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Ethnic Differences in Carotid Artery Diameter and Stiffness: The Northern Manhattan Study

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Abstract

Objective—Race/ethnic differences in carotid arterial function and structure exist among those with cerebrovascular disease, but whether differences persist among healthy populations is unknown. Our objective was to investigate differences in carotid artery diameter and stiffness between race/ethnic groups, and examine whether these race/ethnic differences were age-dependent.

Methods—Carotid diameters were assessed by B-mode ultrasound among 1536 participants from the Northern Manhattan Study (NOMAS), and carotid stiffness metrics were calculated. We used multivariable linear regression models to determine the relationship between race/ethnicity and both carotid arterial stiffness and carotid diastolic diameter.

Results—Mean participant age was 70 ± 9 years (Hispanics= 68 ± 8 , blacks= 72 ± 9 , and whites= 74 ± 9 , $p < 0.0001$). Mean DDIAM was 6.2 ± 1.0 mm (Hispanics= 6.2 ± 0.9 mm, blacks= 6.3 ± 1.0 mm, and whites= 6.3 ± 1.0 mm, $p < 0.005$) and mean STIFF was 8.7 ± 6.3 (Hispanics= 8.5 ± 5.7 , blacks= 9.2 ± 6.2 and whites= 8.9 ± 6.9 , $p < 0.02$). In a model that adjusted for sociodemographics and vascular risk factors including hypertension, diabetes, dyslipidemia, renal function, physical activity and a history of known coronary artery diseases; age was positively associated with greater DDIAM in Hispanics ($p < 0.0001$) but not among blacks or whites. Older age was associated with greater stiffness among Hispanics ($p < 0.0001$) and blacks ($p < 0.003$), but not among whites.

Conclusions—We found race/ethnic differences in the association between age and arterial stiffness and diameter, including age-dependent arterial dilation observed in Hispanics that was not observed among blacks or whites.

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Keywords

arterial stiffness; atherosclerosis; diastolic diameter; carotid artery; race/ethnicity; carotid ultrasound

Introduction

Carotid arterial stiffness is a measurement of the vessel wall's tendency to resist deformation by systolic blood pressure during the cardiac cycle, [1] is greater among people with atherosclerosis, and is an early predictor of cardiovascular disease and stroke [2]. The process of age-related arteriosclerosis includes compensatory dilation of the larger vessels following separation of the elastic lamellae within the arterial media. Intima-medial thickening and hyperplasia of the collagenous components result in a more stiff vascular wall until elevated shear stress at the location of a stenosis induces expansion of the luminal area. Stiffness has been associated with atherosclerosis[3], advanced age, type II diabetes, the metabolic syndrome[4], hypertension[5] and smoking[6].

Although several studies have examined stiffness or luminal measures in populations, [7–11] few have studied stiffness in populations that include Hispanics, blacks and whites living in the same community. Further, race/ethnic variations in stiffness with aging is not well understood, but these differences, and those in diastolic diameter, may explain race/ethnic differences in stroke risk, in particular increased stroke incidence among blacks and Hispanics as compared to whites, and decreased mortality among Hispanics compared to blacks and whites[12].

We investigated race/ethnic differences in carotid stiffness and arterial diameter in a multiethnic population-based cohort, the Northern Manhattan Study (NOMAS). We also examined whether these differences are age-dependent.

Materials and Methods

Study Population

The Northern Manhattan Study (NOMAS) is an ongoing prospective cohort study approved by the institutional review boards (IRBs) of both the Columbia University Medical Center and the University of Miami. NOMAS is designed to investigate traditional and novel stroke risk factors and incidence, as well as cognitive decline in the multiethnic, urban population of northern Manhattan[10]. The NOMAS cohort consists of 3298 participants enrolled between 1993–2001, identified through random digit dialing. Subjects were eligible if they never had a stroke diagnosed, were 40 years of age or older, and had been residents of Northern Manhattan for at least 3 months in a household with a telephone. Subjects from the telephone sample were recruited for in-person assessment. The overall response rate was 68%. The methodology for the NOMAS study has been described previously[13], including for the determination of hypertension, body-mass index, diabetes, and other vascular risk factors that are reported here. Standardized questionnaires were adapted from the validated Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System. The validity of these questions in the northern Manhattan cohort have also been described previously[14]. Race-ethnicity was determined by self-identification in response to a questionnaire modeled after the 2000 US census. Most Hispanics in our cohort did not identify with any particular race after self-identifying as Hispanic, and over 80% originated from the Caribbean (Dominican Republic and Puerto Rico).

High-resolution carotid ultrasound was performed as a part of the NOMAS sub-clinical atherosclerosis ancillary study among 1700 individuals and out of this sample, carotid stiffness metrics were available for 1536 participants. Sociodemographics and vascular risk factors did not significantly differ between the participants included in this study (=1536) and non-participants (1762), except for the greater prevalence of Hispanics included (participants: 62% Hispanics, 21% black, 17% white; non-participants: 52% Hispanics, 24% black, 24% white). Written informed consent was obtained from all participants.

Ultrasound measurements of carotid diameter and stiffness

We collected high-resolution carotid ultrasound data with a GE LOGIQ 700 system (GE Healthcare, Milwaukee, WI) equipped with a multifrequency 9/13-MHz linear array transducer. Both internal and common carotid arteries as well as bifurcations were imaged in transverse (short axis) and longitudinal planes (anterior, lateral, and posterior views) with standardized scanning and reading protocols that had a high degree of reproducibility and reliability. Images were divided into three segments, defined as: segment 1 = from 10–20 mm proximal to the tip of the flow divider into the common carotid artery (CCA); segment 2 = the near and far walls of the carotid bifurcation beginning at the tip of the flow divider and extending 10mm proximal to the flow divider tip; and segment 3 = the near and far walls of the proximal 10mm of the internal carotid artery (ICA). A real-time digital clip of the CCA was recorded for 10 seconds. We measured the CCA intraluminal systolic and diastolic diameters off-line with IMAGE-Pro analysis software on a specialized work station. We traced the best-visualized intima-media boundaries from up to 10 cardiac cycles on the M mode ultrasound and computed the systolic (SDIAM) and diastolic (DDIAM) intraluminal CCA diameters that were averaged and then stored in a data file. We noted the presence of carotid plaque in any of the carotid segments and recorded the number of plaques in each segment. The high reliability of the SDIAM and DDIAM measurements between the two readers in our laboratory was reported previously. The inter-reader correlation coefficients were 0.96 for SDIAM and 0.95 for DDIAM.

The blood pressure (BP) in the right brachial artery was measured and recorded by a Dinamap Pro100 (Critikon Inc) automatic sphygmomanometer after the participants had rested for 10 minutes in a supine position. Blood pressure was repeated after ultrasound scanning was completed, and the average of the pre- and post-scanning systolic and diastolic BP measurements were averaged and used in the analyses. Although BP is best measured in the arterial segment being studied for stiffness, brachial artery pressures have served as a suitable substitute for carotid artery pressure^[15]. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg based on the mean of 2 blood pressure measurements, self-report of previous diagnosis of hypertension, or medical treatment thereof.

Strain represents a ratio of the amount of stress deformation relative to the unstressed state, and stiffness is a dimensionless quantity that expresses the tendency of an individual's arteries to deform from a given change in blood pressure. We therefore defined STRAIN = (SDIAM-DDIAM)/DDIAM, and stiffness as: STIFF (β) = $[\ln(SBP/DBP)] / \text{STRAIN}$, where SBP and DBP were mean brachial blood pressures in the systolic and diastolic cardiac cycle, respectively.

Statistical Analysis

Demographics and vascular risk factors were tested for differences across race/ethnic groups by Analysis of Variance (ANOVA). The differences in stiffness and DDIAM across race/ethnic groups (Hispanic white, black, and non-Hispanic white) were analyzed with linear regression models adjusting for age, sex, years of education, and vascular risk factors that

were significantly ($p < 0.05$) associated with stiffness or DDIAM in univariate analyses. We constructed the following models: 1) univariate for race-ethnicity, 2) adjusted for age, sex, years of education, and 3) Model 2 + BMI, hypertension, diabetes, LDL-cholesterol, HDL-cholesterol, triglycerides, lipid lowering medication use, an estimated glomerular filtration rate (eGFR), presence/absence of carotid plaque, pack-years history of smoking, physical activity, alcohol consumption, and a history of coronary artery disease or medications for a heart condition. Stiffness and diastolic diameter were each analyzed as dependent variables, and stiffness was log-transformed to satisfy normality assumptions. After discovering significant interactions between age and race/ethnicity in relation to stiffness and DDIAM, we performed stratified analyses of the effect of age on stiffness and DDIAM using the fully-adjusted model 3. The strength and direction of associations were presented with the beta β coefficients derived from the linear regression models with corresponding p values. A test for slope of the linear regression line for the fully adjusted model was conducted using white race as a reference line.

Results

Demographic characteristics for the study population ($n=1536$) stratified by race/ethnicity are shown in Table 1. The mean age was 70 ± 9 years, and 61% of participants were women; 62% identified themselves as white race and Hispanic ethnicity, 20% as black race and non-Hispanic, and 18% as white race and non-Hispanic. We found significant ($p < 0.05$) differences in risk factors across race/ethnic groups for age, hypertension, diabetes, level of education, moderate/heavy physical activity, smoking status and pack/years history, alcohol intake, stiffness, DDIAM, SBP, DBP, plasma cholesterol (total, LDL, HDL), plasma triglycerides, estimated Glomerular filtration rate, and number of carotid plaques (Table 1).

Average values for stiffness and DDIAM (overall and by race/ethnicity across age-groups) are presented in Table 2. Also presented are values for stiffness and DDIAM that are adjusted for subject height (mm/m). We found a positive relationship between the mean DDIAM and age for Hispanics but not for blacks or whites in our fully adjusted model. Although all race/ethnic groups showed greater stiffness with older age, the association between age and stiffness among Hispanics and blacks was more pronounced than among whites (Figure 1a), consistent with their expected risk profile.

The associations of race/ethnicity with stiffness and DDIAM in sequential multivariate models are shown in Table 3. Hispanic ethnicity was significantly associated with DDIAM compared to whites in the fully adjusted model. We found an interaction between race/ethnicity and age for DDIAM ($p=0.0081$) and for stiffness ($p=0.013$). We then did stratified analyses using the fully adjusted model (Table 4). Diastolic diameter was greater with age among Hispanics ($\beta = 0.02$, $p < 0.001$) but not among blacks or whites. Stiffness also was greater with age among Hispanics ($\beta = 0.01$, $p < 0.0001$) and blacks ($\beta = 0.01$, $p = 0.006$) but not among whites. Associations with age are strongly significant for stiffness and DDIAM in Hispanics. Other potential confounders of subject height, mean arterial pressure, pulse-pressure, and carotid intima-medial thickness were both as covariates and as interaction terms, and were not shown to have an effect on model significance. When we categorized age by group according to distribution within the total cohort ($1 \leq 64$ years, $2 = 65-74$ years, $3 \geq 75$ years) we found age-group was related to stiffness ($\beta = 0.14$, $p < 0.001$) and DDIAM ($\beta = 0.21$, $p < 0.001$) in Hispanics but was not associated with either in whites. In Hispanics, when compared to younger subjects (age-group 1), stiffness ($\beta = 0.13$, $p = 0.002$) and DDIAM ($\beta = 0.28$, $p < 0.001$) were both greater among the oldest (age-group 3) compared to younger participants. Although absolute diastolic diameter is lower in Hispanics, adjusting so that diastolic diameter is shown as a proportion of subject height (mm/m) helps better illustrate

the relative increase with age that differs compared to blacks or whites (Figure 2b, $p_{\text{slope}} < 0.001$).

Discussion

In the race/ethnically diverse NOMAS urban population-based cohort, we found greater carotid stiffness among blacks and Hispanic whites compared to non-Hispanic whites. We also found that age is independently associated with greater carotid artery diameter among Hispanics but not among blacks or whites. The regression coefficients contained in the tables indicate the per/unit change in diameter or stiffness associated with a 1-year increase in age, and their associated significance values. The strongest association between age and diastolic diameter in Hispanics was found in the oldest group (≥ 75 years) even though the average age of those elder Hispanics (mean age 80.7 years) was lower than in blacks (mean age 81.3 years) or whites (mean age 82 years) in the same age group. Likewise, the association between age and carotid stiffness was strongest among Hispanics, followed by blacks, and was not apparent among whites.

This study was motivated in part by our prior research showing that an increased incidence of stroke among blacks and Hispanics compared to whites in the NOMAS cohort. Carotid arterial stiffness has been associated with an increased risk for stroke, especially in the elderly population,^{[11], [7, 16]} and the race/ethnic differences found in our study might in part explain observed differences in stroke risk among the different elderly race/ethnic groups^[10, 12].

We know of no other multi-ethnic studies that involve Hispanics that have examined age-related race/ethnic differences in carotid arterial stiffness and diameter, although increases in other markers of subclinical atherosclerosis such as carotid intima medial thickness (cIMT) have been shown among Afro-Caribbean participants in a small study. Considerable work has been done to characterize absolute race/ethnic differences in carotid arterial stiffness^[17–19]. Traditional vascular risk factors that have been associated with stiffness did not explain the race/ethnic disparities in carotid stiffness associated with age observed in our study. Although stiffness is associated with increased stroke risk^[2, 11, 20], it is plausible arteries that widen as they stiffen could limit brain ischemia by allowing more blood flow than narrower arteries. Our findings are consistent with results from The National Longitudinal Mortality Study, which found that Hispanics have a similar risk compared to whites at younger ages, but that the risk for Hispanics is marginally lower at older ages^[21]. Another review of all age-specific strokes and deaths from stroke in the United States from 1995–1998 ($n=507,256$) showed that Hispanics have a significantly reduced rate of mortality from ischemic stroke compared to whites (RR 0.51, 95%CI 0.50–0.52). Our findings, that Hispanics have a relative widening of diameters with older age which may be protective regardless of increased stiffness, may in part explain these observations. Increases in both DDIAM and stiffness are usually considered markers of atherosclerosis and therefore associated with an increased risk of stroke, these complex associations need to be investigated in other large prospective studies.

Greater arterial stiffness is an important phenotype associated with vascular aging in humans^[9]. The principal structural changes in the arterial wall with aging are medial degeneration, which leads to progressive stiffening of the large elastic arteries, and calcium deposition^[22]. The carotid is the most susceptible among all arteries studied thus far for the effect of aging and hypertension on increased wall-material stiffness. Stiffer arteries include calcifications, large amounts of collagen, and fragmentation and rupture of elastic tissue, that result in greater pulse-wave velocity and alterations of amplitude and timing of wave reflections^[23]. Several mechanisms underlay the change in artery wall structure and

composition with aging, and those involved with the arterial remodeling are well described. Genetic factors be involved in the mechanisms of arterial stiffening and may have different race-ethnic predispositions^[24]. In particular, oxidative stress plays a pivotal role in the progression of vascular aging^[25]. High levels of inflammatory factors (e.g. cytokines) contribute to a pro-inflammatory microenvironment that facilitates the development of vascular wall dysfunction by increasing macrophage infiltration and atheroma (plaque) formation. Other mechanisms such as variability in levels and activity of coagulation factors lead to an increase of artery wall modification, and different levels of circulating lipids increase arterial stiffness while lipid-lowering therapy may reduce it.

We found greater arterial stiffness with older age among Hispanics that was greater than age-related differences among Blacks, and we found no differences with age among whites. We also found changes in carotid artery diastolic diameters with older age among Hispanics that were not found among blacks or among whites. When we express diameters as a ratio of subject height (mm/m), we find that there is a relative increase in diameter with age compared to whites and to blacks. These findings were independent of traditional vascular risk factors, and adjusting the models for plaque, carotid intima-medial thickness, pulse-pressure, or mean-arterial pressure did not diminish the effect. The mechanisms of aging, oxidative stress and changes in inflammatory and other age-related factors may have differential effects on carotid artery stiffness across race-ethnicities, explaining, at least in part, the difference in greater carotid artery diameter we found in older Hispanics compared to whites and blacks. Telomere length has recently emerged as a marker of exposure to oxidative stress and aging and has been specifically identified as corresponding with senescence in atherosclerotic vascular smooth muscle cells. One recent study found that shorter leukocyte telomeres are associated with increased stiffness and with increased oxidized-LDL^[26]. Race/ethnic differences in telomere length with age have already been shown, with blacks and Hispanics having greater differences in leukocyte telomere length associated with age than whites indicating a different exposure and response to oxidative stress. Whether changes in telomere length in vascular smooth muscle also differs across race/ethnic groups, and whether those differences translate into stress-related arterial wall changes still needs to be demonstrated.

Race-ethnic variation in carotid geometry is another important factor affecting changes in atherosclerosis and carotid arterial stiffness. Disturbances in local blood flow are influenced by arterial geometry, and contribute to atherogenesis through increases in shear stress that occur with arterial narrowing and asymmetric CCA branching. Significant race/ethnic differences in the anatomy of the carotid bifurcation were found for African Americans, who seem to have a proportionally narrower internal carotid artery and larger external carotid artery than whites or Caribbean Hispanics^[27].

The primary limitation to our study was the cross-sectional design, and the larger population of Hispanics. Power for detecting effect of age on DDIAM or stiffness was greater than 85% for each race/ethnic group when examining the entire cohort; although stratification may have left age-related changes in diameter and stiffness undetected in whites. We have inferred effects of aging on DDIAM and stiffness using individuals of different ages at the time of carotid ultrasound, but future studies are needed to calculate DDIAM and stiffness within individuals over a time series to understand the changes in vasculature that occur with aging. There is also no consensus on the best method for measuring arterial stiffness^[16, 28], although a previously published study showed significant reliability of our method^[29]. Comparison with a 'gold' standard (such as pathology) is yet to be performed, but ultrasound is a valid and effective method for evaluating subclinical carotid vascular disease^[30].

Conclusion

Our results suggest that Hispanics and blacks have increased stiffness with age in comparison to whites. In addition, aging is associated with increased carotid intraluminal diameter among Hispanics but not among blacks or whites. These findings may offer a possible explanation for reported disparities in stroke morbidity and mortality among Hispanics compared to blacks and whites and require further study.

References

1. Hoeks A, et al. Assessment of the Distensibility of Superficial Arteries. *Ultrasound Med Biol.* 1990; 16:121–128. [PubMed: 2183458]
2. Bots ML, et al. Carotid intima-media thickness, arterial stiffness and risk of cardiovascular disease: current evidence. *Journal of Hypertension.* 2002; 20(12):2317–2325. [PubMed: 12473847]
3. van Popele NM, et al. Association Between Arterial Stiffness and Atherosclerosis : The Rotterdam Study. *Stroke.* 2001; 32(2):454–460. [PubMed: 11157182]
4. Della-Morte D, et al. Metabolic syndrome increases carotid artery stiffness: The Northern Manhattan Study. *International Journal of Stroke.* 5(3):138–144.
5. Alecu C, et al. Determinants of arterial stiffness in an apparently healthy population over 60 years. *J Hum Hypertens.* 2006; 20(10):749–756. [PubMed: 16855622]
6. Mahmud A, Feely J. Effect of Smoking on Arterial Stiffness and Pulse Pressure Amplification. *Hypertension.* 2003; 41(1):183–187. [PubMed: 12511550]
7. Laurent S, et al. Aortic Stiffness Is an Independent Predictor of Fatal Stroke in Essential Hypertension. *Stroke.* 2003; 34(5):1203–1206. [PubMed: 12677025]
8. Ruan L, et al. Correlates of Common Carotid Artery Lumen Diameter in Black and White Younger Adults: The Bogalusa Heart Study. *Stroke.* 2009; 40(3):702–707. [PubMed: 19131651]
9. Mitchell GF, et al. Changes in Arterial Stiffness and Wave Reflection With Advancing Age in Healthy Men and Women: The Framingham Heart Study. *Hypertension.* 2004; 43(6):1239–1245. [PubMed: 15123572]
10. Northern Manhattan Stroke Study Collaborators, et al. Stroke Incidence among White, Black, and Hispanic Residents of an Urban Community: The Northern Manhattan Stroke Study. *Am J Epidemiol.* 1998; 147(3):259–268. [PubMed: 9482500]
11. Mattace-Raso FUS, et al. Arterial Stiffness and Risk of Coronary Heart Disease and Stroke: The Rotterdam Study. *Circulation.* 2006; 113(5):657–663. [PubMed: 16461838]
12. Fields LE. Absolute Stroke Mortality Burden for Non-Hispanic Non-Latino Whites Was Disproportionately Higher Than Expected Simply Based on the US Population in 2001. *Stroke.* 2005; 36(5):e48–49. [PubMed: 15817894]
13. Sacco RL, et al. Race-Ethnicity and Determinants of Intracranial Atherosclerotic Cerebral Infarction : The Northern Manhattan Stroke Study. *Stroke.* 1995; 26(1):14–20. [PubMed: 7839388]
14. Kargman D, et al. Validity of Telephone Interview Data for Vascular Disease Risk Factors in a Racially Mixed Urban Community: The Northern Manhattan Stroke Study. *Neuroepidemiology.* 1999; 18:174–184. [PubMed: 10364718]
15. Dobrin P. Mechanical Properties of Arteries. *Physiol Rev.* 1978; 58:397–460. [PubMed: 347471]
16. Oliver JJ, Webb DJ. Noninvasive Assessment of Arterial Stiffness and Risk of Atherosclerotic Events. *Arterioscler Thromb Vasc Biol.* 2003; 23(4):554–566. [PubMed: 12615661]
17. Lemogoum D, et al. Ethnic differences in arterial stiffness and wave reflections after cigarette smoking. *J Hypertens.* 2006; 24(4):683–9. [PubMed: 16531796]
18. Din-Dzietham R, et al. Arterial stiffness is greater in African Americans than in whites: evidence from the Forsyth County, North Carolina, ARIC cohort. *Am J Hypertens.* 2004; 17(4):304–13. [PubMed: 15062883]
19. Malayeri AA, et al. Relation of Aortic Wall Thickness and Distensibility to Cardiovascular Risk Factors (from the Multi-Ethnic Study of Atherosclerosis [MESA]). *The American Journal of Cardiology.* 2008; 102(4):491–496. [PubMed: 18678312]

20. Dijk JM, et al. Increased Arterial Stiffness Is Independently Related to Cerebrovascular Disease and Aneurysms of the Abdominal Aorta: The Second Manifestations of Arterial Disease (SMART) Study. *Stroke*. 2004; 35(7):1642–1646. [PubMed: 15143289]
21. Howard G, et al. Ethnic differences in stroke mortality between non-Hispanic whites, Hispanic whites, and blacks. The National Longitudinal Mortality Study. *Stroke*. 1994; 25(11):2120–2125. [PubMed: 7974531]
22. Ungvari Z, et al. Mechanisms of vascular aging: new perspectives. *J Gerontol A Biol Sci Med Sci*. 2010; 65(10):1028–41. [PubMed: 20576649]
23. Safar ME, et al. Stiffness of carotid artery wall material and blood pressure in humans: application to antihypertensive therapy and stroke prevention. *Stroke*. 2000; 31(3):782–90. [PubMed: 10700519]
24. Yasmin, O'Shaughnessy KM. Genetics of arterial structure and function: towards new biomarkers for aortic stiffness? *Clin Sci (Lond)*. 2008; 114(11):661–77. [PubMed: 18442360]
25. Donato AJ, et al. Direct evidence of endothelial oxidative stress with aging in humans: relation to impaired endothelium-dependent dilation and upregulation of nuclear factor-kappaB. *Circ Res*. 2007; 100(11):1659–66. [PubMed: 17478731]
26. Nawrot TS, et al. Telomere length and its associations with oxidized-LDL, carotid artery distensibility and smoking. *Frontiers in Bioscience*. 2:1164–1168.
27. Koch S, et al. Race-ethnic variation in carotid bifurcation geometry. *J Stroke Cerebrovasc Dis*. 2009; 18(5):349–53. [PubMed: 19717017]
28. Asmar R, et al. Assessment of Arterial Distensibility by Automatic Pulse Wave Velocity Measurement : Validation and Clinical Application Studies. *Hypertension*. 1995; 26(3):485–490. [PubMed: 7649586]
29. Godia EC, et al. Carotid Artery Distensibility: A Reliability Study. *J Ultrasound Med*. 2007; 26(9): 1157–1165. [PubMed: 17715309]
30. James HS, et al. Use of Carotid Ultrasound to Identify Subclinical Vascular Disease and Evaluate Cardiovascular Disease Risk: A Consensus Statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force Endorsed by the Society for Vascular Medicine. *Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography*. 2008; 21(2):93–111. [PubMed: 18261694]

Fig 1a) Slope of linear regression for age and stiffness

Fig 1b) Slope of linear regression for age and diastolic diameter

Figure 1.

Fig 2a) Slope of linear regression for age and adjusted stiffness

Fig 2b) Slope of linear regression for age and adjusted diastolic diameter

Figure 2.

Table 1

Cohort Descriptive Statistics

Risk Factor	(ANOVA/ χ^2 *p< 0.05)	(Mean $\pm$ SD)			
		Total Cohort	Hispanic	Black	White
*Age					
Agegroup 50–64	(1536)	70.0 $\pm$ 9.2	68.1 $\pm$ 8.4	72.5 $\pm$ 9.2	74 $\pm$ 9.7
Agegroup 65–74	(503)	60.1	60.1	60.3	59.6
Agegroup $\geq$ 75	(577)	69.9	69.6	70.5	70.1
Female	(456)	81.2	80.7	81.3	82.0
*Hypertension	(940)	61 %	62 %	62 %	55 %
*Diabetes	(1073)	70 %	70 %	76 %	61 %
History of CAD	(294)	19 %	21 %	21 %	9 %
*Education	(198)	13 %	8 %	2 %	(3) %
$\leq$ 8th Grade	(602)	39 %	58 %	9 %	7 %
Some HS	(200)	13 %	15 %	14 %	6 %
Completed HS	(266)	17 %	13 %	32 %	17 %
Some College	(209)	14 %	8 %	24 %	22 %
$\geq$ College Grad	(263)	17 %	7 %	22 %	48 %
*Mod/High Phys. Activity	(159)	10 %	8 %	12 %	18 %
*Ever Smoked	(804)	52 %	48 %	60 %	59 %
Pack Years		12 $\pm$ 23	10 $\pm$ 23	14 $\pm$ 20	17 $\pm$ 24
*Alcohol use (drinks/mo)		4.1 $\pm$ 5.4	5.1 $\pm$ 6.2	3.2 $\pm$ 3.9	2.2 $\pm$ 2.5
*Stiffness		8.63 $\pm$ 6.01	8.40 $\pm$ 5.65	9.24 $\pm$ 6.21	8.74 $\pm$ 6.91
*DDIAM (mm)		6.24 $\pm$ 0.96	6.17 $\pm$ 0.93	6.33 $\pm$ 0.99	6.35 $\pm$ 1.01
*SBP mmHg		140 $\pm$ 20	140 $\pm$ 20	144 $\pm$ 20	138 $\pm$ 19
*DBP mmHg		83 $\pm$ 11	84 $\pm$ 11	84 $\pm$ 12	79 $\pm$ 10
*Height (inches)		64 $\pm$ 4	63 $\pm$ 3	65 $\pm$ 4	65 $\pm$ 4
*BMI kg/m²		28.2 $\pm$ 4.9	28.5 $\pm$ 4.7	28.6 $\pm$ 5.3	26.6 $\pm$ 5.2
Waist : Hip Ratio		0.90 $\pm$ 0.1	0.90 $\pm$ 0.1	0.90 $\pm$ 0.1	0.91 $\pm$ 0.1
*Cholesterol mg/dL		201 $\pm$ 39	202 $\pm$ 39	197 $\pm$ 40	205 $\pm$ 35

Risk Factor	(ANOVA/X ² *p<0.05)				
	(n)	Total Cohort	(Mean ± SD)		
	(n)		Hispanic	Black	White
*LDL mg/dL		128 ± 35	129 ± 35	123 ± 37	129 ± 33
*HDL mg/dL		47 ± 15	44 ± 13	52 ± 16	50 ± 17
*Triglycerides mg/dL		135 ± 81	145 ± 82	109 ± 62	133 ± 89
eGFR ml/min		75 ± 22	73 ± 20	77 ± 23	79 ± 24
*Carotid Plaques (n)		1.5 ± 1.7	1.2 ± 1.6	1.7 ± 1.7	1.9 ± 1.8

Hypertension = at least two recordings of >140mmHg Systolic, or >90mmHg Diastolic, or with a history of diagnosis, or currently taking medication to control volume or pressure.

Diabetes = at least one fasting glucose recording of at least 126mg/dL, or with a history of diagnosis, or currently taking medication to control blood sugar.

History of CAD =bypass surgery or angioplasty to correct coronary artery disease, or currently taking medication for a heart condition with diagnosed coronary artery disease, or a history of angina

Table 2
Carotid Stiffness (STIFF) and Diastolic Diameter (DDIAM) by race/ethnicity and age-groups

	Total (Mean±SD)			Hispanic			Black			White		
	n	STIFF	DDIAM	n	STIFF	DDIAM	n	STIFF	DDIAM	n	STIFF	DDIAM
All Ages	(1536)	8.60 ± 6.01	6.24 ± 0.96	(948)	8.40 ± 5.65	6.17 ± 0.93	(317)	9.24 ± 6.21	6.33 ± 0.99	(271)	8.74 ± 6.91	6.35 ± 1.01
Age : 50-64	(503)	7.36 ± 4.47	6.07 ± 0.89	(377)	7.32 ± 4.46	5.97 ± 0.79	(75)	8.01 ± 4.75	6.45 ± 1.07	(51)	6.65 ± 4.05	6.19 ± 1.13
65-74	(577)	8.68 ± 6.02	6.27 ± 0.95	(379)	8.34 ± 5.45	6.28 ± 0.96	(111)	9.00 ± 6.34	6.18 ± 0.96	(87)	9.79 ± 7.67	6.34 ± 0.90
≥75	(456)	9.98 ± 7.10	6.37 ± 1.02	(192)	10.64 ± 7.29	6.34 ± 1.05	(131)	10.13 ± 6.72	6.39 ± 0.97	(133)	8.86 ± 7.12	6.40 ± 1.02
	n			adjSTIFF			adjDDIAM			n		
	adjSTIFF			adjDDIAM			adjSTIFF			adjDDIAM		
All Ages	(1536)	5.30 ± 3.80	3.83 ± 0.58	(948)	5.24 ± 3.55	3.84 ± 0.58	(317)	5.60 ± 3.85	3.82 ± 0.60	(271)	5.30 ± 4.30	3.83 ± 0.60
Age : 50-64	(503)	4.52 ± 2.78	3.71 ± 0.51	(377)	4.54 ± 2.79	3.70 ± 0.48	(75)	4.84 ± 2.97	3.85 ± 0.59	(51)	3.92 ± 2.40	3.64 ± 0.58
65-74	(577)	5.33 ± 3.69	3.84 ± 0.58	(379)	5.19 ± 3.41	3.90 ± 0.58	(111)	5.39 ± 3.80	3.68 ± 0.56	(87)	5.85 ± 4.61	3.78 ± 0.56
≥75	(456)	6.22 ± 4.50	3.96 ± 0.64	(192)	6.72 ± 4.58	4.00 ± 0.68	(131)	6.23 ± 4.24	3.92 ± 0.61	(133)	5.50 ± 4.57	3.94 ± 0.62

* Adjustment uses diastolic diameter as a proportion of subject height in meters (mm/m), and the standard calculation for stiffness also adjusted for height in meters

Table 3

Multivariable Linear Regression Models

Race : [ref]	Model 1			Model 2			Model 3					
	STIFF	DDIAM		STIFF	DDIAM		STIFF	DDIAM				
	β	p	β	p	β	p	β	p	β	p		
Hispanic : [White]	-0.004	0.93	-0.17	0.01	0.04	0.42	-0.13	0.10	0.02	0.75	-0.19	0.02
Black : [White]	0.10	0.04	-0.01	0.89	0.11	0.02	0.03	0.73	0.09	0.06	-0.07	0.42
Hispanic : [Black]	-0.10	0.01	-0.16	0.01	-0.15	0.06	-0.16	0.02	-0.08	0.08	-0.10	0.09

β = Regression parameter estimate, the average difference in STIFF or DDIAM in that race/ethnic group vs. reference P = probability that the null hypothesis is correct, that there is no difference between the group vs. reference

Model 1: Univariate

Model 2: Age at Ultrasound, Sex, Education

Model 3: Age at Ultrasound, Sex, Education, BMI, Hypertension, Diabetes, LDL, HDL, Presence of Plaque, Pack Years Smoking, Alcohol Use, Triglycerides, estimated Glomerular Filtration Rate, Moderate/Heavy Physical Activity, Lipid Lowering Medications, History of CAD

Table 4
Association of Age with Arterial Stiffness and Diameter Using the Fully Adjusted Model 3, stratified by Race/Ethnicity

	Hispanic						Black						White					
	STIFF			DDIAM			STIFF			DDIAM			STIFF			DDIAM		
	(n)	β	p	β	p	(n)	β	p	(n)	β	p	(n)	β	p	(n)	β	p	
Age	(948)	0.01	<0.001	0.02	<0.001	(317)	0.01	0.006	0.002	0.75	(271)	0.003	0.51	-0.005	0.49			
Agegroup	-	0.14	<0.001	0.21	<0.001	-	0.10	0.03	0.02	0.74	-	0.032	0.58	0.02	0.85			
ref: Age (under 65)	(377)	-	-	-	-	(75)	-	-	-	-	(51)	-	-	-	-			
Age (65-74)	(379)	-0.08	0.06	-0.001	0.98	(111)	-0.02	0.72	-0.28	0.03	(87)	0.048	0.57	-0.12	0.37			
Age (75-up)	(192)	0.13	0.002	0.28	<0.001	(131)	0.12	0.08	-0.01	0.93	(133)	0.10	0.28	0.03	0.82			

Model : Age at Ultrasound (or Age Group), Sex, Education, BMI, Hypertension, Diabetes, LDL, HDL, Presence of Plaque, Pack Years Smoking, Alcohol Consumption, Level of Triglycerides, estimated Glomerular Filtration Rate, Moderate/Heavy Physical Activity, Lipid Lowering Medications, History of CAD