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Influence on Aerobic Fitness on Aortic Stiffness in Apparently Healthy Caucasian and African-American Subjects

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Abstract

Background— Previous research suggests that arterial stiffness may be significantly higher in African-Americans compared to Caucasians. However, the influence of aerobic fitness on the putative difference in arterial stiffness between these groups has not been previously investigated.

Methods— Two hundred forty-eight subjects (215 Caucasian, 33 African-American) participated in this study. Within one week following enrollment, subjects underwent body mass index (BMI, kg/m²) assessment, cardiopulmonary exercise testing and measurement of aortic wave velocity (AWV, m/s) via magnetic resonance imaging. Initially, 33 Caucasian subjects were randomly age (± 4 years) and sex-matched (10 male/23 female) to the African-American subjects. 25 Caucasian subjects were then randomly matched for age (± 4 years), sex (7 male/18 female) and maximal oxygen consumption ($\text{VO}_{2\text{Max}} \pm 7 \text{ mL O}_2 \bullet \text{kg}^{-1} \bullet \text{min}^{-1}$) to the African-American subjects. Matching based upon $\text{VO}_{2\text{Max}}$ criteria was not possible for 8 African-American subjects.

Results— In the age and sex-matched analysis, Caucasian subjects demonstrated a significantly higher $\text{VO}_{2\text{Max}}$ (38.3 ± 9.6 vs. $27.9 \pm 8.6 \text{ mL O}_2 \bullet \text{kg}^{-1} \bullet \text{min}^{-1}$, $p < 0.001$) and lower BMI (24.5 ± 3.2 vs. $29.3 \pm 6.2 \text{ kg/m}^2$, $p < 0.001$) and AWV (5.8 ± 1.7 vs. $6.7 \pm 1.5 \text{ m/s}$, $p = 0.03$). However, when subjects were matched for age, sex and $\text{VO}_{2\text{Max}}$, the differences in both BMI (26.8 ± 5.5 vs. $27.9 \pm 5.6 \text{ kg/m}^2$, $p = 0.45$) and AWV (6.1 ± 1.8 vs. $6.5 \pm 1.6 \text{ meters/second}$, $p = 0.77$) were insignificant.

Conclusions— The results of the present study suggest that previously reported differences in arterial stiffness between Caucasians and African-Americans is at least partially a consequence of a lower level of aerobic fitness in the latter group, a phenomenon that has also been previously demonstrated.

Keywords

Exercise Testing; Oxygen Consumption; Aortic Wave Velocity; Ethnic Differences

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Introduction

In recent years, arterial stiffness has been shown to significantly predict cardiovascular dysfunction. Specifically, a number of investigations have found that decreased aortic compliance (increased stiffness) possesses both diagnostic[1] and prognostic value.[2–8] Covic et al.[1] found increasing degrees of aortic stiffness to be reflective of worsening coronary artery disease. Laurent et al.[5] reported that aortic stiffness significantly predicted all-cause and cardiovascular mortality independent of age, previous cardiovascular disease and diabetes in a group of subjects with essential hypertension. Cruickshank et al.[7] likewise found that aortic stiffness predicted all-cause and cardiovascular mortality in diabetic and glucose intolerant groups independent of age, sex and systolic blood pressure.

Furthermore, several previous investigations have reported arterial stiffness to be significantly higher in African-Americans compared to Caucasians.[9–14] The disparity between these ethnic groups has been attributed to differences in exposure to cardiac risk factors,[9,13,14] beta-adrenergic sensitivity,[10] vascular remodeling[11] and mechanical properties of large vessels.[12] All of these studies compared ethnic groups of similar age, an important determinant of arterial stiffness.[15] However, comparison of differences in arterial stiffness between ethnic groups with comparable levels of aerobic fitness has, to our knowledge, not been performed. This is an important consideration, given the significant relationship between $\text{VO}_{2\text{Max}}$ and arterial stiffness.[15–17]

The purpose of the present investigation is to therefore: (1) compare the differences in large artery stiffness between African-American and Caucasian cohorts matched for age and sex, and (2) compare the differences in large artery stiffness between African-American and Caucasian subjects matched for age, sex and aerobic fitness.

Methods

Study Population

Two hundred and fifteen Caucasian and 33 African American subjects participated in a study examining the relationship between arterial stiffness and a number of traditional cardiovascular risk factors. Inclusion criteria consisted of the ability to successfully put forth a near-maximal to maximal effort during exercise testing without an abnormal hemodynamic/ECG response. Exclusion criteria included: history of myocardial infarction, angina or stroke, evidence of coronary heart disease, peripheral arterial disease or diabetes, pregnancy, age < 21 years and magnetic resonance (MR) contraindications (e.g. ferromagnetic implants, claustrophobia). Written informed consent was obtained from all subjects prior to testing. Approval from the institutional review board at Virginia Commonwealth University was obtained before study initiation.

Data Collection

Body Mass Index (BMI) in kilograms per meters squared (kg/m^2) was calculated and recorded for each subject on the day of maximal exercise testing. Resting HR and blood pressure (BP) were additionally recorded prior to exercise testing and at the time of the MR examination. Resting BP values reported in the present investigation are the average of six separate recordings for each subject (three before exercise testing and three after MR).

Ventilatory expired gas analysis was obtained using a metabolic cart (Vmax Spectra29, SensorMedics, Inc., Yorba Linda, CA) during exercise testing. The oxygen and carbon dioxide sensors were calibrated using gases with known oxygen, nitrogen, and carbon dioxide concentrations prior to each exercise test. The flow sensor was also calibrated before each test using a three-liter syringe.

Physician-supervised maximal exercise tests were conducted using a modified Balke treadmill exercise protocol. Monitoring consisted of continuous 12-lead electrocardiography, BP measurements at regular intervals during the exercise test, HR recordings every stage via the electrocardiogram, and rating of perceived exertion (Borg 6–20 scale). Subjects were encouraged to exercise to muscular fatigue. Test termination criteria followed American College of Sports Medicine guidelines.[18] Monitoring of HR and BP persisted at least five minutes into the recovery phase following exercise testing. Oxygen consumption (in $\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) was collected throughout the exercise test. $\text{VO}_{2\text{Max}}$ and peak respiratory exchange ratio were defined as the final 20-second averaged value during the last stage of the exercise test. Percent of age-predicted maximum HR (APMHR) achieved during exercise was determined by dividing maximal exercise HR by 220-age and multiplying that value by 100. Percent predicted $\text{VO}_{2\text{Max}}$ was also calculated for each subject.[19]

Measurement of Aortic Wave Velocity

All MR examinations were performed on a 1.5T whole-body MR unit (Vision, Siemens Medical Solutions, Erlangen, Germany). Subjects were positioned supine on a standard spine array receiver coil, and centered in the magnet using the xiphisternum as an anatomical landmark. Electrocardiogram gating was used to synchronize MR acquisitions to the early systolic portion of the cardiac cycle. After acquiring transaxial and sagittal scout images of the thoracic aorta, cardiac-triggered aortic wave velocity (AWV) measurements were performed as described previously.[20] The strategy of the measurement is to simultaneously record the initial systolic flow velocity waveforms at two sites within the descending thoracic aorta, separated by a known distance (84 mm). Since the flow propagation rate is finite, a distinct delay can be discerned between the two velocity waveforms. The separation distance divided by this observed delay time yields the AWV.

After each AWV measurement, MR data analysis was performed offline, by downloading the raw data to a laptop PC. Using customized software based on Matlab Version 6.5 (The MathWorks Inc., Natick, MA), various processing steps, including complex fast Fourier transform with zero-filling, flow image construction, and automated AWV calculation, could be completed within approximately 30 s of data acquisition. The mean of five individual measurements was used to compute an overall AWV for each subject.

We have performed a separate test-retest reliability analysis of the AWV measurement technique in a group of 10 apparently healthy individuals. The intraclass correlation coefficient for the two AWV determinations was 0.97, $p < 0.001$. The standard error of measurement (95% confidence intervals) for AWV was ± 0.18 m/s. These results demonstrate excellent reliability of our AWV measurement method.

Statistical Analysis

Mean and standard deviation were calculated for baseline and exercise testing variables as well as AWV. Paired sample t-tests compared differences in variables of interest between age/sex and age/sex/ $\text{VO}_{2\text{Max}}$ -matched African-American and Caucasian subjects. All statistical tests with a p-value < 0.05 were considered significant.

For this sub-analysis, 33 Caucasian subjects were first randomly selected and matched for age (± 4 years) and sex (10 male/23 female) to the African-American subjects. Next, 25 Caucasian subjects were then randomly selected and matched for age (± 4 years), sex (7 male/18 female) and maximal oxygen consumption ($\text{VO}_{2\text{Max}} \pm 7 \text{ mlO}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ or 2 metabolic equivalents) to the African-American Subjects. During both matching processes, the investigator (RA) only considered the minimum data required for matching (Random selection 1: age and sex, Random

selection 2: age, sex and $\text{VO}_{2\text{Max}}$). Matching based upon $\text{VO}_{2\text{Max}}$ was not possible for 8 African-American subjects.

Results

All exercise tests were terminated secondary to subject fatigue. Mean peak RER was greater than 1.1 (Caucasian: 1.14 ± 0.06 , African-American: 1.17 ± 0.07) and percent APMHR achieved was greater than 95% (Caucasian: $101.1 \pm 6.1\%$, African-American: $97.0 \pm 7.7\%$) in the age/sex-matched groups. Likewise, mean peak RER was greater than 1.1 (Caucasian: 1.17 ± 0.07 , African-American: 1.15 ± 0.04) and percent APMHR achieved was greater than 95% (Caucasian: $100.4 \pm 6.8\%$, African-American: $99.4 \pm 6.8\%$) in the age/sex/ $\text{VO}_{2\text{Max}}$ -matched groups. These findings indicate that subjects put forth an excellent effort in both groups.

Subject characteristics for the age/sex-matched comparison are listed in Table 1. Caucasian subjects had a significantly lower BP, BMI and AWW and a significantly higher aerobic capacity compared to the African-American subjects. Figure 1 illustrates the significant difference in AWW between age/sex matched groups.

Subject characteristics for the age/sex/ $\text{VO}_{2\text{Max}}$ -matched comparison are listed in Table 2. Caucasian subjects had a significantly lower diastolic BP; in all other respects differences were not significant. Figure 2 illustrates the (insignificant) difference in AWW between age/sex/ $\text{VO}_{2\text{Max}}$ -matched groups.

Discussion

In age-sex matched Caucasian and African-American groups, African-American subjects had a higher resting BP and BMI as well as a lower level of aerobic fitness. These findings are consistent with United States trends reported by the American Heart Association.[21] The age-sex-fitness matched comparison indicates that the disparities in systolic BP and BMI between ethnic groups may be explained by differences in fitness level. This finding is not surprising given the positive influence of fitness on resting hemodynamics and body weight.

The age-sex matched findings regarding a significantly higher level of arterial stiffness in the African-American subjects is also consistent with several previous investigations.[9–14] To our knowledge, however, the present study is the first to assess differences in arterial stiffness between Caucasian and African American subjects in age-sex-fitness matched groups. These results indicate that, like systolic blood pressure and BMI, differences in arterial stiffness between African American and Caucasian subjects can be at least partially explained by differences in fitness level. The inverse relationship between aerobic fitness and arterial stiffness,[15–17] therefore appears to be consistent in both Caucasian and African-American subjects.

Several mechanisms for differences in arterial stiffness between African American and Caucasian subjects have been postulated by previous investigations. Din-Dzietham et al.[9] proposed that significant differences in arterial stiffness between African American and Caucasian subjects may be the result of earlier exposure to cardiovascular risk factors, such as hypertension, in the African American population. Urbina et al.[13,14] likewise demonstrated a significantly higher level of arterial stiffness in African American subjects and cited the importance of other cardiovascular risk factors. Conversely, Chaturvedi et al.[11] hypothesized that a higher level of arterial stiffness in individuals of African compared to European descent may be due to differences in vascular remodeling. Lemogoum et al.[10] and Ferreira et al.[12] postulated there may be differences in beta-adrenergic sensitivity and arterial mechanical properties, respectively, between African and Caucasian subjects contributing to differences in arterial stiffness. While not discounting the possibility of ethnic-based differences in arterial

characteristics, the results of the present study indicate that aerobic fitness level is a mitigating factor in observed differences in arterial stiffness between African American and Caucasian subjects. Although fitness level was not assessed in the studies by Din-Dzietham et al.[9] and Urbina et al.,[13,14] low fitness has been clearly established as a cardiovascular risk factor. Therefore, the results of the present study support the contention that differences in arterial stiffness between African American and Caucasian individuals are at least partly explained by differences in cardiovascular risk factor exposure between groups. Furthermore, increasing levels of aerobic fitness appear to subdue other risk factors such as a higher BMI and systolic blood pressure.

Although a number of noninvasive techniques have been widely employed to assess arterial compliance, most suffer fundamental methodological problems that undermine their accuracy, reproducibility or relevance to the central arteries. Consequently, none can be presently considered a “gold standard” method. Magnetic resonance imaging does not suffer from the acoustic window limitations of ultrasound, and is therefore, in principle, better suited for studying the central arteries. Slice positioning accuracy and distance determinations are also generally superior using MR. Both direct distensibility[16,22] and indirect wave velocity measurements[23–25] have been described using MR. The MR sequence[20] employed herein was designed to measure wave velocity in the human descending thoracic aorta within a single cardiac cycle. Careful validation using *in vitro* standards has demonstrated high accuracy of the method, and *in vivo* trials have yielded excellent reproducibility (coefficient of variation below 8%).[26] This lends confidence in the validity of the AWW assessments.

The small sample size of the present study is a weakness that must be rectified by future research. This will allow, e.g. studies of gender differences in various ethnic groups. Several studies have demonstrated that aerobic exercise significantly reduces large vessel stiffness in apparently healthy individuals as well as in subjects possessing characteristics that elevate the risk for cardiovascular disease.[27–29] Another important direction for future research is the comparison of alterations in arterial stiffness as a result of aerobic exercise training between African American and Caucasian subjects. Such an investigation would further help to determine if arterial architecture/function varies by ethnicity.

In conclusion, the results of the present study indicate that aerobic fitness level may be an important determinant in the differences in arterial stiffness previously demonstrated between African American and Caucasian subjects. These findings support the notion that arterial stiffness is a modifiable cardiovascular risk factor, irrespective of race.

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***p<0.05**

Figure 1.
Difference in AWV between African-American and Caucasian Subjects: age/sex-Matched Groups

p=0.46

Figure 2.
Difference in AWW between African-American and Caucasian Subjects: age/sex/ $\text{VO}_{2\text{Max}}$ -matched groups

Table 1

Comparison between age/sex-matched Caucasian and African-American Subjects

	Caucasian	African-American
Age (years)	42.8±13.0	44.0±13.2
BMI (kg/m ²)	24.5±3.3	29.3±6.2**
SBP (mmHg)	120.3±13.5	129.0±17.8*
DBP (mmHg)	72.7±9.4	78.0±10.3*
VO _{2Max} (mlO ₂ · kg ⁻¹ · min ⁻¹)	38.3±9.6	27.9±8.6**
Percent predicted VO _{2Max} (%)	114.0±28.7	81.1±29.0**
AWV (m/s)	5.8±1.5	6.7±1.7*

*
p<0.05**
p<0.001

Table 2Comparison between age/sex/ $\text{VO}_{2\text{Max}}$ -matched Caucasian and African American Subjects

	Caucasian	African-American
Age (years)	45.5±13.5	44.5±13.1
BMI (kg/m^2)	26.8±5.5	27.9±5.6
SBP (mmHg)	121.3±13.5	126.6±17.4
DBP (mmHg)	72.5±7.2	77.1±9.7*
$\text{VO}_{2\text{Max}}$ ($\text{mlO}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$)	32.7±7.0	30.6±8.0
Percent predicted $\text{VO}_{2\text{Max}}$ (%)	96.6±20.1	91.2±25.4
AWV (m/s)	6.1±1.8	6.5±1.6

*
p<0.05