



Ethnic Difference in Proximal Aortic Stiffness

An Observation From the Dallas Heart Study

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ABSTRACT

OBJECTIVES This study aims to compare ethnic difference in proximal aortic pulse wave velocity (PWV) and characteristic impedance (Zc).

BACKGROUND Increased aortic stiffness is an independent predictor of target organ damage, incident hypertension, and all-cause mortality. However, previous studies have not directly assessed proximal aortic function in Blacks, the ethnic population with disproportionately high risk for incident hypertension and target organ complications.

METHODS We evaluated the multiethnic, population-based DHS (Dallas Heart Study) participants (N = 2,544, 54.2% women, 49.7% Black) who underwent cardiac magnetic resonance at 1.5-T. Aortic stiffness and Zc were determined from aortic arch PWV and lumen area measurements. Linear regression was used to evaluate ethnic differences in proximal aortic wall stiffness using aortic arch PWV and Zc as dependent variables with and without adjustment for traditional cardiovascular risk factors. Because cardiac output was significantly higher in Blacks compared to Whites and Hispanics, additional comparisons of PWV and Zc were performed after adjustment for cardiac output and peripheral vascular resistance.

RESULTS Compared with Whites, both Blacks and Hispanics had higher levels of aortic arch PWV (4.25, 95% confidence interval [CI]: 4.15 to 4.35 m/s, vs. 4.72, 95% CI: 4.64 to 4.81 m/s, vs. 4.48, 95% CI: 4.33 to 4.63 m/s, respectively, both $p < 0.05$ vs. White), and Zc (64.9, 95% CI: 63.3 to 66.6 dyne · s/cm⁵, vs. 75.6, 95% CI: 74.0 to 77.2 dyne · s/cm⁵, vs. 70.1, 95% CI: 67.6 to 72.8 dyne · s/cm⁵, respectively, both $p < 0.01$ vs. White) after adjustment for age, age squared, sex, body mass index, height, mean arterial blood pressure, antihypertensive treatment, heart rate, total cholesterol, diabetes mellitus, and smoking. Compared with Hispanics, Blacks also had higher level of both PWV and Zc (both $p < 0.01$). Ethnic differences in PWV and Zc persisted after adjustment for cardiac output and peripheral vascular resistance.

CONCLUSIONS In a multiethnic population-based-sample, Blacks and Hispanics had higher proximal aortic stiffness compared with Whites independent of blood pressure and relevant risk factors. (J Am Coll Cardiol Img 2017;10:54-61)
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Blacks suffer a disproportionately increased risk for hypertension and hypertensive target organ damage (1). The mechanisms underlying these ethnic differences have been explored but remain incompletely elucidated. Properties of the arterial system, such as aortic stiffness, may contribute to risk for developing hypertension (2). Increased aortic stiffness may also represent a consequence of

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long-standing hypertension. Blacks have higher pulse pressure (3) which is a measure of arterial pressure pulsatility and is closely related to arterial stiffness. Various measures have been developed to assess aortic stiffness directly, with the best-characterized noninvasive measurement being pulse wave velocity (PWV) (4). PWV is an independent risk predictor of target organ damage (5,6), cardiovascular events (7,8), incident hypertension (2), and all-cause mortality (4). Characteristic impedance of the proximal aorta (Zc) is another useful measure of arterial stiffness that is related to clinical outcomes (9). Zc is related to PWV but is also highly sensitive to aortic lumen area, which also influences arterial pressure pulsatility. For some subgroups of patients, such as diabetics, Zc is a more sensitive measure of central aortic stiffness than PWV (10). Because of differing relations with aortic wall stiffness and diameter, PWV and Zc each provide distinct insights and can change discordantly under certain circumstances. If the aortic wall stiffens and diameter is unchanged, PWV and Zc will change proportionately. On the other hand, if stiffness and diameter both change, the resulting change in PWV and Zc can differ dramatically and may even change in opposite directions. Between young adulthood and midlife, aortic diameter is expected to increase while the wall stiffens; PWV could therefore increase while Zc and pulse pressure decrease (11).

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Prior population-based studies assessing ethnic differences in aortic stiffness (12,13) used measures derived from radial artery tonometry, which are indirect and less precise than PWV (14). Carotid and femoral artery applanation tonometry is the most widely used technique for measuring aortic PWV; however, the proximal arch (proximal to the origin of the brachiocephalic artery) cannot be assessed with this technique (4). In this regard, cardiac magnetic resonance (CMR) has the potential advantage of being able to measure stiffness in multiple user-specified segments of the aorta, including measurement of aortic arch PWV (15). Further, with the advent of automated post-processing techniques, CMR-derived aortic arch PWV is readily obtained during routine CMR with minimal additional scan time (16).

Accordingly, our study aimed to use CMR-derived aortic arch PWV and Zc in a large multiethnic, population to assess ethnic differences in proximal aortic stiffness across different ages. To understand these relationships we will also adjust for risk factors that may influence stiffness as well as potential contributions of aortic lumen area. As a secondary aim, we evaluate ethnic differences in pulse pressure.

METHODS

STUDY SAMPLE. Written informed consent was obtained from all participants. The study was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center. Participants were enrolled in the DHS (Dallas Heart Study), a multiethnic, population-based probability sample of Dallas County. The study design and methodology have been described previously (17). Briefly, the DHS phase 1 consisted of 3 sequential visits, including 2 home visits and a clinical visit. During the first 2 visits, a survey was administered through a face-to-face interview and self-reported ethnicity was obtained. In the third visit, 2,971 participants returned for various imaging studies, including CMR. Participants were excluded from analysis if CMR image quality was insufficient for interpretation (n = 340) or if self-reported ethnicity was not Black, White, or Hispanic (n = 84). A total of 2,544 participants (54.2% women, 49.7% Black) ages 19 to 67 years comprised the analysis cohort.

COVARIATE DEFINITIONS. Brachial blood pressure was measured noninvasively using a non-ferromagnetic arm blood pressure cuff and automated blood pressure monitor. Four separate blood pressure measurements were acquired at various time points: 1) before scanning, outside the magnet; 2) before scanning, inside the magnet; 3) after scanning, inside the magnet; and 4) immediately after scanning, outside the magnet. The second and third blood pressure measurements were averaged for each subject. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or use of blood pressure lowering medication. Pulse pressure was defined as the difference between systolic and diastolic blood pressure. Mean arterial pressure was defined as: $(2 \times \text{diastolic blood pressure} + \text{systolic blood pressure})/3$. Diabetes mellitus was defined as a fasting glucose ≥ 125 mg/dl or use of hypoglycemic medications. Body mass index (BMI) was calculated using the equation $\text{weight}/\text{height}^2$ (kg/m²). Ethnicity, cigarette smoking, and use of antihypertensive medication were determined by self-report.

CMR. Participants underwent CMR using a 1.5-T whole-body system (Intera, Philips Medical Systems, Best, the Netherlands). All CMR studies were acquired with a 4-element surface array coil. Aortic arch PWV was assessed using a breath-hold, velocity-encoded, phase-contrast gradient echo sequence acquired perpendicular to the course of the ascending aorta 4 cm above the aortic valve plane. The ascending and

ABBREVIATIONS AND ACRONYMS

BP = blood pressure

CMR = cardiac magnetic resonance

PWV = proximal aortic pulse wave velocity

Zc = characteristic impedance

descending thoracic aorta were imaged in cross-section with a temporal resolution of <40 ms, 256 × 256 matrix, 34-cm field of view, 20° flip angle, 10 ms repetition time, 5 ms echo time, ±150 cm/s through-plane velocity encoding, and 8-mm slice thickness. Images were acquired using prospective electrocardiogram gating. The time-velocity curve was interpolated to a temporal resolution of 10 ms by using a cubic spline for subsequent analysis. The aortic arch was also evaluated with an oblique sagittal, double inversion-recovery spin echo image (“candy cane” view) with the following parameters: 33 cm field of view, electrocardiographically gated repetition time, 5.3 ms echo time, and 32 echo train length. Images were analyzed with MASS/FLOW (Medis, Leiden, the Netherlands), which has been validated in prior studies (18). Area contours of the ascending and descending thoracic aorta were manually traced through all phases of the cardiac cycle, and maximum and minimum cross-sectional areas of the ascending aorta were measured. The operator assessing magnetic resonance area contours was blind to the racial status of participants. Specific details of our technique have been described previously (7).

CALCULATION OF AORTIC ARCH PWV, IMPEDANCE, AND CARDIAC OUTPUT. Time-velocity flow curves of the ascending and descending aorta were produced using MASS/FLOW. Transit time was calculated as the time difference between the ascending and descending upstroke velocities at half-maximum velocity. Arch distance was determined by drawing a freehand line through the center of the aorta between the ascending aorta position and descending aorta position where flow measurements were made (19). Aortic arch PWV was calculated by dividing arch distance by transit time with larger velocities indicating greater aortic stiffness (4).

Zc is a measure of the opposition of the circulation to oscillatory flow input (20). We estimated Zc, by using the water hammer equation, as the product of aortic arch PWV and blood density divided by the ascending aortic area in diastole. Blood density was assumed to be fixed at 1.06 gram/cm³ as previously described (21).

CMR imaging included a cine steady state free precession series of 10 to 13 short axis slices spanning the cardiac apex through the ventricular base, for measurement of left ventricular stroke volume. Cardiac output was measured as stroke volume multiplied by heart rate as previously described (22).

STATISTICAL ANALYSIS. Ethnic differences in baseline characteristics (Black vs. Hispanic, Black vs. White, and Hispanic vs. White) were evaluated using analysis of variance. Because 22 baseline characteristic

variables were compared between each ethnicity, we only performed a post hoc comparison if the main interaction p value was <0.0023 (0.05 per 22.00). Multivariable linear regression was used to further evaluate the relationship between ethnicity and minimal aortic area with adjustment for age and height and for age and BMI. Aortic arch PWV and Zc were log transformed for regression analysis to produce a normal distribution. Ethnic differences in aortic arch PWV and Zc were then analyzed in univariable and multivariable linear regression models with the latter models adjusted for age, age squared, sex, BMI, height, mean arterial blood pressure, use of antihypertensive medication, heart rate, total cholesterol level, diabetes mellitus, and cigarette smoking. Least squares means estimates of PWV and Zc for Blacks, Whites, and Hispanics were calculated adjusting for the foregoing covariates. In secondary analysis, ethnic differences in pulse pressure were explored using linear regression with adjustment for age, age squared, sex, BMI, height, mean arterial blood pressure, use of antihypertensive medication, heart rate, total cholesterol level, diabetes mellitus, and cigarette smoking. The linear regression evaluated the relationship between Black ethnicity and Hispanic ethnicity against White ethnicity. The significance of differences between Black and Hispanic ethnic groups was determined by a linear contrast of the regression coefficients from the linear regression models.

Statistical significance was defined as a 2-tailed p value <0.05. All analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, North Carolina) and MedCalc 8.1.0.0 for Windows (MedCalc Software, Mariakerke, Belgium).

RESULTS

Table 1 shows demographic and baseline characteristics of the study sample. Systolic blood pressure, diastolic blood pressure, and pulse pressure were higher in Blacks than non-Blacks ($p < 0.01$). Prevalence of diabetes mellitus was higher in Blacks than in Whites but was similar to Hispanics and other ethnic groups. Serum triglyceride level was lower whereas high-density cholesterol was higher in Blacks than all other ethnic groups. Cardiac output was significantly higher in Blacks compared to Whites and Hispanics (both $p < 0.001$), although cardiac index was similar in all ethnic groups (all $p > 0.1$) (**Table 1**). In univariate analysis, aortic area was smaller in Hispanics than Blacks and Whites (both $p < 0.01$) whereas the areas were similar in Blacks and Whites (**Table 1**). In multivariate analysis, Hispanics in our sample were shorter ($p < 0.0001$) and younger ($p < 0.0001$)

TABLE 1 Characteristics of Study Participants (N = 2,544)

	Black (n = 1,264)	White (n = 830)	Hispanic (n = 450)	p Value			
				Black vs. White	Hispanic vs. White	Black vs. Hispanic	Interaction
Age, yrs	45 ± 10	45 ± 10	41 ± 9	0.991	<0.0001	<0.0001	<0.0001
Female	56	50	58	NA	NA	NA	0.006
Blood pressure, mm Hg							
Systolic	130 ± 18	124 ± 14	120 ± 15	<0.0001	<0.0001	<0.0001	<0.0001
Diastolic	80 ± 10	77 ± 9	75 ± 9	<0.0001	<0.0001	<0.0001	<0.0001
Pulse pressure	51 ± 15	46 ± 11	46 ± 12	<0.0001	0.918	<0.0001	<0.0001
Hypertension	45	25	16	<0.0001	0.0008	<0.0001	<0.0001
Cigarette smoking (current)	31	27	20	0.0103	0.0035	<0.0001	<0.0001
Diabetes mellitus	13	6	12	<0.0001	0.0002	0.4188	<0.0001
Antihypertensive medication	26	16	11	<0.0001	0.0115	<0.0001	<0.0001
Lipid lowering medication	6	7	4	NA	NA	NA	0.098
Fasting lipids, mg/dl							
Triglycerides	105 ± 92	137 ± 106	150 ± 129	<0.0001	0.068	<0.0001	<0.0001
Total cholesterol	179 ± 40	185 ± 37	180 ± 40	0.0005	0.029	0.649	0.0018
High-density	52 ± 15	49 ± 15	46 ± 12	<0.0001	0.0001	<0.0001	<0.0001
Low-density	106 ± 38	109 ± 34	105 ± 33	NA	NA	NA	0.087
Weight, kg	90 ± 92	84 ± 20	79 ± 19	<0.0001	<0.0001	<0.0001	<0.0001
Height, cm	168 ± 10	170 ± 10	161 ± 9	0.0005	<0.0001	<0.0001	<0.0001
Body mass index, kg/m ²	31 ± 8	29 ± 6	30 ± 6	<0.0001	<0.0001	0.06	0.0001
Minimum aortic area, cm ²	7.1 ± 2.0	7.2 ± 1.9	6.3 ± 1.7	0.249	<0.0001	<0.0001	<0.0001
Stroke volume, ml	74 ± 19	73 ± 17	70 ± 15	0.209	0.001	<0.0001	0.0002
Heart rate, beats/min	77 ± 12	76 ± 12	75 ± 11	NA	NA	NA	0.006
Cardiac output, l/min	5.0 ± 1.4	4.9 ± 1.2	4.7 ± 1.2	0.081	<0.0001	<0.0001	0.0003
Cardiac index, l/min/m ²	2.5 ± 0.6	2.5 ± 0.5	2.5 ± 0.6	NA	NA	NA	0.984

Values are mean ± SD or %.
 NA = not applicable.

compared with Whites and Blacks. Hispanic ethnicity was no longer significantly associated with smaller aortic area ($p = 0.1$) after adjustment for age and height. After adjustment for age and BMI, however, aortic area was smaller in Blacks ($p = 0.005$) and Hispanics ($p < 0.0001$) compared to Whites.

Percentiles for aortic arch PWV and Zc by age and ethnicity are shown in [Online Table 1](#). Multivariable models of log-transformed aortic arch PWV, Zc, and pulse pressure are shown in [Table 2](#). Blacks and Hispanics had higher levels of aortic arch PWV (Black vs. White, $p < 0.0001$; Hispanic vs. White, $p = 0.017$), Zc (Black vs. White, $p < 0.0001$; Hispanic vs. White, $p = 0.002$) and pulse pressure (Black vs. White, $p < 0.0001$; Hispanic vs. White, $p = 0.037$) compared with Whites after adjustment for age, age squared, sex, BMI, mean arterial blood pressure, antihypertensive treatment, heart rate, total cholesterol, diabetes mellitus, and smoking.

Compared with Hispanic ethnicity, Black ethnicity was associated with higher aortic arch PWV ($p = 0.007$) and Zc ($p = 0.0005$) but not pulse pressure ($p = 0.058$). Least squares means estimates calculated for PWV by Black, White, and Hispanic ethnicity adjusting for the covariates in the models

are shown in [Figure 1](#) and estimates for Zc are shown in [Figure 2](#).

To account for ethnic difference in cardiac output and potential influence of peripheral vascular resistance, analysis was repeated after cardiac output and total peripheral resistance (mean arterial pressure divided by cardiac output) was included in the model separately along with relevant variables (age, age squared, sex, BMI, height, systolic blood pressure, antihypertensive treatment, heart rate, total cholesterol, diabetes mellitus, and cigarette smoking). We found that ethnic difference in PWV and Zc persisted despite accounting for cardiac output or peripheral vascular resistance ([Online Tables 2 and 3](#)).

DISCUSSION

In the multiethnic, community-based DHS cohort, Blacks and Hispanics, as compared to Whites, displayed greater proximal aortic stiffness, whether assessed as aortic arch PWV or Zc, in models that adjusted for various standard vascular risk factors. Blacks demonstrated higher prevalence of numerous cardiovascular disease risk factors that may contribute to aortic stiffness ([4,23](#)). However, these

TABLE 2 Multivariable Linear Regression Models of Aortic Arch PWV, Zc, and Pulse Pressure

	Log Aortic Arch PWV			Log Zc			Pulse Pressure		
	Regression Coefficient*	Standard Error	p Value	Regression Coefficient	Standard Error	p Value	Regression Coefficient*	Standard Error	p Value
Black vs. White ethnicity	0.104	0.015	<0.0001	0.152	0.017	<0.0001	2.6	0.48	<0.001
Hispanic vs. White ethnicity	0.051	0.021	0.017	0.074	0.024	0.002	1.4	0.67	0.037
Black vs. Hispanic ethnicity	0.054	0.20	0.007	0.078	0.022	0.0005	1.2	0.63	0.058

*Exponentiation of the regression coefficient values indicates fold difference in the variables between each ethnicity. For example, a coefficient of 0.104 indicates that aortic arch PWV is 11% higher in Blacks than Whites (i.e., $e^{0.104} = 1.11$ = the fold higher in blacks as compared to whites). Multivariable models of log-transformed aortic arch PWV, Zc, and Pulse Pressure, after adjustment for age, age squared, sex, BMI, height, mean arterial blood pressure, antihypertensive treatment, heart rate, total cholesterol, diabetes mellitus, and cigarette smoking. The regression coefficient is in reference to the 2 ethnicity variables.

BMI = body mass index; PWV = proximal aortic pulse wave velocity; Zc = characteristic impedance.

risk factors do not explain the ethnic differences in aortic arch PWV and Zc, as we adjusted for them in our analysis. Thus, mechanisms underlying higher aortic stiffness in Blacks and Hispanics are uncertain and represent important targets for future research.

Previous large epidemiological studies have provided conflicting evidence regarding ethnic differences in aortic stiffness (12,13). Although the Bogalusa Heart Study showed increased large artery stiffness in Blacks for the age range 18 to 44 years, the Multi-ethnic Study of Atherosclerosis evaluated participants 45 to 84 years of age and found no ethnic differences in arterial stiffness after adjustment for height (12,13). These studies may have obtained different results due to their differences in age ranges; the use of radial artery tonometry in these studies also has several potential limitations (24-30). Our study uses a validated technique that directly assesses central aortic stiffness and our sample has an age range that encompasses most of the adult lifespan (19 to 67 years of age).

Stiffness may be considered as factors related to wall stiffness but is also related to pressure pulsatility. PWV is a good measure of wall stiffness because it is relatively insensitive to geometry (i.e., diameter). We further assessed Zc which is a sensitive indicator of the contribution of aortic stiffening and matching between flow and aortic diameter to the pathogenesis of high pulse pressure and systolic hypertension (31,32). From the water hammer equation, Zc is directly proportional to PWV and inversely proportional to vessel lumen area (10). Pulse pressure is, of course, the best measure of pressure pulsatility. An important question is whether increased pulsatility in Blacks can be explained by a stiffer wall or by other factors such as higher flow or smaller aortic diameter. To completely address these factors strays beyond our scope, but we will explore some essential

relationships, starting with the relationship between diameter and stiffness.

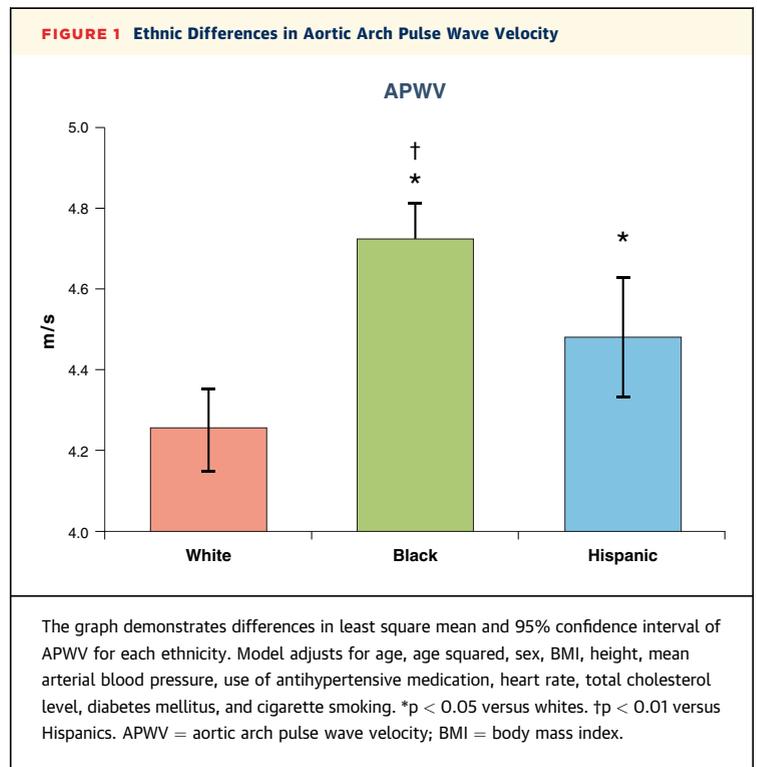
Higher levels of Zc in Hispanics and Blacks compared with Whites in our study was driven in part by smaller aortic area, suggesting a possible impairment in aortic remodeling. Univariate analysis shows Hispanics had significantly smaller aortic area as a group than non-Hispanic Whites or Blacks. Further exploration shows that this association is lost after adjusting for the lower age and height of Hispanics in our study. The observation that aortic lumen area seems appropriate for height may reflect strong, parallel genetic contributions to height and aortic area, which have heritabilities that exceed 0.5 (33,34). Both Hispanic and Black ethnicity were associated with smaller aortic areas, however, when adjustment was made for BMI. The latter observation suggests there may be a mismatch between aortic diameter and adiposity in Hispanics and Blacks. Another interesting finding is the contrasting relation of BMI with pulse pressure (positive) and Zc (negative). With increasing adiposity, cardiac output increases and the aorta remodels, driving down Zc. However, the increase in peak flow presumably exceeds the decrease in Zc, resulting in an increase in pulse pressure.

Beyond the factors we explore here, age-related differences in aortic stiffening may also be due in part to genetic differences in vascular collagen content and endothelial response to cell injury (35). Other factors, including male sex, elevated blood pressure (BP), cigarette smoking, obesity, and diabetes are not likely to explain ethnic difference in Zc or PWV in our study as the difference persisted after adjustment for these relevant factors. Increased aortic stiffening may also be related to excess sodium intake or low potassium intake which has been shown to be associated with larger increase in BP in Blacks in the DHS (36) and other large population studies (37).

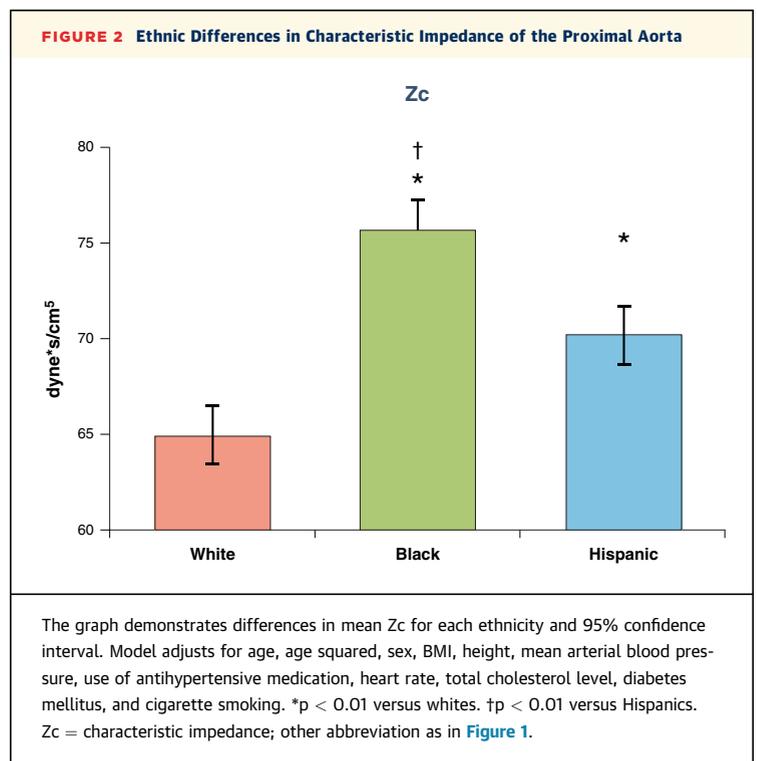
Secondary analysis of ethnic differences in pulse pressure reveals some interesting relationships. Aortic lumen area, wall stiffness, and blood flow are the primary determinants of forward pressure wave amplitude, which is a major determinant of pulse pressure. Even after accounting for distending pressure (mean arterial pressure), aortic wall stiffness (PWV), and lumen area, Blacks and Hispanics have higher pulse pressure than whites. This suggests that either there is higher relative flow in Blacks and Hispanics (i.e., there is mismatch between flow and Zc) or that there is a difference in wave reflection or amplification between the central aorta (where we measured stiffness and lumen area) and the arm (where we measured pulse pressure). This will need to be explored in future studies.

Our demonstration of ethnic differences in arterial stiffness is an important step in understanding the mechanisms that mediate ethnic differences in cardiovascular disease. In light of prior prospective observations showing that PWV was an independent predictor of incident hypertension in a White cohort (2), our study may provide a potential explanation for excess risk of hypertension and target organ complication in Blacks. Beyond the factors we explore here, ethnic differences in aortic stiffening may be due in part to genetic differences in vascular collagen content and endothelial response to cell injury (35).

STUDY LIMITATIONS. The study uses a cross-sectional design and hence does not allow inferences on causality or longitudinal change. However, this sample will be studied over time to ascertain whether longitudinal measurements confirm our present cross-sectional findings. Limited temporal resolution of CMR measurements may confound our measurements of PWV, as a higher temporal resolution allows for more precise estimates of aortic arch PWV (38). We assumed that the water hammer equation is applicable when calculating Zc in the proximal aorta, which is a reasonable assumption (39). However, use of the water hammer is expected to provide lower estimates of Zc (40), which was the case in our study as compared to prior reports based on pressure-flow relations (11). A limitation of flow-based PWV, in general, is that wave reflection blunts the upstroke of flow, leading to progressive over-estimation of the arrival time of the flow waveform at more distal locations within the aorta and hence a longer transit time. Our study used brachial BP measurements, which often differ from the central BPs within the aorta due to peripheral pulse amplification. This amplification will result in an increased systolic and pulse pressure in the arm compared with the aorta for some individuals. Further, this



amplification is not necessarily fixed and may decrease with age as the aorta stiffens. Strengths of our study include a large sample of ethnically diverse participants with routinely ascertained, detailed



measurements of aortic structure and function, and related risk factors.

CONCLUSIONS

In a probability-sampled, multiethnic population, we have identified higher stiffness of the proximal aorta in Blacks and Hispanics as compared to Whites, even after adjustment for traditional cardiovascular disease risk factors. Future studies are needed to identify interventions that ameliorate or prevent abnormal large artery function in these high-risk ethnic groups.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In a multiethnic population-based study, Blacks and Hispanics displayed higher proximal aortic stiffness when compared to Whites, independent of BP and other standard vascular risk factors.

TRANSLATIONAL OUTLOOK: Although mechanisms underlying higher aortic stiffness in Blacks and Hispanics are unknown, the increased proximal aortic stiffness may explain the disproportionately increased cardiovascular risk in these 2 ethnic populations when compared to Whites.

REFERENCES

- Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation* 2014;129:e28-292.
- Kaess BM, Rong J, Larson MG, et al. Aortic stiffness, blood pressure progression, and incident hypertension. *JAMA* 2012;308:875-81.
- Gazes PC, Lackland DT, Mountford WK, Gilbert GE, Harley RA. Comparison of cardiovascular risk factors for high brachial pulse pressure in blacks versus whites (Charleston Heart Study, Evans County Study, NHANES I and II Studies). *Am J Cardiol* 2008;102:1514-7.
- Cavalcante JL, Lima JA, Redheuil A, Al-Mallah MH. Aortic stiffness: current understanding and future directions. *J Am Coll Cardiol* 2011;57:1511-22.
- Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM. Impact of aortic stiffness on survival in end-stage renal disease. *Circulation* 1999;99:2434-9.
- King KS, Chen KX, Hulsey KM, et al. White matter hyperintensities: use of aortic arch pulse wave velocity to predict volume independent of other cardiovascular risk factors. *Radiology* 2013;267:709-17.
- Maroules CD, Khera A, Ayers C, et al. Cardiovascular outcome associations among cardiovascular magnetic resonance measures of arterial stiffness: the Dallas heart study. *J Cardiovasc Magn Reson* 2014;16:33.
- Ben-Shlomo Y, Spears M, Boustred C, et al. Aortic pulse wave velocity improves cardiovascular event prediction: an individual participant meta-analysis of prospective observational data from 17,635 subjects. *J Am Coll Cardiol* 2014;63:636-46.
- Cooper LL, Rong J, Benjamin EJ, et al. Components of hemodynamic load and cardiovascular events: the Framingham Heart Study. *Circulation* 2015;131:354-61; discussion 61.
- Sweitzer NK, Shenoy M, Stein JH, et al. Increases in central aortic impedance precede alterations in arterial stiffness measures in type 1 diabetes. *Diabetes Care* 2007;30:2886-91.
- Mitchell GF, Wang N, Palmisano JN, et al. Hemodynamic correlates of blood pressure across the adult age spectrum: noninvasive evaluation in the Framingham Heart Study. *Circulation* 2010;122:1379-86.
- Bhuiyan AR, Li S, Li H, Chen W, Srinivasan SR, Berenson GS. Distribution and correlates of arterial compliance measures in asymptomatic young adults: the Bogalusa Heart Study. *Am J Hypertens* 2005;18:684-91.
- Duprez DA, Jacobs DR Jr., Lutsey PL, et al. Race/ethnic and sex differences in large and small artery elasticity—results of the multi-ethnic study of atherosclerosis (MESA). *Ethn Dis* 2009;19:243-50.
- Heffernan KS, Jae SY, Wilund KR, Woods JA, Fernhall B. Racial differences in central blood pressure and vascular function in young men. *Am J Physiol Heart Circ Physiol* 2008;295:H2380-7.
- Nichols WW, McDonald DA. Wave-velocity in the proximal aorta. *Med Biol Eng* 1972;10:327-35.
- Goel A, McColl R, King KS, Whittemore A, Peshock RM. Fully automated tool to identify the aorta and compute flow using phase-contrast MRI: validation and application in a large population based study. *J Magn Reson Imaging* 2014;40:221-8.
- Victor RG, Haley RW, Willett DL, et al. The Dallas Heart Study: a population-based probability sample for the multidisciplinary study of ethnic differences in cardiovascular health. *Am J Cardiol* 2004;93:1473-80.
- van der Geest RJ, Niezen RA, van der Wall EE, de Roos A, Reiber JH. Automated measurement of volume flow in the ascending aorta using MR velocity maps: evaluation of inter- and intraobserver variability in healthy volunteers. *J Comp Assist Tomogr* 1998;22:904-11.
- Dogui A, Redheuil A, Lefort M, et al. Measurement of aortic arch pulse wave velocity in cardiovascular MR: comparison of transit time estimators and description of a new approach. *J Magn Reson Imaging* 2011;33:1321-9.
- Nichols W, O'Rourke M, Vlachopoulos C. *McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles*. Boca Raton, FL: CRC Press, 2011.
- Mitchell GF, Gudnason V, Launer LJ, Aspelund T, Harris TB. Hemodynamics of increased pulse pressure in older women in the community-based Age, Gene/Environment Susceptibility-Reykjavik Study. *Hypertension* 2008;51:1123-8.
- Markham DW, Dries DL, King LP, et al. Blacks and whites have a similar prevalence of reduced left ventricular ejection fraction in the general population: the Dallas Heart Study (DHS). *Am Heart J* 2008;155:876-82.
- Milan A, Tosello F, Fabbri A, et al. Arterial stiffness: from physiology to clinical implications. *High Blood Press Cardiovasc Prev* 2011;18:1-12.
- Richardson CJ, Maki-Petaja KM, McDonnell BJ, Hickson SS, Wilkinson IB, McEniery CM. Comparison of estimates of central systolic blood pressure and peripheral augmentation index obtained from the Omron HEM-9000AI and SphygmoCor systems. *Artery Res* 2009;3:24-31.
- Zhang Y, Agnoletti D, Safar ME, et al. Comparison study of central blood pressure and wave reflection obtained from tonometry-based devices. *Am J Hypertens* 2013;26:34-41.
- Rietzschel E-R, Boeykens E, De Buyzere ML, Duprez DA, Clement DL. A comparison between systolic and diastolic pulse contour analysis in the

- evaluation of arterial stiffness. *Hypertension* 2001;37:e15-22.
27. Segers P, Qasem A, De Backer T, Carlier S, Verdonck P, Avolio A. Peripheral "oscillatory" compliance is associated with aortic augmentation index. *Hypertension* 2001;37:1434-9.
28. Manning TS, Shykoff BE, Izzo JL Jr. Validity and reliability of diastolic pulse contour analysis (windkessel model) in humans. *Hypertension* 2002;39:963-8.
29. Oliver JJ, Webb DJ. Noninvasive assessment of arterial stiffness and risk of atherosclerotic events. *Arterioscler Thromb Vasc Biol* 2003;23:554-66.
30. Laurent S, Boutouyrie P. Recent advances in arterial stiffness and wave reflection in human hypertension. *Hypertension* 2007;49:1202-6.
31. Mitchell GF, Lacourciere Y, Ouellet JP, et al. Determinants of elevated pulse pressure in middle-aged and older subjects with uncomplicated systolic hypertension: the role of proximal aortic diameter and the aortic pressure-flow relationship. *Circulation* 2003;108:1592-8.
32. Torjesen AA, Sigurethsson S, Westenberg JJ, et al. Pulse pressure relation to aortic and left ventricular structure in the Age, Gene/Environment Susceptibility (AGES)-Reykjavik Study. *Hypertension* 2014;64:756-61.
33. Bella JN, MacCluer JW, Roman MJ, et al. Genetic influences on aortic root size in American Indians: the Strong Heart Study. *Arterioscler Thromb Vasc Biol* 2002;22:1008-11.
34. Vasani RS, Glazer NL, Felix JF, et al. Genetic variants associated with cardiac structure and function: a meta-analysis and replication of genome-wide association data. *JAMA* 2009;302:168-78.
35. Hall JL, Duprez DA, Barac A, Rich SS. A review of genetics, arterial stiffness, and blood pressure in African Americans. *J Cardiovasc Transl Res* 2012;5:302-8.
36. Hedayati SS, Minhajuddin AT, Ijaz A, et al. Association of urinary sodium/potassium ratio with blood pressure: sex and racial differences. *Clin J Am Soc Nephrol* 2012;7:315-22.
37. Stamler J, Brown JJ, Yap IK, et al. Dietary and urinary metabolomic factors possibly accounting for higher blood pressure of black compared with white Americans: results of International Collaborative Study on macro-/micronutrients and blood pressure. *Hypertension* 2013;62:1074-80.
38. Ibrahim el-SH, Johnson KR, Miller AB, Shaffer JM, White RD. Measuring aortic pulse wave velocity using high-field cardiovascular magnetic resonance: comparison of techniques. *J Cardiovasc Magn Reson* 2010;12:26.
39. Hanya S. Validity of the water hammer formula for determining regional aortic pulse wave velocity: comparison of one-point and two-point (Foot-to-Foot) measurements using a multi-sensor catheter in human. *Ann Vasc Dis* 2013;6:150-8.
40. Segers P, Swillens A, Taelman L, Vierendeels J. Wave reflection leads to over- and underestimation of local wave speed by the PU- and QA-loop methods: theoretical basis and solution to the problem. *Physiol Meas* 2014;35:847-61.

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APPENDIX For supplemental tables, please see the online version of this article.