Distributions of Subclinical Cardiovascular Disease in a Socioeconomically and Racially Diverse Sample

Carrington R. Wendell, PhD; Shari R. Waldstein, PhD; Michele K. Evans, MD; Alan B. Zonderman, PhD

Background and Purpose—Differential subgroup vulnerability to subclinical cardiovascular disease is likely, and yet few, if any, studies have addressed interactive relations of age, sex, race, and socioeconomic status (SES) to these conditions to examine nuances of known health disparities. We examined distributions of carotid atherosclerosis and arterial stiffness in a socioeconomically diverse, biracial, urban sample.

Methods—Participants (n=2270) in the population-based HANDLS study (Healthy Aging in Neighborhoods of Diversity Across the Life Span; 30–64 years old, 44% men, 57% African American, 39% with household income <125% federal poverty threshold) underwent carotid intimal medial thickness (IMT) and pulse wave velocity assessment.

Results—In cross-sectional hierarchical regression analyses, interactive race×SES effects were identified for IMT and pulse wave velocity, such that high SES African Americans had significantly thicker IMTs and faster pulse wave velocities than all other subgroups (ie, low SES African Americans, low SES whites, and high SES whites). A race×sex effect was also identified for IMT, such that the IMT discrepancy between white men and women was more pronounced than the discrepancy between African American men and women. Finally, an SES×sex effect indicated that while IMTs of high SES and low SES men did not significantly differ, high SES women had marginally thicker IMTs than low SES women.

Conclusions—High SES African Americans may be particularly vulnerable to subclinical cardiovascular diseases, placing them at enhanced risk for clinical cardiovascular diseases, including stroke. These findings suggest that male sex, low SES, and African American ancestry may represent imprecise generalizations as risk factors for subclinical cardiovascular disease. **(*Stroke*. 2017;48:850-856. DOI: 10.1161/STROKEAHA.116.015267.)**

Key Words: arterial stiffness ■ atherosclerosis ■ health disparities ■ intima–media thickness ■ pulse wave velocity ■ subclinical cardiovascular disease

Subclinical cardiovascular diseases (CVDs), including carotid atherosclerosis and arterial stiffness, are asymptomatic stepping stones to clinical CVDs and stroke[1] and predict a variety of poor health outcomes, including accelerated aging, frailty, cognitive decline, and all-cause mortality.[2–4] For example, individuals in the highest quintile of carotid intimal medial thickness (IMT) are up to 4.5× as likely to experience a stroke.[4] Prevalence of any subclinical CVD is typically described as 35% to 40% of community-dwelling older adults.[5] There are substantial race and socioeconomic status (SES) discrepancies in CVD and stroke prevalence,[6,7] but less is known about differential patterns of subclinical CVDs among sociodemographic groups.

Subclinical disease rates increase with age, male sex, racial minority status, and lower SES.[5,8–12] None of these directionalities are surprising given their parallels with the clinical CVD literature. However, little is known about interactive relations of these sociodemographic factors to subclinical disease prevalence. Investigations of interactive patterns are critical given frequent confounding among different characteristics (eg, race and SES[13]) that may lead to inaccurate presumptions of risk. Early data from the ARIC study (Atherosclerosis Risk in Communities) failed to show interactive race–sex or race–SES interactions in relation to carotid atherosclerosis, although there was a trend for whites to benefit more from higher SES than African Americans.[12] More recently, a race–sex interaction was identified among ≥65-year-old ARIC participants for a marker of arterial stiffness, such that white men had higher carotid–femoral pulse wave velocities (PWVs) than white women, with no significant sex difference between African Americans.[14] In a different population-based study (MESA [Multi-Ethnic Study of Atherosclerosis]), low SES was

Received August 26, 2016; final revision received December 19, 2016; accepted December 29, 2016.

From the Department of Psychology, University of Maryland, Baltimore County (C.R.W., S.R.W.); Laboratory of Epidemiology and Population Sciences, Intramural Research Program, National Institute on Aging, NIH (C.R.W., M.K.E., A.B.Z.); Division of Gerontology & Geriatric Medicine, Department of Medicine, University of Maryland School of Medicine (S.R.W.); and Geriatric Research Education and Clinical Center, Baltimore VAMC, MD (S.R.W.).

The online-only Data Supplement is available with this article at http://stroke.ahajournals.org/lookup/suppl/doi:10.1161/STROKEAHA.116.015267/-/DC1.

Correspondence to Carrington R. Wendell, PhD, UMBC Department of Psychology, 1000 Hilltop Circle, Baltimore, MD 21250. E-mail crwendell@umbc.edu

associated with greater carotid atherosclerosis, but African American women were most vulnerable to greater exposure to neighborhood poverty.[15] A separate analysis of MESA data showed no statistically significant race by sex interactions for IMT, but did show more pronounced sex differences in coronary artery calcification among non-Hispanic whites than in other racial/ethnic groups.[16] Although these studies represent important steps toward understanding subgroup-specific patterns of subclinical CVDs, to our knowledge, no study has comprehensively addressed interactive associations between multiple sociodemographic indicators and multiple subclinical CVDs. Most, if not all, studies have assessed racially or socioeconomically homogenous samples, included only men or women, focused on fewer sociodemographic characteristics, measured just 1 subclinical disease, or have not examined interactive terms.

The present study evaluated interactive associations among 4 sociodemographic risk factors (age, sex, race, and SES) and 2 common subclinical CVDs, carotid atherosclerosis and arterial stiffness, in participants in the HANDLS study (Healthy Aging in Neighborhoods of Diversity Across the Life Span). The HANDLS study design presents a unique opportunity to assess the synergistic influences of age, sex, race, and poverty status. We also explored whether other SES indicators and clusters of pertinent biopsychosocial risk factors mediated these findings.

Methods

Participants

HANDLS enrolled a fixed cohort of participants (August 2004 to March 2009) in a prospective, population-based, longitudinal study examining the influences and interaction of race and SES on development of health disparities. Data for the present analyses were exclusively cross-sectional because repeat subclinical disease data are not yet available. Comprehensive information regarding HANDLS study design and procedures has been published elsewhere.[17] Participants were recruited from separate clusters of contiguous census tracts containing sufficient numbers of residents to fill a factorial cross of age (30–64 years), sex, race (African American or white), and poverty status. Of 8150 eligible individuals, 3720 participants met study criteria. Inclusion criteria were age 30 to 64 years and able to give informed consent, perform ≥5 measures on the mobile medical research vehicle, and provide picture identification. Exclusion criteria were pregnancy, AIDS, and within 6 months of active cancer treatment. Examinations were deferred when blood pressure(s) exceeded 160/100. HANDLS was approved by the MedStar Institutional Review Board and National Institute of Environmental Health Science of the National Institutes of Health. All participants provided informed consent.

Among 2707 individuals who completed the HANDLS protocol, 2670 participants completed subclinical CVD assessment. Exclusions specific to carotid ultrasonography were blood pressure >200/100 at ultrasound, bruit, and weight ≥295 pounds. We further excluded individuals with stroke, dementia, carotid endarterectomy, heart failure, dialysis, HIV, and other neurological/psychiatric illness. The final sample included 2270 participants: 1903 and 2003 of whom underwent IMT and PWV assessment, respectively.

Carotid IMT Assessment

High-resolution B-mode ultrasonography of the left common carotid artery was performed with standard transducer (5.OL45) and equipment (Acuson CV 70, Siemens). At a region 1.5 cm proximal to carotid bifurcation, far-wall IMT was evaluated as the distance between intimal–luminal and medial–adventitial interfaces in areas devoid of plaque, at 5 contiguous sites at 1 mm intervals, with the mean used in the analyses. A single sonographer performed measurements. Intraobserver correlation between repeated IMT measurements on 10 participants was 0.96 ($P<0.001$).[18]

PWV Assessment

To measure carotid–femoral PWV, a minimum of 10 arterial flow waves from the right common carotid and femoral arteries were recorded using nondirectional transcutaneous Doppler probes (Model 810A, 9- to 10-MHz probes; Parks Medical Electronics, Inc) and averaged using QRS for synchronization. PWV was calculated as distance traveled by the flow wave divided by the time differential. A single technologist assessed PWV.

Demographic Characteristics

Demographic characteristics of interest included age, sex, self-identified race, and SES assessed by household income above or below 125% of poverty threshold, based on household size and reported family income relative to the 2004 federal guidelines (eg, $18 850 per year for family of 4) published by the Department of Health and Human Services. In Baltimore, 125% of the poverty threshold better approximates economic hardship because of the city's higher cost of living relative to the national average.

Covariates

Covariates included years of education, literacy, depressive symptoms, substance use, body mass index, total cholesterol, lipid-lowering medication use, hypertension, diabetes mellitus, and CVD. Literacy was estimated via the reading subtest of the Wide Range Achievement Test–3rd edition,[19] and depressive symptoms were measured by the 20-item Center for Epidemiological Studies-Depression scale.[20] Fasting venous blood specimens for total cholesterol and glucose assay were analyzed at the NIA Clinical Research Branch Core Laboratory (Baltimore, MD) and Quest Diagnostics Inc (Baltimore, MD, and Chantilly, VA) using a spectrophotometer (AU5400 Immuno Chemistry Analyzer; Olympus, Center Valley, PA). Body mass index was calculated as the ratio of weight (kg) to height (m) squared. Resting brachial systolic and diastolic blood pressure was measured bilaterally with an aneroid manometer and stethoscope and averaged across arms. The assessor recorded any diagnosable medical conditions and medication use. Individual hypertension and diabetes mellitus diagnostic variables were coded as positive when the participant self-reported the condition, was taking medications for the condition, or produced a resting systolic blood pressure average of ≥140 mm Hg/diastolic blood pressure average of ≥90 mm Hg or a fasting glucose of ≥126 mg/dL, respectively. Lipid-lowering medication use was coded dichotomously. A CVD cluster variable was based on diagnoses of coronary artery disease, myocardial infarction, peripheral artery disease, atrial fibrillation, angioplasty, and coronary artery bypass surgery. Each medical condition was coded dichotomously, and a summation score was calculated to represent the cluster variable. Self-reported alcohol, cigarette smoking, and illicit drug status were each coded dichotomously as not current user (ie, never tried, never used regularly, or used >6 months ago) or used within the past 6 months.

Statistical Analyses

Statistical analyses were performed using SAS v9.3 (Cary, NC). Hierarchical multiple regression analyses (PROC GLM) evaluated interactive and independent associations of age, sex, race, and poverty status with subclinical CVD measures, IMT, and PWV, which served as outcome variables. IMT and PWV were examined in separate models. Age was analyzed continuously. Dichotomous variables were coded as follows: sex (0=female and 1=male), race (0=white and 1=African American), SES (0=high SES and 1=low SES), substance use (0=not current user and 1=current user), and lipid-lowering medications, hypertension, and diabetes mellitus as 0=absent and 1=present.

Consistent with HANDLS' factorial design, initial models examined interactions of age×sex×race×SES and all possible lower-order interactive and independent terms. In the absence of any significant 4-way or 3-way interactions, these terms were backward eliminated from all models for the sake of parsimony. (Post-hoc power analysis showed >99% power to detect a significant 3- or 4-way interaction in step 1 models with P=0.05 and f^2=0.02.) Final step 1 models, thus, included age, sex, race, SES, and interactive terms of race×SES, race×sex, and SES×sex (n_{IMT}=1903 and n_{PWV}=2003). Additional clusters of variables were entered in subsequent steps as follows: step 2: education, literacy; step 3: alcohol use, smoking, illicit drug use; step 4: depressive symptoms; and step 5: body mass index, total cholesterol, lipid-lowering medication use, hypertension, diabetes mellitus, and CVD (n_{IMT}=1704 and n_{PWV}=1811 because of missing covariate data). Coefficients with P<0.05 were considered statistically significant.

Results

Sample Characteristics

Table 1 presents descriptive statistics for the full sample, as well as stratified by race and SES. Please see online-only Data Supplement for further descriptive stratification and the findings of Waldstein et al[21] for information regarding variability of cardiovascular risk factors across groups. Overall, participants were ≈44% men, 57% African American, and ranged in age from 30 to 64 years (mean=48 years). Approximately 39% of participants reported having a household income below the 125% federal poverty threshold.

Hierarchical Regression Models

Tables 2 and 3 present results from each of the 5 steps of hierarchical regression models predicting IMT and PWV, respectively.

Race×SES

Significant interactive race×SES effects were identified for IMT (b=−0.026, SE=0.012; P<0.05) and PWV (b=−0.619, SE=0.241; P<0.05) in step 1 models. These effects remained significant through step 4 for both IMT (b=−0.028, SE=0.012; P<0.05) and PWV (b=−0.629, SE=0.252; P<0.05). For both IMT and PWV (Figure 1), high SES African Americans had significantly thicker IMTs and faster PWVs than all other subgroups (ie, low SES African Americans, low SES whites, and high SES whites; all P<0.01). For IMT only, low SES African Americans also had thicker IMTs than both white subgroups (P<0.05).

Race×Sex

A significant interactive race×sex effect was identified for IMT, but not for PWV, in the step 1 model (b=−0.028, SE=0.011; P<0.05). This effect persisted through step 4 of the IMT hierarchical regressions (b=−0.029, SE=0.012; P<0.05). As depicted in Figure 2A, African Americans had thicker IMTs than whites, and men had thicker IMTs than women. Interestingly, the IMT discrepancy between white men and women was more pronounced (M_{men}=0.69 mm [0.007], M_{women}=0.65 mm [0.006], F=18.09; P<0.0001) than the discrepancy between African American men and women (M_{men}=0.71 mm [0.006], M_{women}=0.70 mm [0.005], F=4.20; P=0.041).

SES×Sex

A significant interactive SES×sex effect arose for IMT, but not for PWV, in step 1 models only (b=0.024, SE=0.012; P<0.05). Figure 2B shows that men had significantly thicker IMTs than women. The IMTs of high SES and low SES men did not

Table 1. Descriptive Statistics

	Mean (SD) or %				
	Full Sample (n=2270)	African American Low SES (n=592)	African American High SES (n=705)	White Low SES (n=287)	White High SES (n=686)
Age, y	47.7 (9.3)	46.7 (9.1)	48.3 (9.4)	47.1 (9.4)	48.2 (9.4)
Male, %	43.7	42.2	45.0	37.6	46.4
African American, %	57.1	N/A	N/A	N/A	N/A
SES, % below poverty line	38.7	N/A	N/A	N/A	N/A
Education, y	12.6 (3.0)	11.7 (2.3)	12.9 (2.6)	11.5 (3.0)	13.5 (3.6)
WRAT-3 reading (total)	42.4 (8.1)	39.4 (8.2)	41.5 (7.2)	41.9 (8.3)	46.2 (7.3)
Alcohol, % ever	54.9	52.2	54.9	50.9	59.0
Cigarettes, % ever	44.3	56.3	38.0	55.4	35.9
Illicit drugs, % ever	15.5	22.5	15.0	13.6	10.8
CES-D (total)	14.1 (10.9)	16.2 (11.1)	12.5 (10.0)	17.0 (11.6)	12.8 (10.7)
Body mass index, kg/m^2	29.9 (7.6)	28.8 (7.7)	30.6 (7.5)	30.7 (8.5)	29.6 (7.2)
Total cholesterol, mg/dL	187.6 (42.3)	183.4 (41.9)	185.8 (43.7)	188.3 (43.2)	192.5 (40.3)
Lipid-lowering medications, %	12.1	8.6	11.9	10.5	16.0
Hypertension, %	42.6	46.2	47.1	36.9	37.4
Diabetes mellitus, %	15.3	14.2	17.8	17.8	12.6
Cardiovascular disease, %≥1 disease	4.0	4.7	3.7	5.2	3.1
Intimal medial thickness, mm	0.69 (0.13)	0.69 (0.14)	0.71 (0.12)	0.67 (0.13)	0.67 (0.13)
Pulse wave velocity, m/s	8.05 (2.66)	7.81 (1.96)	8.49 (3.29)	7.85 (1.93)	7.89 (2.65)

CES-D indicates Center for Epidemiologic Studies Depression scale; SES, socioeconomic status; and WRAT-3, Wide Range Achievement Test-3rd edition.

Table 2. Results From Hierarchical Regression Models Predicting Carotid Intimal Medial Thickness

	b (SE)				
	Step 1	Step 2	Step 3	Step 4	Step 5*
Age, y	0.004 (0.0003)†	0.004 (0.0003)†	0.005 (0.0003)†	0.005 (0.0003)†	0.004 (0.0004)†
Sex	0.032 (0.009)†	0.033 (0.009)†	0.032 (0.010)†	0.033 (0.010)†	0.033 (0.010)†
Race	0.061 (0.009)†	0.064 (0.009)†	0.064 (0.009)†	0.064 (0.009)†	0.056 (0.010)†
SES	0.0002 (0.010)	0.002 (0.011)	0.003 (0.011)	0.002 (0.011)	0.001 (0.011)
Race×SES	−0.026 (0.012)‡	−0.028 (0.012)‡	−0.029 (0.012)‡	−0.028 (0.012)‡	−0.021 (0.013)
Race×sex	−0.028 (0.011)‡	−0.029 (0.012)‡	−0.029 (0.012)‡	−0.029 (0.012)‡	−0.013 (0.012)
SES×sex	0.024 (0.012)‡	0.021 (0.012)	0.021 (0.012)	0.021 (0.012)	0.018 (0.012)
Education	…	−0.0004 (0.001)	−0.0005 (0.001)	−0.0004 (0.001)	0.0004 (0.001)
WRAT-3	…	0.0004 (0.0004)	0.0004 (0.0004)	0.0004 (0.0004)	0.0005 (0.0004)
Alcohol	…	…	0.005 (0.006)	0.006 (0.006)	0.006 (0.006)
Smoking	…	…	−0.0004 (0.006)	−0.0006 (0.006)	0.009 (0.006)
Illicit drugs	…	…	−0.002 (0.008)	−0.002 (0.008)	0.004 (0.009)
CES-D	…	…	…	0.0002 (0.0003)	0.0001 (0.0003)
Body mass index	…	…	…	…	0.003 (0.0004)†
Total cholesterol	…	…	…	…	0.0002 (0.0001)†
Lipid-lowering medications	…	…	…	…	0.005 (0.010)
Hypertension	…	…	…	…	0.019 (0.007)†
Diabetes mellitus	…	…	…	…	0.012 (0.009)
Cardiovascular disease	…	…	…	…	0.007 (0.006)

CES-D indicates Center for Epidemiologic Studies Depression scale; SES, socioeconomic status; and WRAT-3, Wide Range Achievement Test-3rd edition.
*Significance of Step 5 results remained unchanged after removal of nonsignificant covariates.
†$P<0.01$, ‡$P<0.05$.

significantly differ ($M_{highSES}$=0.70 mm [0.005], M_{lowSES}=0.71 mm [0.008], F=0.42; P=0.517), while high SES women had marginally thicker IMTs than low SES women ($M_{highSES}$=0.68 mm [0.005], M_{lowSES}=0.67 mm [0.006], F=2.97; P=0.085). In a sensitivity analysis that eliminated participants with CVD (n=90), overall results were identical, except SES×sex became nonsignificant for IMT (b=0.020, SE=0.012; P>0.05).

Discussion

We identified multiple 2-way interactive effects of sex, race, and SES in relation to carotid atherosclerosis and arterial stiffness. We found that high SES African Americans had significantly greater subclinical CVD, in the form of thicker IMTs and faster PWVs, than any other subgroup. Cardiovascular risk factors and comorbidities at least partially accounted for this race×SES effect for both IMT and PWV, given nonsignificance of the interaction in fully adjusted models. Sex-specific interactive effects for IMT also showed individual subgroup vulnerabilities. The typical sex difference in IMT (with men>women) was present for both whites and African Americans, but the discrepancy was more pronounced among whites, suggesting that African American women may be at heightened risk relative to white women. African American men, nevertheless, had the greatest IMTs overall. Additionally, high SES women had marginally thicker IMTs than low SES women, a pattern that was absent among men. Taken together, our results underscore the importance of including interactive terms when assessing sociodemographic risk for subclinical CVD.

Our finding that high SES African Americans had significantly thicker IMTs and faster PWVs than all other subgroups may seem unexpected at first glance, given known health-related correlates of low SES (eg, reduced healthcare access, food insecurity, reduced leisure-time physical activity because of neighborhood safety concerns). However, the diminishing returns hypothesis posits that African Americans often do not experience commensurate health benefits (or returns) of higher SES as whites.[13] Experiences of unfair treatment and racial discrimination are significantly associated with poor cardiovascular outcomes, including increased IMT[22] and heightened cardiovascular reactivity,[23,24] and higher SES minorities often report greater discrimination than lower SES minorities, potentially because of more extensive exposure to majority groups (ie, reduced segregation in higher SES neighborhoods and occupational environments).[25,26] Higher SES African Americans may also reasonably expect reduced discrimination with achievement of higher SES, which may lead to increased emotional and physiological reactivity to discrimination if/when this expectation proves false.

To our knowledge, a significant race×sex effect has not previously been identified for IMT, although subgroup differences have been examined individually in at-risk cohorts.[27] Similar

Table 3. Results From Hierarchical Regression Models Predicting Pulse Wave Velocity

	b (SE)				
	Step 1	Step 2	Step 3	Step 4	Step 5*
Age	0.084 (0.006)†	0.083 (0.006)†	0.083 (0.006)†	0.083 (0.006)†	0.071 (0.007)†
Sex	0.215 (0.186)	0.187 (0.195)	0.188 (0.196)	0.200 (0.196)	0.258 (0.197)
Race	0.768 (0.179)†	0.770 (0.190)†	0.765 (0.190)†	0.781 (0.191)†	0.553 (0.193)†
Poverty status	−0.040 (0.210)	−0.121 (0.222)	−0.095 (0.223)	−0.115 (0.224)	−0.252 (0.224)
Race×SES	−0.619 (0.241)‡	−0.627 (0.251)‡	−0.627 (0.252)‡	−0.629 (0.252)‡	−0.391 (0.255)
Race×sex	−0.395 (0.233)	−0.372 (0.243)	−0.350 (0.243)	−0.361 (0.244)	−0.165 (0.246)
SES×sex	0.312 (0.238)	0.340 (0.247)	0.338 (0.248)	0.353 (0.248)	0.392 (0.251)
Education	…	−0.083 (0.022)†	−0.090 (0.023)†	−0.086 (0.023)†	−0.062 (0.023)†
WRAT-3	…	0.013 (0.009)	0.013 (0.009)	0.013 (0.009)	0.009 (0.009)
Alcohol	…	…	0.088 (0.125)	0.091 (0.125)	0.177 (0.126)
Smoking	…	…	−0.170 (0.129)	−0.176 (0.129)	0.082 (0.133)
Illicit drugs	…	…	−0.049 (0.172)	−0.057 (0.173)	0.015 (0.176)
CES-D	…	…	…	0.007 (0.006)	0.005 (0.006)
Body mass index	…	…	…	…	0.062 (0.009)†
Total cholesterol	…	…	…	…	0.001 (0.001)
Lipid-lowering medications	…	…	…	…	0.033 (0.199)
Hypertension	…	…	…	…	0.239 (0.139)
Diabetes mellitus	…	…	…	…	0.829 (0.178)†
Cardiovascular disease	…	…	…	…	−0.007 (0.120)

CES-D indicates Center for Epidemiologic Studies Depression scale; SES, socioeconomic status; and WRAT-3, Wide Range Achievement Test-3rd edition.
*Significance of Step 5 results remained unchanged after removal of nonsignificant covariates.
†$P<0.01$, ‡$P<0.05$.

to the race×SES effect described earlier, cardiovascular risk factors and comorbidities at least partially mediated the interaction, given nonsignificance of the interactive race×sex term in fully adjusted models. Meyer et al[14] demonstrated a pattern similar to our results among older adult ARIC participants, but for PWV. They found white men had significantly faster PWVs than white women, but there was no significant sex difference among African Americans. In our study, a significant sex difference in IMT arose for both whites and African Americans. However, the significant interaction was driven by a more substantial sex discrepancy among whites than among African Americans. One interpretation of our findings, combined with Meyer et al's[14] results, is that African American women are at heightened risk for increased subclinical CVD given the sex difference was less pronounced than expected (or absent). This is consistent with observations of heightened risk of clinical CVD among African American women compared with white women.[6,28,29] Such a pattern could potentially

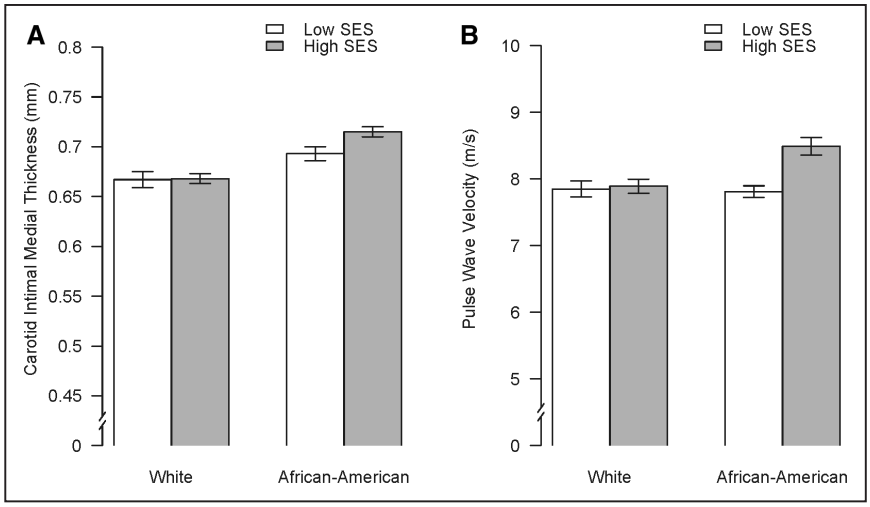

Figure 1. Unadjusted interactive associations of race×socioeconomic status (SES) to (**A**) carotid intimal medial thickness and (**B**) pulse wave velocity.

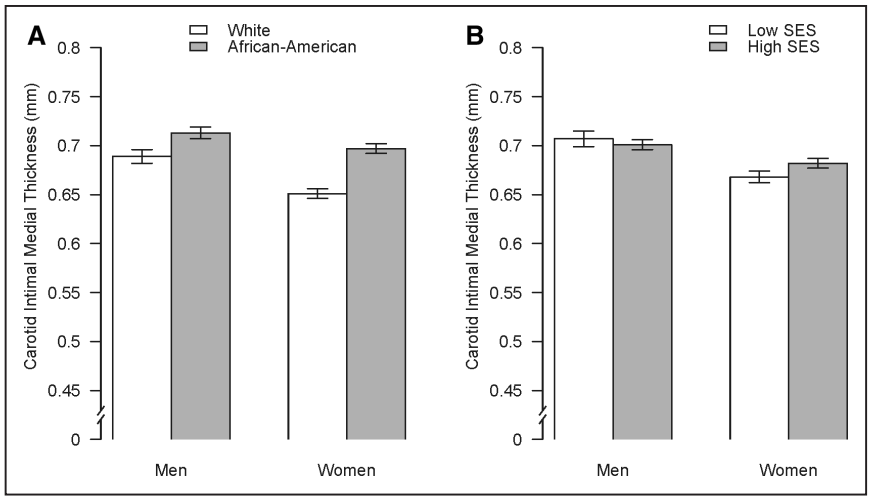

Figure 2. Unadjusted interactive associations of (**A**) race×sex and (**B**) socioeconomic status (SES)×sex to carotid intimal medial thickness.

be explained by the double jeopardy experienced by women of color who cope with discrimination on ≥2 fronts.[7]

We found that high SES women had marginally greater IMTs than low SES women, whereas there was clearly no significant SES-related difference in men. This pattern ostensibly contrasts with data from at least 3 epidemiological studies that identified inverse associations between other SES indices (eg, occupational status,[9] childhood SES as measured by parental education,[15] neighborhood SES as measured by proportion of residents with secondary education[30]) and IMT in women. The variability in directionality may be explained by our use of poverty status as an index of SES. Specifically, the interactive SES×sex term was rendered nonsignificant after the addition of education and literacy to the model, suggesting that other aspects of SES may be more pertinent or mediate the significant interactive effect. The interaction was also rendered nonsignificant in a sensitivity analysis without prevalent CVD, so differential survival may have biased this finding.

Replication in other racially and socioeconomically diverse samples is recommended prior to clinical application of these findings. African Americans are most likely to experience temporal delays in endarterectomy for carotid stenosis, and socioeconomic disadvantage does not seem to explain this pattern entirely.[31] Accordingly, if replicated, the present findings suggest counterintuitively that high SES African Americans may require increased clinical attention. While carotid ultrasonography is not recommended for widespread screening of asymptomatic individuals, in part because of limited guidelines,[6] knowing who to target could help facilitate the creation of such guidelines and, thus, augment stroke prevention on both individual and population levels.[32,33] Regardless, a substantial portion of the variance in carotid atherosclerosis cannot be explained by demographic or traditional risk factors (>60%),[34] and variable cardiovascular risk profiles are associated with subclinical CVD across subgroups,[35] so researchers and clinicians alike are reminded to avoid generalizations that overlook individual differences and presently unknown contributors to subclinical diseases. Early intervention is also critical because sex and race/ethnicity differences are detectable as early as young adulthood,[36] and African Americans develop cardiovascular risk factors such as obesity and hypertension earlier and more severely than other groups[37]—a finding that may help explain disproportionate subclinical CVD and stroke in this group. Nevertheless, the present study extends the dearth of information regarding subgroup vulnerability to subclinical CVD. Future mechanistic investigations are crucial to understand the reasons for differential vulnerability. Consideration of cumulative risk for aggregated subclinical diseases, rather than individual diseases, are also worthwhile to identify those at exceptionally heightened risk.

The primary strength of this investigation involves its comprehensive assessment of up to 4-way interactive associations among age, sex, race, SES, and subclinical CVDs. Inclusion of both IMT and PWV allowed examination of 2 different subclinical diseases, carotid atherosclerosis and arterial stiffness, respectively. The HANDLS study design also provided an unusual opportunity to disentangle typically confounded sociodemographic characteristics. Our use of far-wall IMT also represents a strength because near-wall IMT is known to be less reliably assessed. An important limitation of the present study is the absence of data regarding other operationalized definitions of SES, such as continuous household income, occupational status, or early childhood SES indicators. These findings also may not extend (and should not be directly applied) to other ethnic minorities within the United States or worldwide. Finally, longitudinal data regarding subclinical CVDs were not available, although HANDLS will provide such opportunities in the future. The cross-sectional nature of our analyses, thus, limits our ability to account for differential survival and other intraindividual time-dependent variables.

Summary

In this population-based, biracial, socioeconomically diverse cohort, high SES African Americans demonstrated the greatest subclinical CVD assessed by thickest IMTs and fastest PWVs. These findings suggest that singular consideration of male sex, low SES, or African American ancestry may prompt an imprecise conception of risk for subclinical CVD and, thus, downstream clinical events, such as stroke.

Acknowledgments

We thank the HANDLS Mobile Medical Research Vehicle Staff with special recognition to the technologists, Mary Lassiter and Clare Jefferson, for their careful evaluation of participants.

Sources of Funding

This work was supported by the National Institute on Aging Intramural Research Program of the National Institutes of Health (NIH) and NIH grant RO1 AG034161.

Disclosures

None.

References

1. Devereux RB, Alderman MH. Role of preclinical cardiovascular disease in the evolution from risk factor exposure to development of morbid events. *Circulation*. 1993;88(4 pt 1):1444–1455.
2. Chaves PH, Kuller LH, O'Leary DH, Manolio TA, Newman AB; Cardiovascular Health Study. Subclinical cardiovascular disease in older adults: insights from the Cardiovascular Health Study. *Am J Geriatr Cardiol*. 2004;13:137–151.
3. Newman AB, Arnold AM, Naydeck BL, Fried LP, Burke GL, Enright P, et al; Cardiovascular Health Study Research Group. "Successful aging": effect of subclinical cardiovascular disease. *Arch Intern Med*. 2003;163:2315–2322. doi: 10.1001/archinte.163.19.2315.
4. 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;340:14–22. doi: 10.1056/NEJM199901073400103.
5. Kuller L, Borhani N, Furberg C, Gardin J, Manolio T, O'Leary D, et al. Prevalence of subclinical atherosclerosis and cardiovascular disease and association with risk factors in the Cardiovascular Health Study. *Am J Epidemiol*. 1994;139:1164–1179.
6. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics-2016 update. *Circulation*. 2016;133:e38–e360.
7. Williams DR, Mohammed SA, Leavell J, Collins C. Race, socioeconomic status, and health: complexities, ongoing challenges, and research opportunities. *Ann N Y Acad Sci*. 2010;1186:69–101. doi: 10.1111/j.1749-6632.2009.05339.x.
8. Carson AP, Rose KM, Catellier DJ, Kaufman JS, Wyatt SB, Diez-Roux AV, et al. Cumulative socioeconomic status across the life course and subclinical atherosclerosis. *Ann Epidemiol*. 2007;17:296–303. doi: 10.1016/j.annepidem.2006.07.009.
9. Nash SD, Cruickshanks KJ, Klein R, Klein BE, Nieto FJ, Ryff CD, et al. Socioeconomic status and subclinical atherosclerosis in older adults. *Prev Med*. 2011;52:208–212. doi: 10.1016/j.ypmed.2010.12.009.
10. Thurston RC, El Khoudary SR, Derby CA, Barinas-Mitchell E, Lewis TT, McClure CK, et al. Low socioeconomic status over 12 years and subclinical cardiovascular disease: the study of women's health across the nation. *Stroke*. 2014;45:954–960. doi: 10.1161/STROKEAHA.113.004162.
11. Bauer M, Delaney JA, Möhlenkamp S, Jöckel KH, Kronmal RA, Lehmann N, et al; Multi-Ethnic Study of Atherosclerosis; Investigator Group of the Heinz Nixdorf Recall Study. Comparison of factors associated with carotid intima-media thickness in the Multi-Ethnic Study of Atherosclerosis (MESA) and the Heinz Nixdorf Recall Study (HNR). *J Am Soc Echocardiogr*. 2013;26:667–673. doi: 10.1016/j.echo.2013.03.011.
12. Diez-Roux AV, Nieto FJ, Tyroler HA, Crum LD, Szklo M. Social inequalities and atherosclerosis. The atherosclerosis risk in communities study. *Am J Epidemiol*. 1995;141:960–972.
13. Farmer MM, Ferraro KF. Are racial disparities in health conditional on socioeconomic status? *Soc Sci Med*. 2005;60:191–204. doi: 10.1016/j.socscimed.2004.04.026.
14. Meyer ML, Tanaka H, Palta P, Cheng S, Gouskova N, Aguilar D, et al. Correlates of segmental pulse wave velocity in older adults: the Atherosclerosis Risk in Communities (ARIC) study. *Am J Hypertens*. 2016;29:114–122. doi: 10.1093/ajh/hpv079.
15. Lemelin ET, Diez Roux AV, Franklin TG, Carnethon M, Lutsey PL, Ni H, et al. Life-course socioeconomic positions and subclinical atherosclerosis in the multi-ethnic study of atherosclerosis. *Soc Sci Med*. 2009;68:444–451. doi: 10.1016/j.socscimed.2008.10.038.
16. Kim C, Diez-Roux AV, Nettleton JA, Polak JF, Post WS, Siscovick DS, et al. Sex differences in subclinical atherosclerosis by race/ethnicity in the multi-ethnic study of atherosclerosis. *Am J Epidemiol*. 2011;174:165–172. doi: 10.1093/aje/kwr088.
17. Evans MK, Lepkowski JM, Powe NR, LaVeist T, Kuczmarski MF, Zonderman AB. Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS): overcoming barriers to implementing a longitudinal, epidemiologic, urban study of health, race, and socioeconomic status. *Ethn Dis*. 2010;20:267–275.
18. Nagai Y, Metter EJ, Earley CJ, Kemper MK, Becker LC, Lakatta EG, et al. Increased carotid artery intimal-medial thickness in asymptomatic older subjects with exercise-induced myocardial ischemia. *Circulation*. 1998;98:1504–1509.
19. Wilkinson GS. *Wide Range Achievement Test (WRAT-3)*. Wilmington, DE: Wide Range; 1993.
20. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1:385–401.
21. Waldstein SR, Moody DL, McNeely JM, Allen AJ, Sprung MR, Shah MT, et al. Cross-sectional relations of race and poverty status to cardiovascular risk factors in the Healthy Aging in Neighborhoods of Diversity Across the Lifespan (HANDLS) study. *BMC Public Health*. 2016;16:258. doi: 10.1186/s12889-016-2945-9.
22. Troxel WM, Matthews KA, Bromberger JT, Sutton-Tyrrell K. Chronic stress burden, discrimination, and subclinical carotid artery disease in African American and Caucasian women. *Health Psychol*. 2003;22:300–309.
23. Clark R. Perceptions of interethnic group racism predict increased vascular reactivity to a laboratory challenge in college women. *Ann Behav Med*. 2000;22:214–222.
24. Guyll M, Matthews KA, Bromberger JT. Discrimination and unfair treatment: relationship to cardiovascular reactivity among African American and European American women. *Health Psychol*. 2001;20:315–325.
25. Bécares L, Nazroo J, Stafford M. The buffering effects of ethnic density on experienced racism and health. *Health Place*. 2009;15:670–678. doi: 10.1016/j.healthplace.2008.10.008.
26. Borrell LN, Kiefe CI, Diez-Roux AV, Williams DR, Gordon-Larsen P. Racial discrimination, racial/ethnic segregation, and health behaviors in the CARDIA study. *Ethn Health*. 2013;18:227–243. doi: 10.1080/13557858.2012.713092.
27. Urbina EM, Srinivasan SR, Tang R, Bond MG, Kieltyka L, Berenson GS; Bogalusa Heart Study. Impact of multiple coronary risk factors on the intima-media thickness of different segments of carotid artery in healthy young adults (the Bogalusa Heart study). *Am J Cardiol*. 2002;90:953–958.
28. Health, United States, 2014: with special feature on adults aged 55–64. Hyattsville, MD: National Center for Health Statistics; 2015.
29. Safford MM, Brown TM, Muntner PM, Durant RW, Glasser S, Halanych JH, et al; REGARDS Investigators. Association of race and sex with risk of incident acute coronary heart disease events. *JAMA*. 2012;308:1768–1774. doi: 10.1001/jama.2012.14306.
30. Grimaud O, Lapostolle A, Berr C, Helmer C, Dufouil C, Kihal W, et al. Gender differences in the association between socioeconomic status and subclinical atherosclerosis. *PLoS One*. 2013;8:e80195. doi: 10.1371/journal.pone.0080195.
31. Wise ES, Ladner TR, Song J, Eagle SS, Mocco J, Wergin JE, et al. Race as a predictor of delay from diagnosis to endarterectomy in clinically significant carotid stenosis. *J Vasc Surg*. 2015;62:49–56. doi: 10.1016/j.jvs.2015.01.057.
32. Poredos P. Intima-media thickness: indicator of cardiovascular risk and measure of the extent of atherosclerosis. *Vasc Med*. 2004;9:46–54.
33. Simon A, Levenson J. May subclinical arterial disease help to better detect and treat high-risk asymptomatic individuals? *J Hypertens*. 2005;23:1939–1945.
34. Santos IS, Alencar AP, Rundek T, Goulart AC, Barreto SM, Pereira AC, et al. Low impact of traditional risk factors on carotid intima-media thickness: the ELSA-Brasil cohort. *Arterioscler Thromb Vasc Biol*. 2015;35:2054–2059. doi: 10.1161/ATVBAHA.115.305765.
35. Kuller L, Fisher L, McClelland R, Fried L, Cushman M, Jackson S, et al. Differences in prevalence of and risk factors for subclinical vascular disease among black and white participants in the Cardiovascular Health Study. *Arterioscler Thromb Vasc Biol*. 1998;18:283–293.
36. Breton CV, Wang X, Mack WJ, Berhane K, Lopez M, Islam TS, et al. Carotid artery intima-media thickness in college students: race/ethnicity matters. *Atherosclerosis*. 2011;217:441–446. doi: 10.1016/j.atherosclerosis.2011.05.022.
37. Freedman DS, Dietz WH, Tang R, Mensah GA, Bond MG, Urbina EM, et al. The relation of obesity throughout life to carotid intima-media thickness in adulthood: the Bogalusa Heart study. *Int J Obes Relat Metab Disord*. 2004;28:159–166. doi: 10.1038/sj.ijo.0802515.

Stroke
Journal of the American Heart Association

Distributions of Subclinical Cardiovascular Disease in a Socioeconomically and Racially Diverse Sample

Carrington R. Wendell, Shari R. Waldstein, Michele K. Evans and Alan B. Zonderman

Stroke. 2017;48:850-856; originally published online February 24, 2017;
doi: 10.1161/STROKEAHA.116.015267
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628

SUPPLEMENTAL MATERIAL

Supplemental Table I. Descriptive Statistics, Stratified by Race, Sex, and SES

	Intimal Medial Thickness (mm)		Pulse Wave Velocity (m/s)	
	High SES	Low SES	High SES	Low SES
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
African-American men	0.716 (0.129)	0.710 (0.152)	8.35 (3.89)	7.88 (2.08)
African-American women	0.714 (0.113)	0.679 (0.135)	8.62 (2.68)	7.76 (1.86)
White men	0.686 (0.127)	0.699 (0.132)	8.03 (2.00)	8.17 (2.00)
White women	0.652 (0.122)	0.650 (0.120)	7.77 (3.11)	7.66 (1.88)

Supplemental Table II. Descriptive Statistics, Stratified by Race, Sex, and Age

	Intimal Medial Thickness (mm)		Pulse Wave Velocity (m/s)	
	<48 years old	≥48 years old	<48 years old	≥48 years old
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
African-American men	0.671 (0.117)	0.756 (0.147)	7.45 (1.56)	8.82 (4.18)
African-American women	0.670 (0.109)	0.728 (0.134)	7.59 (2.44)	8.82 (2.15)
White men	0.645 (0.116)	0.729 (0.125)	7.31 (1.50)	8.67 (2.14)
White women	0.621 (0.099)	0.681 (0.134)	6.94 (1.38)	8.47 (3.43)