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Racial Differences in the Association between Carotid Plaque and Aortic and Coronary Artery Calcification Among Women Transitioning the Menopause

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Abstract

Background—Carotid atherosclerosis is a marker for atherosclerotic disease in other vascular beds; however, racial differences in this association have not been fully examined. The purpose of this report is to evaluate racial differences in the relationship between carotid plaque and calcification in the aorta and coronary arteries among women transitioning the menopause.

Methods—540 African American and White women with a median age of 50 years were evaluated from the Study of Women's Health Across the Nation. Carotid plaque (none versus any) was assessed with B-mode ultrasound and aortic (AC; 0, >0–100, >100) and coronary artery calcification (CAC; 0, >0–10, >10) with computed tomography.

Results—For the total cohort, higher prevalence of plaque was significantly associated with higher levels of AC, but not CAC. The interaction of race and carotid plaque was significant in models with AC and CAC as dependent variables ($p=0.03$, 0.002 , respectively). Among African Americans, there was an inverse relationship, although not significant, between carotid plaque and high AC (>100) (OR 0.75, 95%CI: 0.10–5.48), and between plaque and high CAC (>10) (OR 0.20, 95%CI: 0.03–1.52) in fully adjusted models. In contrast, for Whites, significant positive associations existed between carotid plaque and high AC (OR 4.12, 95%CI: 1.29–13.13) and borderline for high CAC (OR 1.83, 95%CI: 0.66–5.19).

Conclusions—This study demonstrated the presence of carotid plaque appeared to be a marker for AC and potentially CAC in White women during the menopause transition, but not African American middle-aged women.

Keywords

Atherosclerosis; Plaque; Carotid Arteries; Coronary Disease; African Americans and Calcium

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INTRODUCTION

Atherosclerosis is a generalized process that is the major cause of cardiovascular disease (CVD), the leading cause of death in the United States¹. Many noninvasive subclinical measures have been examined to better characterize the extent of atherosclerosis in the body. These include the use of computed tomography to measure aortic calcification (AC) and coronary artery calcification (CAC), and the use of B-mode ultrasound to assess carotid plaque. CAC has been shown to be associated with the extent of coronary atherosclerosis and to predict future cardiovascular events^{2,3}. AC has been related to CVD and is significantly higher in patients with coronary artery disease⁴. In addition, carotid ultrasound has been used as a measure of atherosclerosis and as a surrogate for coronary atherosclerosis in clinical trials for cholesterol-lowering agents⁵. It has also been reported that carotid plaque is correlated with the extent of coronary artery disease, and carotid atherosclerosis can be used to predict future coronary events^{6,7}. Although these subclinical measures are useful in risk stratification for future coronary events, the associations across vascular beds have not been fully examined to account for racial differences in women during the menopausal transition.

It has been shown since the late 1960's that racial differences exist in the anatomic distribution of atherosclerosis. African Americans are more likely to have atherosclerosis in the intracranial cerebral vessels, while Whites tend to have extracranial disease^{8,9}. More recent data from the Multi-Ethnic Study of Atherosclerosis (MESA) revealed that among a population of Whites, Hispanics, African Americans, and Chinese, ethnic differences existed in the prevalence of extra-coronary calcification, with Whites having the highest prevalence¹⁰. Furthermore, ethnic differences in atherosclerosis have been reported to be independent of well known cardiovascular risk factors¹¹. Studies have proposed that these differences could be due to differences in lifestyle, environment, and mechanisms of the disease itself^{10,12,13}.

Although it is known that racial differences exist in the anatomic distribution of atherosclerosis, differences in associations between noninvasive subclinical measures of atherosclerosis in their respective anatomic locations have not been fully examined. A recent study from MESA examined ethnic differences in the association of carotid intima media thickness with CAC. The authors found that CAC was less strongly associated with carotid atherosclerosis, as measured by intima media thickness, in African Americans, particularly African American women, compared with other ethnic groups¹⁴. Additionally, carotid plaque was shown to have a significant positive association with CAC in a predominantly White population in The Rotterdam Coronary Calcification Study¹⁵.

The purpose of this report is to examine the association of carotid plaque with AC and CAC and to evaluate whether this association differs by race in women at various stages of the menopausal transition.

METHODS

Study Population

The Study of Women's Health Across the Nation (SWAN) is a multi-site longitudinal study designed to examine the biological and psychological changes of women during the menopause transition. The SWAN conforms to the ethical principles for medical research involving human subjects. The institutional review board at each site approved the protocol, and all participants provided informed consent. Recruitment details have previously been described¹⁶.

A sub-cohort of women (n=608) from the Chicago and Pittsburgh SWAN sites participated in SWAN Heart, an ancillary study to assess subclinical CVD. Baseline enrollment for SWAN Heart occurred between 2001 and 2003 (corresponding to the 4th – 7th annual SWAN visits). Women were excluded if they reported a history of CVD (n=2), hysterectomy/oophorectomy (n=16), diabetes (n=1) or hormone therapy (n=32). Additional women were excluded for missing menopausal status or subclinical data, resulting in a final sample size of 540 (89%) for this analysis.

Measures of Subclinical Disease

AC and CAC were quantified using electron beam computed tomography (GE Imatron C-150 Ultrafast Scanner, San Francisco, CA). All scans were saved to optical disc and read centrally at the University of Pittsburgh using a DICOM workstation and Acumage software (South San Francisco, CA). The Agatston scoring method, 3 contiguous pixels >130 Hounsfield units, was used to define the presence of calcified lesions within the vessel. A total calcium score was calculated summing the scores in four major coronary arteries, while the aorta total score was from the whole aortic vessel. One blinded physician, centrally trained with a standardized protocol, analyzed all scans from the two sites. A reproducibility study in 40 consecutive subjects previously reported an intrareader intraclass correlation (ICC) of 0.98 for AC and 0.99 for CAC ¹⁷.

Carotid plaque assessment was made using B-mode ultrasound (Pittsburgh: Toshiba American Medical Systems, Tustin, CA and Chicago: Hewlett Packard, Andover, MA). Sonographers were centrally trained with a standardized protocol. Right and left carotid arteries were scanned to obtain a total of 8 images: near and far wall of common carotid (1cm proximal to bulb), far wall of carotid bulb (starting from the point where the common carotid walls are no longer parallel and ending at the flow divider) and far wall of internal carotid artery (distal 1cm from flow divider). Carotid plaques were identified as discrete focal protrusions into the lumen >50% of the surrounding wall thickness. Images obtained from the comparable ultrasound machines were read centrally at the University of Pittsburgh, Ultrasound Research Laboratory. Interreader reproducibility of carotid plaque during annual recertifications were reported as ICC of 0.86–0.93 for plaque ^{18, 19}.

Covariate Measures

During annual visits, SWAN administered standard questionnaires, collected fasting blood samples and obtained anthropometric and blood pressure measures. In this crosssectional analysis, data from these annual SWAN visits (4th: n=272, 5th: n=231, 6th: n=20 and 7th: n=17) were matched to participant's baseline SWAN Heart subclinical measures. Based on self-reported bleeding history, menopausal status was classified as premenopausal (menses in the last 3 months with no irregularity), early-perimenopausal (menses in the last 3 months with irregularity), late-perimenopausal (no menses for at least 3 months, but less than 12 months) and postmenopausal (no menses for at least 12 months). Fasting blood samples were analyzed at the Medical Research Laboratories (Lexington, KY). Total cholesterol and triglycerides were analyzed with the Hitachi 747 analyzer, HDL cholesterol was isolated using heparin-2M manganese chloride and LDL cholesterol was estimated with the Friedewald equation ^{2021, 22}. Assays for estradiol levels were performed on the ACS-180 automated analyzer (Bayer Diagnostics, Tarrytown, NY) using a double-antibody chemiluminescent ²³. Two blood pressure measurements were averaged on the right arm after five minutes of rest in a seated position. Height was measured using a stadiometer and weight was measured using a balance beam, digital scale, or portable scale. BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured over undergarments or light clothing.

Statistical Analysis

Descriptive statistics were used to characterize the sample based on age, race, obesity measures, lipids, and other covariates. In order to compare racial t-tests, Wilcoxon signed-rank tests, and chi-square tests were performed. Carotid plaque was evaluated as presence or absence of any carotid plaque. As previously reported, calcification scores were categorized for the aorta and coronary vessels given the skewed nature of the variables: no AC (0), moderate AC (>0–100), and high AC (>100) ²⁴. CAC was categorized as no CAC (0), moderate CAC (>0–10), and high CAC (>10). Menopausal status was divided into 3 categories: pre-, peri-, and post-menopausal.

Well-known cardiovascular risk factors, such as LDL, SBP, smoking, and waist circumference, as well as risk factors that were potential confounders ($p < 0.10$) in univariate analysis, such as menopausal status and site, were examined in multivariable models in relation to the subclinical measures of atherosclerosis. Stepwise logistic regressions were used to analyze the associations between the risk factors and the outcome variable carotid plaque. Multinomial logistic regressions were used to determine the associations between the risk factors and the two outcome variables AC and CAC, respectively, because models did not consistently meet the assumption of proportional odds. The prevalence of carotid plaque was then examined at the various levels of both AC and CAC. Chi-square and Cochran-Armitage trend tests were performed to determine univariate associations in this cross-sectional analysis. To understand the relationship between carotid plaque and AC and CAC for the total cohort, carotid plaque was used as the independent variable in univariate and multivariable multinomial logistic regression models predicting AC and CAC. The interaction between carotid plaque and race was also tested, and models were run separately on each of the race strata. All analyses were performed using SAS 9.2.

RESULTS

Descriptive statistics are presented by race and total sample in Table I. Participants had a median age of 50 years, 10.6% were pre-menopausal, 58.7% were peri-menopausal, and 30.7% were post-menopausal. Menopausal status was consistent between African Americans and Whites. Compared to Whites, African Americans had higher measures of obesity (BMI, waist circumference, and weight) and higher measures of blood pressure (SBP, DBP). In addition, African Americans had lower levels of total cholesterol and triglycerides.

Carotid plaque was present in approximately 15% of African American and White women. The unadjusted prevalence of AC and CAC was significantly higher in African Americans; however, after adjustment for age, site, LDL, SBP, waist circumference, smoking and menopausal status, AC or CAC did not significantly vary by race.

Frequencies of carotid plaque by AC and CAC category are depicted by race and total sample in Table II. Higher prevalence of plaque was significantly associated with higher levels of AC in the total group. A similar association was seen with CAC, but this did not reach statistical significance. When stratifying by race, among African Americans, there was no relationship between the prevalence of carotid plaque and AC, and there was a negative association between carotid plaque and CAC; however, this trend did not reach statistical significance ($p = 0.11$). In contrast, for Whites, there were significant positive association between carotid plaque and both AC and CAC.

The association between carotid plaque and AC and CAC was evaluated with multinomial logistic regression (Table III). Carotid plaque was significantly associated with high AC (>100) (OR 2.93, 95% CI 1.53–5.65) compared to women with no AC. After controlling for

age, site, race, LDL, SBP, waist circumference, smoking and menopausal status, the association remained significant. A race by carotid plaque interaction term was significant ($p=0.03$). For African Americans, there was a non-significant association between the presence of carotid plaque and AC in univariate or multivariate analysis. However, for Whites, a significant positive relationship existed between carotid plaque and AC. In univariate analysis, the odds ratio of carotid plaque among women with high AC (>100) was 4.85 (95% CI: 2.19–10.74) compared to women with no AC and remained significant in the fully adjusted model.

In the total cohort, both univariate and multivariable analysis failed to show a significant association between carotid and CAC. When a race by carotid plaque interaction term was added to the model of age, study site, race, and carotid plaque for high CAC, the interaction was significant ($p=0.002$). After stratifying by race, African Americans appeared to have a negative association between carotid plaque and CAC, but this association did not reach statistical significance ($p=0.12$). In contrast, Whites had a significantly positive association between carotid plaque and high CAC (>10) in univariate analysis (OR 3.31, 95% CI 1.63–6.74) compared to no CAC. However, this association was attenuated in the fully adjusted model.

Additionally, estradiol was evaluated as a potential confounder in the multivariable modeling given the known relationship between hormones and atherosclerosis. As seen in Table 1 estradiol levels did not vary by race, and including estradiol in the final fully adjusted models did not change the OR or the significance testing for the AC or CAC models.

DISCUSSION

These findings suggest that the association between carotid plaque and calcification in the aorta and coronary arteries differs by race among women transitioning the menopause. It appears that carotid plaque is a good marker of AC and potentially CAC among Whites; however, this is not the case in African Americans given the significant interaction between carotid plaque and race for both AC and CAC.

The racial difference in the association between carotid plaque and AC and CAC extends what has been previously shown. The MESA study examined the association between intima media thickness and CAC among different ethnicities and showed that CAC is less strongly associated with carotid atherosclerosis in African American women ages 45–84¹⁴. In a previously reported SWAN analysis, African American women had a higher baseline prevalence of AC and CAC compared with Whites, which became non-significant after adjusting for traditional cardiovascular risk factors²⁵. It has been shown that African Americans have a lower prevalence of CAC as compared with Whites^{26, 27}. The younger age of our population may explain this inconsistency. Our results were similar to the results from CARDIA showing that there was no significant difference in CAC between a group of African American females aged 33–45 as compared with Whites²⁸. Racial differences may only become observable as individuals age and existing plaques begin to calcify. This hypothesis is consistent given our population's older age was strongly related to CAC in Whites but not African Americans. It is also consistent data from MESA showing faster progression of CAC in Whites compared to African Americans²⁹.

The racial difference in the associations with AC and CAC in older populations may reflect a racial difference in calcium metabolism. Calcified and non-calcified plaque can be visualized in the carotid arteries, whereas computed tomography can only quantify calcified plaque in the aorta or coronary arteries. Therefore, a higher prevalence of non-calcified

plaque in the aorta or coronary arteries of African American women may explain the lack of an association between carotid plaque and AC and CAC.

A racial difference in calcium metabolism might also contribute to inconsistent reports regarding racial differences in clinical versus subclinical disease. The lower levels of CAC reported in African Americans seem contradictory with higher rates of cardiovascular morbidity and mortality³⁰. It has been suggested that lower levels of CAC may place African Americans at a disadvantage because calcification is thought to stabilize plaque^{31, 32}. If African Americans deposit calcium in their coronary plaques more slowly, they may be at higher risk for rupture or thrombosis.

Differences in calcium metabolism between African Americans and Whites could result in differential rates of coronary plaque calcification. Many studies report lower serum 25(OH)D levels and a higher prevalence of vitamin D deficiency among African Americans^{33–36}. Low vitamin D causes a decrease in calcium and a resulting increase in parathyroid hormone (PTH)³⁷. The rise in PTH stimulates the mobilization of calcium from bone, as reflected in increases in bone turnover. PTH levels appear to be *higher* in African Americans³⁵. Paradoxically, bone turnover markers have been shown to be *lower* among African Americans^{36, 38}. It is possible that African Americans are relatively resistant to the bone resorbing effects of PTH³⁹. In SWAN, significant differences existed in biochemical markers of bone turnover across ethnicity. Urinary measures of a bone resorption marker were similar in African Americans and Whites, while a marker of bone formation were higher in Whites⁴⁰. There is clearly a need to further improve our understanding of racial differences in calcium metabolism but these observations raise the possibility that differences in calcium metabolism could result in differential rates of calcium deposition in the coronary arteries.

If rates of calcium deposition in coronary plaques are indeed lower for African Americans, what effect might this have on the predictive value of CAC in this group? Recent data from MESA has shown that higher levels of CAC are related to increased mortality in African Americans, Asians, Hispanic, and non-Hispanic whites, implying that CAC can be used as a predictor for mortality in both African Americans and Whites⁴¹. Interestingly, the predictive value of CAC for mortality was significantly higher among African Americans compared to Whites. This implies that a given level of CAC is associated with a higher atherosclerotic burden in African Americans compared to Whites. In light of this finding, the question now becomes whether or not carotid atherosclerosis can be used as a marker for coronary disease in both African Americans and Whites. Ongoing studies such as MESA should answer this question.

This study provides evidence of racial differences in the association between atherosclerosis across vascular beds among a well-characterized cohort of women. However, this was a cross-sectional study and the prediction of future cardiovascular events and mortality is not feasible. Although these results were adjusted for important potential confounders, residual confounding could still exist. Specifically, stratification by race identified the association between carotid plaque and AC or CAC varied among African Americans and Whites. However, given the small sample size in some of the strata it is possible that despite adjustment for age and menopausal status, the observed association may have additionally varied between the pre-, peri- and post-menopausal women. Further research is needed among a larger cohort of women across the menopausal transition and even into older adulthood to determine if the association changes with age and/or menopause for African American and White women. Nevertheless, this study provided sufficient power to suggest racial differences given the significant interactions between carotid plaque and race for AC and CAC. Lastly, the few women with high atherosclerotic burden limited the power of this

study, particularly for CAC, and therefore studying older adult women with more advanced CAC would help expand this area of research.

CONCLUSION

Overall, this study demonstrated that the prognostic significance of the association between carotid plaque and AC and CAC is different for African American and White women at various stages of the menopausal transition. We have hypothesized that this may be related to underlying racial differences in calcium metabolism.

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REFERENCES

1. Rosamond W, Flegal K, Friday G, et al. Heart disease and stroke statistics--2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2007; 115(5):e69–e171. [PubMed: 17194875]
2. Arad Y, Goodman KJ, Roth M, Newstein D, Guerci AD. Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study. *J Am Coll Cardiol*. 2005; 46(1):158–165. [PubMed: 15992651]
3. Raggi P, Callister TQ, Shaw LJ. Progression of coronary artery calcium and risk of first myocardial infarction in patients receiving cholesterol-lowering therapy. *Arterioscler Thromb Vasc Biol*. 2004; 24(7):1272–1277. [PubMed: 15059806]
4. Takasu J, Mao S, Budoff MJ. Aortic atherosclerosis detected with electron-beam CT as a predictor of obstructive coronary artery disease. *AcadRadiol*. 2003; 10(6):631–637.

5. Bots ML, Evans GW, Riley WA, Grobbee DE. Carotid intima-media thickness measurements in intervention studies: design options, progression rates, and sample size considerations: a point of view. *Stroke*. 2003; 34(12):2985–2994. [PubMed: 14615619]
6. Sugioka K, Hozumi T, Iwata S, et al. Morphological but not functional changes of the carotid artery are associated with the extent of coronary artery disease in patients with preserved left ventricular function. *Stroke*. 2008; 39(5):1597–1599. [PubMed: 18340102]
7. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. *N Engl J Med*. 1999; 340(1):14–22. [PubMed: 9878640]
8. Solberg LA, McGarry PA. Cerebral atherosclerosis in Negroes and Caucasians. *Atherosclerosis*. 1972; 16(2):141–154. [PubMed: 4634809]
9. Wityk RJ, Lehman D, Klag M, Coresh J, Ahn H, Litt B. Race and sex differences in the distribution of cerebral atherosclerosis. *Stroke*. 1996; 27(11):1974–1980. [PubMed: 8898801]
10. Nasir K, Katz R, Takasu J, et al. Ethnic differences between extra-coronary measures on cardiac computed tomography: multi-ethnic study of atherosclerosis (MESA). *Atherosclerosis*. 2008; 198(1):104–114. [PubMed: 17950742]
11. Manolio TA, Burke GL, Psaty BM, et al. Black-white differences in subclinical cardiovascular disease among older adults: the Cardiovascular Health Study. CHS Collaborative Research Group. *J Clin Epidemiol*. 1995; 48(9):1141–1152. [PubMed: 7636516]
12. Palaniappan L, Wang Y, Fortmann SP. Coronary heart disease mortality for six ethnic groups in California, 1990–2000. *Ann Epidemiol*. 2004; 14(7):499–506. [PubMed: 15310526]
13. Kuller LH. Ethnic differences in atherosclerosis, cardiovascular disease and lipid metabolism. *Curr Opin Lipidol*. 2004; 15(2):109–113.
14. Manolio TA, Arnold AM, Post W, et al. Ethnic differences in the relationship of carotid atherosclerosis to coronary calcification: the Multi-Ethnic Study of Atherosclerosis. *Atherosclerosis*. 2008; 197(1):132–138. [PubMed: 17412347]
15. Odink AE, van der LA, Hofman A, et al. Association between calcification in the coronary arteries, aortic arch and carotid arteries: the Rotterdam study. *Atherosclerosis*. 2007; 193(2):408–413. [PubMed: 16919637]
16. Sowers, MF.; Crawford, S.; Sternfeld, B., et al. Menopause: biology and pathobiology. San Diego: Academic Press; 2000. SWAN: a multicenter, multiethnic, community-based cohort study of women and the menopausal transition; p. 175-188.
17. Sutton-Tyrrell K, Kuller LH, Edmundowicz D, et al. Usefulness of electron beam tomography to detect progression of coronary and aortic calcium in middle-aged women. *Am J Cardiol*. 2001; 87(5):560–564. [PubMed: 11230839]
18. Everson-Rose SA, Lewis TT, Karavolos K, Matthews KA, Sutton-Tyrrell K, Powell LH. Cynical hostility and carotid atherosclerosis in African American and white women: the Study of Women's Health Across the Nation (SWAN) Heart Study. *Am Heart J*. 2006; 152(5):982–913. [PubMed: 17070176]
19. Sutton-Tyrrell K, Wolfson SK Jr, Thompson T, Kelsey SF. Measurement variability in duplex scan assessment of carotid atherosclerosis. *Stroke*. 1992; 23(2):215–220. [PubMed: 1561650]
20. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972; 18(6):499–502. [PubMed: 4337382]
21. Stein EA, Steiner PM, Gartside PS, Glueck CJ. Development and evaluation of a method for quantitation of plasma high-density-lipoprotein cholesterol. *Clin Chem*. 1978; 24(7):1112–1115. [PubMed: 207465]
22. Warnick GR, Albers JJ. A comprehensive evaluation of the heparin-manganese precipitation procedure for estimating high density lipoprotein cholesterol. *J Lipid Res*. 1978; 19(1):65–76. [PubMed: 202660]
23. Thurston RC, Sutton-Tyrrell K, Everson-Rose SA, Hess R, Powell LH, Matthews KA. Hot flashes and carotid intima media thickness among midlife women. *Menopause*. 2011

24. Agatista PK, Matthews KA, Bromberger JT, Edmundowicz D, Chang YF, Sutton-Tyrrell K. Coronary and aortic calcification in women with a history of major depression. *Arch Intern Med*. 2005; 165(11):1229–1236. [PubMed: 15956001]
25. Birru M, Matthews K, Mackey R, Farhat G, Everson-Rose S, Lewis T, Sutton-Tyrrell K. Race, socioeconomic status, and subclinical cardiovascular disease. *Society for Behavioral Medicine Abstract* 2469. 2007 March.
26. Tang W, Detrano RC, Brezden OS, et al. Racial differences in coronary calcium prevalence among high-risk adults. *Am J Cardiol*. 1995; 75(16):1088–1091. [PubMed: 7762490]
27. Bild DE, Detrano R, Peterson D, et al. Ethnic differences in coronary calcification: the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation*. 2005; 111(10):1313–1320. [PubMed: 15769774]
28. Loria CM, Liu K, Lewis CE, et al. Early adult risk factor levels and subsequent coronary artery calcification: the CARDIA Study. *J Am Coll Cardiol*. 2007; 49(20):2013–2020. [PubMed: 17512357]
29. Kronmal RA, McClelland RL, Detrano R, et al. Risk factors for the progression of coronary artery calcification in asymptomatic subjects: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation*. 2007; 115(21):2722–2730. [PubMed: 17502571]
30. Cooper R, Cutler J, Desvigne-Nickens P, et al. Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States: findings of the national conference on cardiovascular disease prevention. *Circulation*. 2000; 102(25):3137–3147. [PubMed: 11120707]
31. Motoyama S, Kondo T, Sarai M, et al. Multislice computed tomographic characteristics of coronary lesions in acute coronary syndromes. *J Am Coll Cardiol*. 2007; 50(4):319–326. [PubMed: 17659199]
32. Schuijff JD, Beck T, Burgstahler C, et al. Differences in plaque composition and distribution in stable coronary artery disease versus acute coronary syndromes; non-invasive evaluation with multi-slice computed tomography. *Acute Card Care*. 2007; 9(1):48–53. [PubMed: 17453539]
33. Looker AC, Dawson-Hughes B, Calvo MS, Gunter EW, Sahyoun NR. Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III. *Bone*. 2002; 30(5):771–777. [PubMed: 11996918]
34. Harris SS, Soteriades E, Dawson-Hughes B. Secondary hyperparathyroidism and bone turnover in elderly blacks and whites. *J Clin Endocrinol Metab*. 2001; 86(8):3801–3804. [PubMed: 11502814]
35. Bell NH, Epstein S, Greene A, Shary J, Oexmann MJ, Shaw S. Evidence for alteration of the vitamin D-endocrine system in obese subjects. *J Clin Invest*. 1985; 76(1):370–373. [PubMed: 2991340]
36. Kleerekoper M, Nelson DA, Peterson EL, et al. Reference data for bone mass, calciotropic hormones, and biochemical markers of bone remodeling in older (55–75) postmenopausal white and black women. *J Bone Miner Res*. 1994; 9(8):1267–1276. [PubMed: 7976509]
37. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocr Rev*. 2001; 22(4):477–501. [PubMed: 11493580]
38. Meier DE, Luckey MM, Wallenstein S, Lapinski RH, Catherwood B. Racial differences in pre- and postmenopausal bone homeostasis: association with bone density. *J Bone Miner Res*. 1992; 7(10):1181–1189. [PubMed: 1456086]
39. Cosman F, Morgan DC, Nieves JW, et al. Resistance to bone resorbing effects of PTH in black women. *J Bone Miner Res*. 1997; 12(6):958–966. [PubMed: 9169356]
40. Finkelstein JS, Sowers M, Greendale GA, et al. Ethnic variation in bone turnover in pre- and early perimenopausal women: effects of anthropometric and lifestyle factors. *J Clin Endocrinol Metab*. 2002; 87(7):3051–3056. [PubMed: 12107200]
41. Nasir K, Shaw LJ, Liu ST, et al. Ethnic differences in the prognostic value of coronary artery calcification for all-cause mortality. *J Am Coll Cardiol*. 2007; 50(10):953–960. [PubMed: 17765122]

Participant Characteristics

Table 1

	Total n=540 ^b		African American n=209		Caucasian n=331		Non- parametric
	Median	25–75%	Median	25–75%	Median	25–75%	p-value
Age (years)	50.0	48–52	50.0	48–52	50.0	48–53	0.26
BMI (kg/m ²)	28.1	25–33	30.3	26–36	27.0	24–32	<.0001
Waist circumference (cm)	87.4	78–98	90.3	81–100	85.0	77–97	0.0001
Weight (kg)	75.2	65–89	79.8	70–96	72.1	63–85	<.0001
Total cholesterol (mg/dl) ^a	200.2	37.6	195.9	37.4	202.9	37.6	0.05
HDL (mg/dl)	55.0	48–65	55.0	47–64	56.0	48–65	0.52
LDL (mg/dl) ^a	119.0	32.8	118.0	33.4	119.6	32.4	0.61
Triglycerides (mg/dl)	97.0	74–37	89.0	71–120	104.0	77–144	0.001
SBP (mmHg)	118.0	108–128	125.0	113–137	113.0	106–124	<.0001
DBP (mmHg)	75.0	69–82	80.0	72–86	72.0	68–79	<.0001
Estradiol (pg/ml)	29.5	16–72	27.8	16–63	31.3	16–77	0.42
	n	%	n	%	n	%	Chi-Square
Smoker							p-value
Yes	78	15.98	29	16.38	49	15.76	0.86
No	410	84.02	148	83.62	262	84.24	
Menopausal Status							
Pre-	57	10.56	19	9.09	38	11.48	0.64
Peri-	317	58.70	123	58.85	194	58.61	
Post-	166	30.74	67	32.06	99	29.91	
	Total n=540 ^b		African American n=209		Caucasian n=331		Chi-Square
Carotid Plaque	n	%	n	%	n	%	p-value
Yes	81	15.14	30	14.63	51	15.45	0.80

	Total n=540 ^b		African American n=209		Caucasian n=331		Non- parametric
	Median	25–75%	Median	25–75%	Median	25–75%	p-value
No	454	84.86	175	85.37	279	84.55	
Aortic Calcification							
0	156	30.23	45	22.84	111	34.80	0.01
0–100	245	47.48	106	53.81	139	43.57	
>100	115	22.29	46	23.35	69	21.63	
Coronary Artery Calcification							
0	271	52.32	83	42.13	188	58.57	0.001
0–10	136	26.25	62	31.47	74	23.05	
>10	111	21.43	52	26.4	59	18.38	

^aNormally distributed, therefore, mean, SD, and T-test results were reported

^bn varies from 472–540 for total sample, 177–209 for African Americans, and 291–311 for Caucasians

Table 2

Prevalence of Carotid Plaque by Aortic and Coronary Calcification

Aortic Calcification	Total		African Americans		Caucasians	
	N	Prevalence of Carotid Plaque, n (%)	N	Prevalence of Carotid Plaque, n (%)	N	Prevalence of Carotid Plaque, n (%)
0	155	17 (10.97)	44	6 (13.64)	111	11 (9.91)
0-100	243	29 (11.93)	105	15 (14.29)	138	14 (10.14)
>100	113	30 (26.55)	44	6 (13.64)	69	24 (34.78)
Chi-Square		0.0004		0.99		<0.0001
Cochran-Armitage Trend		0.001		1.00		<0.0001
Coronary Artery Calcification						
0	271	37 (13.65)	83	15 (18.07)	188	22 (11.70)
0-10	134	17 (12.69)	61	8 (13.11)	73	9 (12.33)
>10	108	22 (20.37)	49	4 (8.16)	59	18 (30.51)
Chi-Square		0.18		0.28		0.002
Cochran-Armitage Trend		0.15		0.11		0.002

N = Number of women with aortic or coronary artery calcification in each category

n = Number of women with carotid plaque

Table 3
Logistic Regressions Depicting Carotid Plaque's Association with Aortic and Coronary Calcification

Carotid Plaque	Aortic Calcification				Coronary Artery Calcification			
	0-100 versus 0		>100 versus 0		0-10 versus 0		>10 versus 0	
Total ^c	N	OR	95%CI	OR	N	OR	95%CI	OR
1. Unadjusted	511	1.10	0.58-2.08	2.93 ^b	513	0.92	0.50-1.70	1.62
2. Fully-Adjusted + race ^d	402	1.14	0.48-2.72	2.93 ^a	404	0.64	0.28-1.46	1.10
African Americans								
1. Unadjusted	193	1.06	0.38-2.93	1.00	193	0.68	0.27-1.73	0.40
2. Fully-Adjusted ^d	143	0.56	0.11-2.86	0.75	143	0.49	0.12-2.08	0.21
Caucasians								
1. Unadjusted	318	1.03	0.45-2.36	4.85 ^b	320	1.06	0.46-2.43	3.31 ^b
2. Fully-Adjusted ^d	259	1.16	0.39-3.44	4.12 ^a	261	0.50	0.16-1.57	1.83

^a p<0.05

^b p<0.01

^c Interaction of carotid plaque and race was significant for aortic >100 (p=0.03) and coronary calcification >10 (p=0.002).

^d Fully-adjusted for adjusted for age, site, LDL, SBP, waist circumference, smoking and menopausal status