Association of African Ancestry with Left Ventricular Hypertrophy Assessed by Electrocardiographic Voltage and Cardiac Magnetic Resonance: the Dallas Heart Study

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Background

- African Americans compared to whites have increased electrocardiographic (EKG) voltage and a concentric hypertrophic response as assessed by cardiac magnetic resonance (CMR)
- It is uncertain whether these ethnic disparities have a genetic basis
- Our study aimed to determine whether African ancestry, as assessed by genetic markers, was associated with EKG voltage and increased LV wall thickness in the Dallas Heart Study

Hypothesis

- A higher degree of African ancestry according to genetic markers will correlate with increased EKG voltage and with increased LV wall thickness as determined by LV concentricity$^{0.67}$ (LV mass/EDV$^{0.67}$)

Methods

Study Participants

- 2077 participants, of whom 1251 self-identified as black, from the Dallas Heart Study, a population-based survey of Dallas County that oversampled African Americans to comprise 50% of the study population
- Participants underwent EKGs, CMRI, genotyping, and completed health questionnaires

Analyses and Statistical Methods

- Analyses restricted to self-identified whites and blacks
- To assess the ancestral admixture, we used genome-wide genotyping data and ADMIXTURE v.1.3.0 software, assuming 3 ancestral populations
- The relation between African ancestry (AFR) and self-reported black race with summated 12-lead EKG voltage, LV concentricity$^{0.67}$, and LV Wall Thickness adjusting for important confounders
- EKG measurements included Q, R, and S wave amplitude measurements in all 12 leads, used to calculated 12-lead sum voltage
- To measure LV concentricity$^{0.67}$ and LV wall thickness, we used short-axis, breath-hold, EKG-gated cine magnetic resonance images obtained from 1.5-T MRI systems and manually traced endo- and epicardial borders of slices from the apex to base of the LV
- All statistical analyses were performed with SAS 9.4

Results

Multivariable Models In Whole Cohort (Blacks and Whites, n = 2077)

Table 1. Black Race is Associated with 12-Lead Voltage and LV Concentric Thickening

Variable	β	12-Lead Voltage	β	LV Concentricity$^{0.67}$	β	LV Wall Thickness
Black Race	18.57	<.0001	0.3034	<.0001	0.4157	<.0001
Age	-0.5675	<.0001	0.0105	<.0001	0.0098	0.0009
Sex	21.10	<.0001	0.5581	<.0001	0.6740	<.0001
Systolic BP	0.4977	<.0001	0.0203	<.0001	0.0245	<.0001
Anti-Htn Meds	7.217	<.0001	0.4478	<.0001	0.5313	<.0001
Lean Mass	-0.1833	0.1121	0.0323	<.0001	0.0501	<.0001
Fat Mass	-0.4185	<.0001	-0.0054	0.0677	-0.0033	0.3235

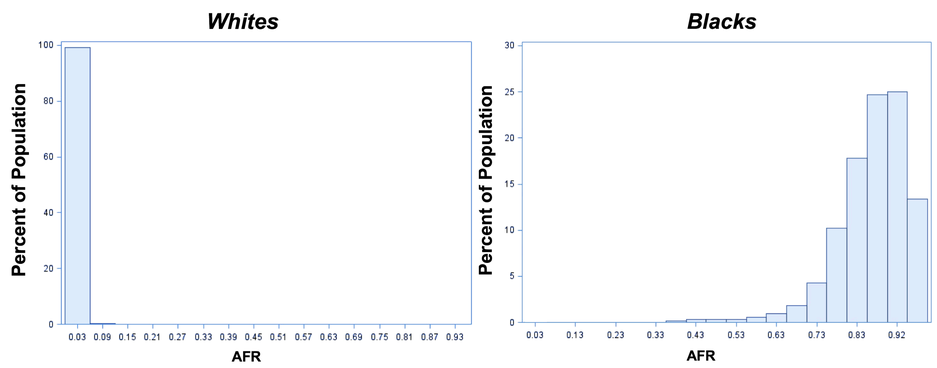
Table 2. AFR is Associated with 12-Lead Voltage and LV Concentric Thickening

Variable	β	12-Lead Voltage	β	LV Concentricity$^{0.67}$	β	LV Wall Thickness
AFR	21.71	<.0001	0.3639	<.0001	0.4957	<.0001
Age	-0.5685	<.0001	0.0105	<.0001	0.0098	0.0009
Sex	21.57	<.0001	0.5698	<.0001	0.6889	<.0001
Systolic BP	0.4951	<.0001	0.0203	<.0001	0.0244	<.0001
Anti-Htn Meds	7.084	<.0001	0.4449	<.0001	0.5277	<.0001
Lean Mass	-0.2064	0.0741	0.0317	<.0001	0.0494	<.0001
Fat Mass	-0.4037	<.0001	-0.0050	0.0865	-0.0028	0.3909

Table 3. AFR, but not Black Race, is Associated with 12-Lead Sum and LV Concentric Thickening When Both are Entered into Models Together

Variable	β	12-Lead Voltage	β	LV Concentricity$^{0.67}$	β	LV Wall Thickness
AFR	21.15	0.0204	0.6359	0.0430	0.7750	0.0287
Black Race	0.4940	0.9503	-0.2402	0.3787	-0.2465	0.4228
Age	-0.5684	<.0001	0.0105	<.0001	0.0098	0.0009
Sex	21.57	<.0001	0.5723	<.0001	0.6916	<.0001
Systolic BP	0.4951	<.0001	0.0203	<.0001	0.0244	<.0001
Anti-Htn Meds	7.086	<.0001	0.4439	<.0001	0.5267	<.0001
Lean Mass	-0.2061	0.0748	0.0316	<.0001	0.0492	<.0001
Fat Mass	-0.4040	<.0001	-0.0049	0.0943	-0.0027	0.4116

Figure 1. Distribution of AFR in Whites and Blacks



Multivariable Models in Blacks Only (n = 1251)

Table 4. AFR remains associated with 12-Lead Voltage and LV Concentric Thickening in Blacks

Variable	β	12-Lead Sum	β	LV Concentricity$^{0.67}$	β	LV Wall Thickness
AFR	20.28	0.0412	0.7021	0.0450	0.8825	0.0241
Age	-0.4723	<.0001	0.0106	0.0045	0.0089	0.033
Sex	19.45	<.0001	0.4821	0.0006	0.6508	<.0001
Systolic BP	0.5024	<.0001	0.0219	<.0001	0.0272	<.0001
Anti-Htn Meds	6.206	0.0067	0.4670	<.0001	0.5607	<.0001
Lean Mass	-0.0026	0.9865	0.0339	<.0001	0.0509	<.0001
Fat Mass	-0.5165	<.0001	-0.0059	0.1493	-0.0038	0.4078

Conclusion

- Genetically inferred African ancestry, as compared to self-identified black race, were more strongly associated with EKG voltage and CMR assessment of LV concentricity$^{0.67}$ and LV Wall Thickness in multivariable models
- African ancestry remained associated with these cardiac phenotypes in analyses restricted to blacks
- These data support a genetic basis for the disparities in EKG voltage and concentric hypertrophic response between blacks and whites in the population
- Currently, a guideline-recommended treatment of systolic heart failure (fixed dose combination of isosorbide dinitrate and hydralazine) is indicated only for patients who self-identify as being black. Our data raise the provocative hypothesis that genetic markers of ancestry could prove more useful than self-identified race when choosing such therapeutics