Title: Defining the Normal Spectrum of Electrocardiographic and Left Ventricular Adaptations in Mixed-Race Male Adolescent Soccer Players.

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Contemporary data regarding exercise-related sudden cardiac death (SCD) reveal that young adolescent athletes (14-18 years old) are the most vulnerable group.[1] Several studies have described the adolescent athlete's heart but have focused only on white or black athletes.[2,3] The demographic landscape for adolescent athletes has changed over the past few decades and consists of an increasing population of mixed-race individuals in whom one parent is black (African or Afro-Caribbean) and the other parent is white. We examined the electrical and structural adaptations within the heart in healthy mixed-race male soccer players and compared them to those of white and black male soccer players.

Ethics approval was granted in accordance with the Research Governance Framework for Health and Social Care (2005) and the English Football Association (FA). Written consent was obtained from all athletes in accordance with the Data Protection Act (1998). The data that support the findings of this study are available from the corresponding author upon reasonable request.

Between 2015-2018, 3,000 consecutive cases of healthy mixed-race, black and white athletes were assessed with EKG and echocardiography. A mixed-race athlete was an individual with one white parent of European origin and one black parent of African/Afro-Caribbean origin.

The 12-lead EKG was interpreted in accordance with international recommendations.[4] Transthoracic echocardiography was performed in accordance with standard American and European protocols. The χ^2 test was used to compare the prevalence of ECG and echocardiogram features between black, white and mixed-race groups.

The mean age was 16.4±1.3 years. Among mixed-race athletes, while one parent was white British in all cases, the other parent was either of African (60%) or Caribbean (40%) origin. Black athletes were of African (61%) or Caribbean origin (39%).

Electrical changes

Sinus bradycardia and Sokolow-Lyon criterion for left ventricular (LV) hypertrophy were most prevalent among mixed-race athletes. Mixed-race and black athletes demonstrated a similar prevalence of voltage criteria for left and right atrial enlargement, which was higher compared with white athletes.

T-wave inversion (TWI) was most common in black athletes, followed by mixed-race and white athletes (12.6%, 8.6%, 2.3% respectively). The prevalence of anterior TWI was higher in black athletes (9.5%) than in mixed-race and white athletes (1.5%).

Mixed-race and black athletes had a similar prevalence of inferior TWI (2% vs. 1.5%; p=0.49). This was higher than in mixed-race than in white athletes (2% vs. 0.5%; p=0.004) and in black than in white athletes (1.5% vs. 0.5%; p=0.04). Mixed-raced and black athletes had a similar prevalence of lateral/ apical TWI (0.6% vs. 1.0%; p=0.33) which was also higher among black athletes than in white athletes (1.0% vs. 0.2%); p=0.02 **(Table 1).** No arrhythmias were identified in any group.

Structural changes

Mixed-race athletes revealed a greater LV wall thickness than white athletes even after indexing for body surface area. Black athletes revealed a greater LV wall thickness compared with both white and mixed-race athletes. In absolute terms, LV hypertrophy >12mm was present in 7.1% black athletes, 5.9% mixed-race athletes

and 1.3% white athletes. The maximal LV wall thickness did not exceed 15mm in any athlete.

White athletes demonstrated the largest LV cavity size and mixed-race athletes had larger LV cavities than black athletes. These differences became more pronounced when indexed for BSA. 5.9% white athletes demonstrated a LV end diastolic dimension >58mm, as did 4.4% mixed-race athletes and 3.2% black athletes. None of the athletes showed a LV end diastolic dimension >62mm.

Among athletes with an abnormal EKG (mixed race interpretation as in white athletes), a LV wall thickness >12 mm, LV cavity >60 mm or LV ejection fraction <50%, we had excluded overt cardiomyopathy on the basis of a normal exercise stress test/echocardiogram, 24-hour EKG monitor and absence scar on cardiovascular magnetic resonance imaging prior to inclusion in the study.

Mixed-race athletes revealed EKG characteristics that were more similar to black athletes than white athletes, with specific reference to left and right atrial enlargement and TWI. Inferior and lateral/ apical TWI was rare in all groups, indicating the need for further investigations and clinical surveillance.

Mixed-race athletes demonstrated a mean LV wall thickness and LV cavity size that fell between values observed in the black and white athlete groups. The electrical and structural parameters for the mixed-race athlete seem to be more similar to the black athlete. One in 14 healthy mixed-race athletes demonstrate TWI or have an LV wall thickness >13mm. Based on our observations, anterior TWI and a marginally increased LV wall thickness may be normal adaptation to athletic training in mixed-race athletes.

The study included only elite male soccer players; soccer however involves a combination of strength and endurance exercises and is the most popular sport worldwide. The cross-sectional nature of study precludes comment on the longitudinal implications of repolarization changes, mild LV hypertrophy or LV dilation with reference to development of cardiomyopathy in the future.

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Table 1: Electrocardiographic and echocardiographic features of 3,000 male adolescent athletes according to ethnicity.

EKG/ echocardiogram feature	White (n= 1,000) %	Black (n= 1,000) %	Mixed (n=1,000) %	p value White vs Black	p value White vs Mixed race	p value Black vs Mixed race
Sinus bradycardia <60bpm	45.4	46.5	67	0.65	<0.0001*	<0.0001*
Sinus arrhythmia	37.3	36.8	35.5	0.85	0.43	0.58
LV hypertrophy	25.6	17.6	30	<0.0001*	0.03*	<0.0001*
RV hypertrophy	2.3	4.2	3.0	0.02*	0.4	0.19
Left atrial enlargement	1	5.9	4.7	<0.0001*	<0.0001*	0.27
Right atrial enlargement	0.7	3.9	3.0	<0.0001*	0.0002*	0.33
T wave inversion (TWI) all	2.3	13.0	8.6	<0.0001*	<0.0001*	0.0019*
TWI- anterior V1-V2	0.9	5.8	3.7	<0.0001*	<0.0001*	0.04*
TWI- anterior beyond V2	0.6	3.7	2.0	<0.0001*	0.0089*	0.03*
TWI- inferior	0.5	1.5	2.0	0.04*	0.0039*	0.49
TWI- lateral/ apical	0.2	1	0.6	0.02*	0.29	0.33
TWI- infero-lateral/ apical	0.1	0.9	0.2	0.02*	1	0.06
ST segment elevation	48.4	63.6	54.7	<0.0001*	0.0055*	<0.0001*
Ascending convex	28.8	38.0	32.7	<0.0001*	0.04*	0.0150*
Ascending concave	16.2	21.8	19.8	0.0017*	0.04*	0.3
Isoelectric	3.2	3.3	2.0	1	0.12	0.09
Depressed	0.2	0.5	0.2	0.45	1	0.45
Left atrial diameter (mm)	32.9 ±5.2	32.8 ±4.7	32.6 ±4.4	0.65	0.16	0.33
LVWT (mm)	9.15 ±1.3	10.1 ±1.4	9.8 ±1.41	<0.0001*	<0.0001*	<0.0001*
Relative wall thickness	0.36 ±0.05	0.38 ±0.04	0.37 ±0.05	<0.0001*	<0.0001*	<0.0001*
LVEDd (mm)	52.4 ±3.9	50.6 ±4	51.1 ±4.03	<0.0001*	<0.0001*	0.0054*
LVEDd i (mm/ m^2)	27.9 ±2.12	26.6 ±2.19	27.2 ±2.05	<0.0001*	<0.0001*	<0.0001*
LVM (g)	168 ±33	171 ±35	173 ±31	0.048*	<0.0001*	0.18
LVM i (b/ m^2)	88.1 ±16.5	89.6 ±17.5	91.2 ±16.5	0.04*	<0.0001*	0.03*
LV E/A	2.10 ±0.6	2.02 ±0.5	2.05 ±0.5	0.0012*	0.04*	0.18
RVD1 (mm)	36.58 ±4.76	36.35 ±4.80	36.45 ±4.11	0.28	0.51	0.62
Aortic root root (mm)	27.56 ±3.22	27.93 ±3.16	27.90 ±3.81	0.01*	0.03*	0.85

* denotes statistically significant ($p<0.05$).

E/A = early filling velocity/ atrial filling velocity, LV = left ventricular, LVEDd = left ventricular end diastolic diameter, LVM = left ventricular mass, LVMi = left ventricular mass indexed to body surface area, LVWT = left ventricular wall thickness, M = mixed-race, RV= right ventricular, RVD1 = right ventricular diameter at level of tricuspid valve, TWI= T wave inversion.