthcare access and utilisation, health status and outcomes for white, African American and Hispanic–American type 2 diabetics has minimal impact on overall health status [15, 16]. Suboptimal health status relative to established treatment goals (i.e. eye examinations, measurement and treatment of high blood pressure, proteinuria, dyslipidaemia, coronary artery disease, and diabetes treatment with insulin/oral agents) were detected in all racial groups.

Recent analyses in nearly 500,000 type 2 diabetic individuals cared for in health maintenance organisations or the VA suggest that African Americans are actually at markedly lower risk of developing diabetes-related coronary artery disease than whites [17, 18]. In addition, the NHANES I Epidemiologic Follow-Up Study and the New York City Medical Examiner's Office autopsy study also observed reduced rates of coronary artery disease in African American men, relative to white [46, 47]. These surprising observations reproduce the long–standing and consistent observation that African American dialysis patients survive longer than their white counterparts [19–23]. Lower rates of coronary artery disease–associated mortality, possibly associated with lesser degrees of calcified coronary artery plaque in type 2 diabetic African Americans with access to Medicare-supported renal replacement therapy, may contribute to this survival advantage [22].

We previously addressed ethnic-specific relationships between subclinical atherosclerosis assessed by carotid artery IMT compared with coronary artery and carotid artery calcified plaque in the DHS [32]. Carotid artery IMT is known to predict incident CHD and is recognised by the Food and Drug Administration as a surrogate marker of atherosclerosis progression or regression [48, 49]. Simple and adjusted correlation coefficients between calcium scores and IMT were of moderate size and statistically significant among whites [32]. In contrast, the correlation coefficients were lower and non-significant for these relationships in African Americans. The most striking racial contrast was for the adjusted correlation coefficient between carotid artery calcium and IMT: 0.25 ($p<0.0001$) in whites and −0.10 ($p=0.64$) in African Americans. Interaction terms (IMT × Ethnicity) were tested in models for coronary artery calcium ($p=0.20$) and carotid artery calcium ($p=0.004$). In both cases, there was a suggestion (weaker for coronary calcium) that the relationship between IMT and vascular calcium differed between racial groups. A significant, positive relationship between coronary and carotid artery calcium and IMT was observed in whites, not in African Americans.

The inherited and environmental factors that underlie the reduced coronary artery and carotid artery calcified plaque in African Americans, despite similar degrees of carotid artery IMT, remain largely unexplored. The DHS detected strong associations between albuminuria and coronary/carotid artery calcified atheroma in white diabetic subjects without advanced nephropathy [50]. Albuminuria, more often observed in diabetic African Americans, would be expected to increase calcified plaque in diabetic African Americans, the opposite of what is observed. African Americans ingest less dietary calcium than do whites [51] and oral calcium supplementation lowers blood pressure in African Americans [52]. Reduced dietary calcium intake could conceivably contribute to the observed racial differences in calcified atherosclerotic plaque. However, reduced dietary calcium intake in African Americans is unlikely to fully explain the racial variation, since increased bone mass and reduced rates of osteoporosis are observed in African Americans [51, 53]. African Americans also manifest skeletal resistance to the effects of parathyroid hormone [51, 53]. It appears likely that racial differences in calcium metabolism contribute to the observed differences in calcified atheroma and bone mineralisation. The deposition of calcium in the arterial wall plaque appears to occur in a process similar to bone formation [54]. The results of the few epidemiological studies that have examined determinants of calcium/bone metabolism and their possible contribution to the variance in coronary artery calcified plaque have been inconsistent.

Potential limitations in our report included the presence of a significantly higher GFR and HDL-cholesterol and reduced levels of triglycerides in African American participants. These effects could translate into protection from the development of calcified atheromatous plaque, since elevated serum triglycerides, reduced renal function and lower HDL-cholesterol levels are potent risk factors for systemic atherosclerosis. We therefore controlled for the variation in GFR and lipid profiles between races and the ethnic disparity in calcified coronary artery plaque persisted. Additionally, differential participation rates between races could have impacted the results. The consistently lower levels of calcified vascular plaque that have been observed in other reports in non-diabetic African Americans make this bias unlikely to fully explain the results.

In summary, reduced amounts of calcified atheromatous plaque were present in the coronary and carotid arteries of African American type 2 diabetic men compared with white. Lower levels of calcified carotid artery plaque were also present in type 2 diabetic African American women, compared with white. These findings were observed despite adverse clinical risk factor profiles in African Americans. Lesser degrees of calcified coronary artery plaque in African Americans are consistent with improved clinical coronary artery disease outcomes among African Americans on dialysis and in those with access to adequate healthcare. Additional studies are urgently needed in order to determine the causes of the ethnic and sex differences that are observed in calcified atheromatous plaque.

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