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The Relationship Between Race, Cigarette Smoking and Carotid Intimal Medial Thickness in Systemic Lupus

Lisabeth V. Scalzi, M.D., M.S.¹, Shweta Bhatt, M.D.², Robert C. Gilkeson, M.D.³, and Michele L. Shaffer, Ph.D.¹

¹Pennsylvania State University/ Milton S. Hershey Medical Center. Hershey, PA, USA

²University of Rochester/ Strong Memorial Hospital, Rochester, NY, USA

³Case Western Reserve University/ University Hospitals of Cleveland, Cleveland, OH, USA

Abstract

Objective—Racial differences are known to account for a higher incidence of systemic lupus erythematosus (SLE), as well as increased disease severity and mortality. The purpose of this study was to determine if there are any race-specific risk factors that affect measures of subclinical atherosclerosis in SLE patients.

Methods—Traditional and SLE-related cardiovascular disease (CVD) risk factors were assessed in 106 female SLE patients. Carotid medial intimal medial thickness (mIMT) and coronary artery calcification (CAC) were measured on all subjects. Differences were evaluated between races for all clinical, serologic, and CVD risk factors and the racial interactions with all covariables. Outcomes included mIMT and CAC.

Results—There were no significant differences between races with regard to mIMT or CAC. Significant covariables in the final model for mIMT included age, triglycerides, glucose, and race-age and race-smoking interactions. A prediction model with fixed significant covariables demonstrated that Black subjects with a smoking history had a significantly higher mIMT than Blacks who had never smoked, an effect not seen in Whites. There were no differences between having CAC or with the CAC scores between the races. In the final model for CAC, age and SLE disease duration were significant covariables impacting CAC.

Conclusion—When controlling for other significant CVD covariables and interactions, Black women, but not White, with SLE with a history of smoking have higher mIMT measurements than those who have never smoked. This is the first report documenting the race-specific effect of smoking on subclinical measures of CVD in SLE.

Keywords

lupus; cardiovascular; smoking; race

Cardiovascular Disease (CVD) has been recognized as a leading cause of morbidity and mortality in systemic lupus erythematosus (SLE). In a recent study, 36% of all SLE deaths were secondary to CVD. (1) Cardiovascular involvement has been noted to be more common in non-Caucasian SLE patients. (2) Racial influence on the clinical heterogeneity of SLE is well established. (3) American black race has been shown to be an independent negative factor on survival in SLE. (4,5) The Centers for Disease Control (CDC) reported that between the

years of 1979 and 1998, crude death rates were greater than 3 times higher in African-Americans with SLE, as compared to Caucasian SLE patients, and death rates increased 70% among black women with SLE aged 45–64 years of age. (6)

Vascular events are also associated with co-morbidities that may be race-related, such as socioeconomic status and health insurance. (7) Many studies have identified potential risk factors that contribute to CVD in SLE. (8–15) Models examining risk factors for measures of CVD as the outcome of interest usually take race into account, but do not specifically examine racial interactions with other traditional, novel, and SLE-specific risk factors that may not be evident without specific attention to these important race-dependent associations. Thus, we sought to examine racial interactions with traditional (e.g. smoking and dyslipidemia) and non-traditional SLE-related CVD risk factors (e.g. homocysteine and SLE duration) to examine whether there may be race-specific risks associated with subclinical CVD that can be identified and potentially targeted in Blacks versus Whites.

PATIENTS AND METHODS

Patient population

Institutional review board approval was obtained from Case Western Reserve University/ University Hospitals of Cleveland (UH), MetroHealth Hospitals, and Pennsylvania State University/ Milton S. Hershey Medical center (HMC). Subjects were recruited from outpatient and University-based rheumatologists from Cleveland, OH and Hershey/ Harrisburg, PA between 2004 and 2008. All subjects fulfilled ≥ 4 of the 1982 American College of Rheumatology criteria. (16) Exclusion criteria included age ≤ 35 or ≥ 78 , pregnancy, history of or presently on dialysis, a known creatinine clearance < 75 ml/min, SLE duration less than 2 years, history of cardiovascular disease (including previous myocardial infarction, coronary stent, revascularization procedure, or known coronary vasculitis), cirrhosis, other inflammatory or autoimmune disease, or any history of malignancy except localized skin and/or cervical cancer. Of a potential 231 subjects, 106 subjects met inclusion criteria.

Clinical Assessments

All subjects received a questionnaire in the mail at least one week in advance of the study visit date. Information from the questionnaire included race, a review of SLE history including disease duration, ACR criteria, and traditional CVD risks (including premature heart disease in first degree relatives (in men less than 55 years of age and women less than 65 years of age), hypertension or use of an antihypertensive (other than an angiotensin converting enzyme for proteinuria), diabetes (or use of insulin or an oral hypoglycemic agent), post-menopausal status (for at least one year), duration of glucocorticoid use, lipid-lowering medication history, and smoking history). Smoking history was defined as ever having smoked. Because smoking history and pack-year history would be expected to have a high correlation, we chose to examine smoking history as the covariable. A glomerular filtration rate was calculated for each subject using the Cockcroft-Gault equation. (17) SLE Disease Activity Scores (SLEDAI) (18) and Systemic Lupus International Collaborating Clinics Damage Index (SLICC) (19) scores were calculated by one trained physician (LS). Body mass index (BMI) was calculated at the time of visit. Both systolic blood pressures (SBP) and diastolic blood pressures (DBP) were calculated as the average of three consecutive blood pressures taken in the right arm while sitting, after 5 minutes at rest.

Laboratory Methods

Blood was drawn during the study visit after an eight hour fasting period. The following laboratories were obtained in order to complete the SLEDAI scoring; urinalysis with microscopy, complement levels (C3 and C4), anti-double-stranded DNA antibody, platelet

count, and white blood cell count. In addition measures of glucose, homocysteine, high-sensitivity CRP (hs-CRP), creatinine, lipid profile (total cholesterol, HDL, VLDL, triglycerides, and calculated LDL (using the Friedewald equation)), were completed.

Carotid Ultrasound

For subjects imaged at UH, one trained sonographer performed all studies using a 7–14 MHz AT 1204 linear array imaging probe (Toshiba American Medical Systems, Tustin, CA) operating at 12 MHz. Subjects imaged at HMC were completed by one trained sonographer and were acquired with a 5–12 MHz linear array imaging probe (Phillips ATL 5000, Bothell, WA) operating at 12 MHz. Images of the bilateral distal common carotids and internal carotid arteries were obtained in longitudinal views. IMT was scored as per the protocol of Riley et al. (20) Images of the near and far wall of the internal carotid artery (ICA) and common carotid artery (CCA), free of plaques, (2sites×2sides×2walls=8 locations) were measured. Of the 106 subjects, 85 had all 8 locations clearly visualized and recorded. All images were scored by a radiologist specialized in ultrasonography (SB) and 12% were reread by another radiologist trained in ultrasonography (RP). The correlation coefficient was 0.97 (95% CI 0.85, 0.99).

Multi-slice CT Scan (MSCT)

Electrocardiographic gating was used such that image acquisition occurred at the same time during diastole to minimize motion artifact. No contrast was administered during the test. Sixty-seven scans were completed on patients from UH/ MH. At UH/MH, CT calcium scoring was performed on a Siemens Sensation 16. Imaging acquisition was performed with 3mm slice thickness and a 1.5mm image reconstruction interval. Images were transferred to a Siemens Leonardo workstation. Thirty-eight subjects from HMC were scanned on a Siemens Sensation 64 scanner using 1.2mm collimation and 3.0mm reconstructed slice width. The images were then transferred to a TeraRecon (3.7.0.7) workstation. All scan results were stored electronically and assessed for quality by a radiologist and CAC was scored according to the Agatston methodology. (21) 10% of the MSCT scans were rescored by one radiologist (RG) to assess inter-reader correlation. The correlation coefficient was 0.99 (95% CI 0.99, 1.0).

Statistical Analysis

Descriptive statistics for SLE-related variables, anthropomorphic data, and CVD-related risk factors for Blacks versus Whites are reported as the mean ± SD for continuous covariables and percentages for categorical covariables. Means were compared using t-tests and comparisons between categorical results were made using chi-square tests. We determined which covariables impact IMT and CAC in an age and race-dependent fashion. Each covariable was independently examined in a regression model controlling for age, race, and interactions (i.e.: CVD outcome = covariable + age + race + (covariable*age) + (covariable*race)). Final modeling included covariables and/or covariable-race interactions with a p-value < 0.10. Those covariables in the final model with a p-value < 0.05 were considered significant. Also calculated are the standardized regression coefficients for the covariables in the final model. As these coefficients have been standardized, they become unitless, which is useful when many covariables with different units of measurement are being compared. The standardized regression coefficients provide vital information about which covariables in the regression model have the greatest effect on the dependent covariable in a multiple regression analysis, IMT or CAC in this case.

RESULTS

Baseline characteristics of the patients

Of the total 118 subjects who met inclusion criteria, 29 were Black (27 women and 2 men), 1 was Asian (female), 85 were White (79 women and 6 men), and 3 were Hispanic (all women). All male, Asian, and Hispanic subjects were excluded from the analyses due to insufficient numbers being present to explore interactions. Of the remaining 106 women, 27 were Black and 79 were White. The mean age for the cohort was 49.9 ± 8.9 years (Table 1). The mean age was 49.0 ± 8.8 years for Black participants and 50.2 ± 9.0 years for White participants ($p=0.57$). The mean duration since SLE diagnosis by a physician was slightly higher in Blacks versus Whites (13.8 years versus 10.7 years; $p=0.09$). There were no significant differences in SLEDAI or SLICC scores between the two groups. White subjects had a significantly higher BMI than Blacks (31.4 versus 27.9, $p=0.03$). Overall, there was not a difference between groups regarding duration of prednisone use ($p=0.29$). 48% of Blacks and 56% of Whites were post-menopausal ($p=0.47$). A greater proportion of Blacks had a smoking history than Whites, 56% versus 33%, $p=0.04$. There were no significant differences between racial groups with regards to SBP, DBP, or a known history of hypertension. The only significant difference between the groups when examining lipid profiles was that the mean triglyceride level for the Blacks was higher than the Whites, 112.0 ± 67.6 versus 84.7 ± 55.8 mg/dL; $p=0.04$. There were no significant differences between groups for fasting glucose levels, homocysteine, hs-CRP, or GFR. Twenty-two percent of White subjects reported taking a lipid lowering medication (ever), while no Black subjects reported having taken medications of this type; $p=0.007$. The mean IMT for White subjects was $0.65 \text{ mm} \pm 0.19 \text{ mm}$ and $0.67 \text{ mm} \pm 0.14 \text{ mm}$ for the Black subjects ($p=0.74$). CAC was present in 28% (22/79) of white subjects and 22% (6/27) of Black subjects ($p=0.57$). For those subjects with a CAC score greater than zero, the mean scores were 79.5 ± 28.3 and 81.3 ± 10.6 , respectively ($p=0.88$). Each covariable was examined for any differences between the subjects from Pennsylvania and Ohio by race. There were no significant differences between sites for any of the covariables (data not shown).

Carotid IMT

Covariable and covariable-race interaction p-values are shown in Table 2. Those covariables or interactions with a p-value < 0.10 were included in the final regression model (see Table 3). Significant covariable and covariable-race interactions (in order of standardized regression coefficient values) were age ($p<0.0001$), race-smoking ($p=0.01$), race-age ($p=0.006$), triglycerides ($p=0.01$), and fasting glucose levels ($p=0.02$). Age had the greatest effect on IMT (standardized regression coefficient = 0.54), with the next being the effect of the race-smoking interaction (standardized regression coefficient = 0.40).

In order to isolate the interaction of race and smoking, the final regression model was used to predict mIMT values in both races. Mean values from the cohort were used to fix other covariables in the final model, including age, glucose, and triglyceride levels. Figures 1a and 1b demonstrate the predicted mIMT values using the regression model. When all other covariables were fixed at the mean values, smoking in Blacks increased the predicted mIMT by 0.18 mm ($p < 0.0001$) and decreased mIMT insignificantly in Whites by 0.05 mm ($p=0.56$). These data demonstrate mIMT values significantly increase in Black SLE patients who smoke, which is not seen in White SLE patients who smoke. In addition, Black smokers have higher predicted mIMT values than non-smoking Black SLE patients, in the model, at all ages.

The interaction of race and age suggested that age significantly impacted the mIMT values in White subjects more than Black subjects, when controlling for other covariables and interactions. In a bivariate analysis, mIMT values significantly increased with age in Whites but not in Blacks, ($p<0.001$ and $p=0.17$, respectively). The mIMT in Blacks versus Whites less

than the age of 50 was 0.56 mm and 0.65 mm, respectively. In those subjects 50 years of age and older, the mIMT was 0.78 mm for Whites and 0.69 for Blacks.

We also examined each of the covariables in bivariate analyses with mIMT as the outcome, without adjusting for age and race to identify which variables may overlap with age. Mean SBP ($p=0.004$), cholesterol ($p=0.07$), triglycerides ($p=0.01$), glucose ($p=0.01$), and history of being on a lipid lowering medication ($p=0.004$) all had p -values of <0.10 , so that they ordinarily would have been included in a final regression model. Both SBP and history of using a lipid lowering medication were significantly associated with increasing age ($p<0.0001$ and $p=0.0007$ respectively). Triglycerides and glucose were not significantly associated with age ($p=0.35$ and $p=0.12$ respectively). Interestingly, race was not a significant predictor in a bivariate model ($p=0.74$).

Coronary Artery Calcification Scores

Covariable and covariable-race interaction p -values are shown in Table 4. Those covariables or interactions with a p -value ≤ 0.10 in the bivariate analyses were included in the final model (see Table 5). These included SLE duration ($p=0.004$), the interaction of SLE duration and race ($p=0.05$), SLICC ($p=0.08$), the interaction of SLICC and race ($p=0.07$), smoking ($p=0.02$), HDL ($p=0.09$), and homocysteine ($p=0.06$). Although SLICC scores were significant in the initial models, there were too few Black subjects ($n=6$) who had values of SLICC and CAC greater than zero to examine a linear relationship. SLICC was therefore excluded in the final modeling. In the final model, significant covariables that were associated with increasing CAC scores were age ($p<0.0001$) and SLE duration ($p=0.007$). There were no race-covariable interactions that were significant with CAC as the outcome.

Discussion

This study underscores the importance of examining potential race-specific risk factor interactions on CVD measures in SLE patients. Examining for specific race-related interactions revealed novel findings. Smoking significantly increased mIMT values in Blacks with SLE, but not in Whites. If race-specific interactions had not been sought in our cohort as potential covariables, smoking would not have been detected as having any impact on the outcome of mIMT. Since race was not significant in the bivariate analysis for mIMT, it would not ordinarily have been included in a regression analysis, and the interaction may not have been investigated. Many studies suggest that there is a SLE specific factor that is contributing to early CVD. Not investigating race and race interactions on CVD outcomes could potentially ignore important covariables that may be specific to the SLE population.

There is great variability in the prevalence of CVD in populations with rheumatic diseases depending on the study and the type of outcome measure used. Both IMT measurements, with or without identification of carotid plaque (8–13,22) and CAC (9,14) have been used as measures of CAD in SLE as predictors of cardiovascular events, as well as in rheumatoid arthritis. (23) In the general population, mean IMT has predictive ability for both myocardial infarction and stroke. (24)

Recent data from the Multi-Ethnic Study of Atherosclerosis (MESA) demonstrates that there are significant differences in IMT and CAC measures depending on age, race, and gender. MESA is a multiethnic study that examined 6814 participants free of any clinical heart disease between the ages of 45–84. (25) Prior to this study, expected CAC scores for race-matched populations were not available. Results from MESA have also shown that there are racial differences between relationships of certain IMT measurements (e.g., common versus internal carotid locations) and CAC. To date, there has never been any examination of inter-racial

comparisons of IMT or CAC, and whether there is any relationship between these two measures in SLE patients.

Similar to our findings, previous studies examining CVD and SLE demonstrated that advancing age (8,10) and elevated fasting glucose levels (10) are associated with increased IMT measurements. Elevated triglycerides have been found to be linked with increasing IMTs in the general population as well as in other groups with inflammatory diseases known to have accelerated atherosclerosis, such as rheumatoid arthritis (26) and psoriatic arthritis (27), but not in SLE. In addition to age, the age-race interaction significantly affected IMT. Mean IMT did not significantly increase in the bivariate analysis in Black subjects in our cohort, but did in White subjects. This racial difference may be a reflection of our cohort. In the MESA study, incremental increases in IMT measures were not as great in Black women as in White women, but did increase with age (28). In addition to age, other studies have reported variables including duration of corticosteroid use (8), higher CRP levels, elevated cholesterol, and increased pulse pressure as being associated with higher IMT measurements. (10) Differing results for covariables between studies are likely multifactorial, including methodological differences, population differences between cohorts, and whether studies are appropriately powered.

Smoking is recognized as a risk factor for development of SLE and for the presence of vascular disease in patients with SLE. A meta-analysis examining the effect of smoking on SLE demonstrated that current smoking increased the odds of developing SLE by 50%. (29) Active cigarette smoking has also been associated with higher disease activity (30) and a 4-fold increased risk of having seropositivity for anti-double stranded DNA antibodies. (31) Smoking contributes independently to vascular events in SLE (7,32) with current smokers having an OR of 3.7 (95% CI 1.4, 10.0) compared to non-smokers. Ethnicity has not been shown to be independently associated with vascular events in SLE. (7,33–35) The total numbers of SLE subjects with a cardiovascular event in any one report have been low and the total numbers of Black SLE subjects even lower; 10/19 in the Hopkins cohort (33), 6 “non-Caucasians”/33 in the Pittsburgh cohort (34), and 15/34 in the LUMINA cohort. (7) It does not appear that the race-smoking interaction was investigated as a potential variable in the regression models in these three studies. Since race was not a significant factor in the bivariate analyses, the interaction of race and smoking was probably not investigated further, even if smoking was found to be a significant univariate variable, as it was in the LUMINA study.

Genetic variability between racial groups may contribute to group differences in measures of cardiovascular disease. It has been demonstrated that different haplotypes for specific genes have an impact on the risk for ischemic stroke and cardiovascular disease that differs between races. (36,37) Potential race-specific interactions impacting accelerated atherosclerosis in patients with chronic inflammatory conditions is an area of great interest. Conditions in the general population associated with inflammation demonstrate gene-environment interactions, such that inflammatory exposures including smoking, obesity/abnormal glucose tolerance, and chronic infections are associated with significantly higher IMTs when patients have inflammatory gene polymorphisms, in particular IL-6 and NADPH oxidase. (38–40) Race differences were not examined in these studies. It is easy for one to imagine that similar gene-environment variations may exist in SLE patients resulting in accelerated atherosclerosis depending on exposures and polymorphisms that may depend on race. Genetic associations with cardiovascular disease have been linked to other rheumatological conditions, including rheumatoid arthritis (RA). RA patients with HLA-DRB1*04 shared epitopes have poorer endothelial dependent vasodilation (41) and an increased risk of CVD mortality. (42) In addition, an interaction of smoking, shared epitopes from the HLA-DRB1 locus, and presence of anti-cyclic citrullinated peptide (anti-CCP) antibodies has been associated with a substantially higher risk of CVD death in RA patients (Hazard Ratio=7.81). (43)

We are unaware of any studies that have examined race interactions with smoking and IMT in the general population. The effects of smoking in different racial groups have been examined using alternative measures of CVD. Arterial stiffness has been shown to be greater in Black subjects that smoke, as compared to White subjects. (44) In a recent study, smoking was found to be independently associated with premature coronary atherosclerosis, via angiogram, in Whites and Blacks without SLE. While smoking was the only factor impacting CVD in Whites, diabetes and dyslipidemia were also independently associated in Blacks. (45) There are also investigations that identify racial differences with regard to the metabolism of nicotine. Blacks are known to have a 30% higher intake of nicotine per cigarette than Whites and have a slower clearance of nicotine metabolites. (46,47) Perhaps the additive effect of inflammatory exposures (including smoking and/or rheumatic disease), race, along with specific gene polymorphisms all contribute to accelerated CVD. Whether our findings are specific to Black SLE patients or whether they reflect a race effect in the general population warrants further investigation.

Limitations of this study include the overall number of SLE subjects, including African-American subjects. The outcome measure of CAC was further limited in that only 22% of African-American subjects had a CAC measurement greater than zero. One further limitation may have included misclassification. We relied on self-report by patients on whether they had ever smoked or not. It appears that in the general population, self-reporting of active smoking is generally accurate. (48) We were unable to determine if the interaction of race and smoking is seen in a similar group of control subjects. This study is the first to examine these racial interactions, and thus future studies are warranted to see if this is indeed a SLE specific finding. We also recognize, as discussed, that carotid IMT may or not be the best measure of subclinical vascular disease. There have not been large studies comparing measures of subclinical disease and CVD outcomes in SLE. Carotid IMT has been shown to be a strong predictor for myocardial infarction and stroke in the general population. (24) Because no Black subjects reported ever having been on a lipid lowering agent, we were unable to assess whether these agents may have impacted any difference in the CVD measures. Of interest is that we did examine whether there were any significant differences between racial groups on fasting cholesterol levels >200 mg/dL, LDL >130 mg/dL, HDL <35 mg/dL, or TG >205 mg/dL. There were no significant differences (data not shown). Despite similar proportions of dyslipidemia in the two populations, 22% of Whites had been on a lipid lowering agent, while none of the Black subjects had. This difference may reflect reporting error or may be consistent with similar trends in the general population. A recent study was done to examine the trends in statin use after the publication of the National Cholesterol Education Program Third Adult Treatment Panel (ATP-III) guidelines in 2001. Results from this report demonstrate that non-Hispanic Blacks are 39% less likely than non-Hispanic Whites to be taking a statin. (49)

In summary, we determined that in a model examining race-specific interactions for measures of subclinical CVD, that there are racial interactions with age and with smoking that impact carotid IMT. In addition, when controlling for age, increasing triglycerides and fasting glucose levels also were associated with higher IMT measurements. We did not detect any racial interactions with other risk factors for CAC. When controlling for age, SLE duration was the only other significant covariable impacting CAC score. Larger studies involving appropriately powered racial groups are warranted to examine racial interactions and their impact on measures of CVD and on CVD events in SLE patients.

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a. White SLE Subjects

b. Black SLE Subjects

Figure 1.
Predicted mIMT values for SLE patients by Smoking Status

Table 1

Descriptive statistics by Race

	Blacks (n=27)	Whites (n=79)	p-value
<u>Age, years</u>	50.2 ± 8.9 (27)	49.0 ± 8.8 (79)	0.57
<u>BMI</u>	27.9 ± 7.3 (27)	31.4 ± 6.9 (76)	0.03
<u>SLE Duration, years</u>	13.8 ± 9.5 (27)	10.7 ± 7.4 (78)	0.09
<u>SLEDAI</u>	4.4 ± 4.7	6.0 ± 5.7	0.22
<u>SLICC</u>	2.9 ± 2.2 (27)	2.8 ± 2.3 (76)	0.82
<u>Prednisone duration</u>			0.29
<u>≤ 1 year</u>	24% (5)	33% (23)	
<u>1–5 years</u>	38% (8)	24% (17)	
<u>5–10 years</u>	24% (5)	14% (10)	
<u>>10 years</u>	14% (3)	29% (20)	
<u>Postmenopausal</u>	48% (11)	56% (44)	0.47
<u>Smoke ever</u>	56% (15)	33% (26)	0.04
<u>SBP, mm Hg</u>	120.3 ± 17.4 (27)	123.1 ± 14.4 (76)	0.42
<u>DBP, mm Hg</u>	74.7 ± 9.5 (27)	77.5 ± 9.7 (76)	0.21
<u>Cholesterol, mg/dL</u>	186.4 ± 44.2 (27)	188.3 ± 34.7 (79)	0.82
<u>LDL, mg/dL</u>	108.0 ± 37.3 (27)	119.8 ± 29.7 (79)	0.12
<u>HDL, mg/dL</u>	55.2 ± 16.0 (27)	50.9 ± 14.9 (79)	0.21
<u>Triglycerides, mg/dL</u>	112.0 ± 67.6 (27)	84.7 ± 55.8 (79)	0.04
<u>Glucose mg/dL</u>	86.3 ± 16.0 (26)	81.3 ± 13.3 (78)	0.13
<u>Homocysteine umol/L</u>	11.6 ± 6.2 (27)	12.6 ± 3.8 (79)	0.31
<u>hs-CRP mg/L</u>	5.52 ± 12.0 (26)	4.47 ± 6.3 (77)	0.57
<u>HTN</u>	54% (12)	46% (41)	0.49
<u>GFR</u>	100.7 ± 35.3 (27)	105.6 ± 32.6 (76)	0.82
<u>Lipid lowering medication (ever)</u>	0% (27)	22% (76)	0.007
<u>mIMT (mm)</u>	0.67 ± 0.14 (20)	0.65 ± 0.19 (65)	0.74
<u>CAC Agatston units</u>	79.5 ± 28.3 (27)	81.3 ± 10.6 (76)	0.88
<u>present</u>	22% (6)	28% (22)	0.57

Table 2

Covariable and Covariable-Race p-values for initial regression models of mIMT

	Covariable (p-value)	Covariable- Race (p-value)
<u>BMI</u>	0.57	0.93
<u>SLE Duration</u>	0.55	0.32
<u>SLEDAI</u>	0.52	0.60
<u>SLICC</u>	0.56	0.96
<u>Prednisone Duration</u>	0.13	0.27
<u>Postmenopausal</u>	0.35	0.27
<u>Smoke ever</u>	0.39	0.03
<u>SBP, mm Hg</u>	0.89	0.16
<u>DBP, mm Hg</u>	0.74	0.61
<u>Cholesterol, mg/dL</u>	0.33	0.23
<u>LDL, mg/dL</u>	0.27	0.14
<u>HDL, mg/dL</u>	0.05	0.40
<u>Triglycerides, mg/dL</u>	0.01	0.99
<u>Glucose, mg/dL</u>	0.01	0.27
<u>Homocysteine, umol/L</u>	0.32	0.61
<u>hs-CRP, mg/L</u>	0.88	0.78
<u>HTN</u>	0.84	0.52
<u>GFR</u>	0.53	0.40
<u>Lipid lowering medication (ever)</u>	0.13	N/A

Table 3

Final multivariate regression analysis of Covariables and Covariable-Race interactions associated with mIMT

Covariable	Regression Coefficient	p-value	Standardized Beta
<u>Age</u>	0.011	<i><0.0001</i>	0.54
<u>Race-Smoking</u>	0.220	<i>0.01</i>	0.40
<u>Race-Age</u>	−0.013	<i>0.006</i>	− 0.34
<u>Triglycerides</u>	0.001	<i>0.01</i>	0.24
<u>Fasting glucose</u>	0.003	<i>0.02</i>	0.21
<u>Race</u>	−0.064	0.25	− 0.15
<u>Smoking (ever)</u>	−0.045	0.23	− 0.12

Table 4

Covariable and Covariable-Race p-values for Initial regression models of ln (CAC+1)

	Covariable (p-value)	Covariable-Race (p-value)
<u>BMI</u>	0.80	0.87
<u>SLE Duration, years</u>	0.004	0.05
<u>SLEDAI</u>	0.97	0.59
<u>SLICC</u>	0.08	0.07
<u>Prednisone duration</u>	0.40	0.75
<u>Postmenopausal</u>	0.82	0.73
<u>Smoke ever</u>	0.02	0.31
<u>SBP</u>	0.12	0.49
<u>DBP</u>	0.38	0.87
<u>Cholesterol</u>	0.37	0.86
<u>LDL</u>	0.54	0.91
<u>HDL</u>	0.09	0.79
<u>Triglycerides</u>	0.43	0.32
<u>Glucose</u>	0.33	0.85
<u>Homocysteine</u>	0.06	0.38
<u>hs-CRP</u>	0.54	0.86
<u>HTN</u>	0.88	0.99
<u>GFR</u>	0.83	0.99
<u>Lipid lowering medication (ever)</u>	0.29	N/A

Table 5

Final multivariate regression analysis of Covariable and Covariable-Race interactions associated with CAC

Covariable	Regression Coefficient	p-value	Standardized Beta
<u>Age</u>	0.10	<i><0.0001</i>	0.48
<u>SLE Duration</u>	0.05	<i>0.007</i>	0.25
<u>Race-SLE Duration</u>	−0.08	0.08	−0.17
<u>Smoke (ever)</u>	0.56	0.09	0.14
<u>Race</u>	−0.59	0.10	−0.14
<u>HDL</u>	−0.01	0.16	−0.11
<u>Homocysteine</u>	0.03	0.30	0.09
<u>Age-Race</u>	0.001	0.97	0.004