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The prevalence, distribution, and clinical outcomes of electrocardiographic repolarization patterns in male athletes of African/Afro-Caribbean origin

Michael Papadakis[1,2], Francois Carre[3], Gaelle Kervio[4], John Rawlins[1,2], Vasileios F. Panoulas[2], Navin Chandra[1,2], Sandeep Basavarajaiah[2], Lorna Carby[2], Tiago Fonseca[2], and Sanjay Sharma[1,2]*

[1]St George's University of London, Cranmer Terrace, SW17 0RE, London, UK; [2]University Hospital Lewisham, London, UK; [3]French Institute of Health and Medical Research (INSERM), U642, Rennes, F-35000, France; and [4]French Institute of Health and Medical Research (INSERM), CIC-IT 804, Rennes, F-35000, France

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Aims Athletic training in male black athletes (BAs) is associated with marked ECG repolarization changes that overlap with hypertrophic cardiomyopathy (HCM). Differentiating between the two entities is prudent since BAs exhibit a higher prevalence of exercise-related sudden death from HCM compared with white athletes (WAs).

Methods and results Between 1996 and 2010, 904 BAs underwent serial cardiac evaluations including ECG and echocardiography. Athletes exhibiting T-wave inversions were investigated further for HCM. Results were compared with 1819 WAs, 119 black controls (BCs), and 52 black HCM patients. Athletes were followed up for 69.7 $\pm$ 29.6 months. T-wave inversions were present in 82.7% HCM patients, 22.8% BAs, 10.1% BCs, and 3.7% WAs. In athletes, the major determinant of T-wave inversions was black ethnicity. T-wave inversions in BAs (12.7%) were predominantly confined to contiguous anterior leads (V1–V4). Only 4.1% of BAs exhibited T-wave inversions in the lateral leads. In contrast, both BCs and HCM patients exhibited lower prevalence of T-wave inversions in leads V1–V4 (4.2 and 3.8%, respectively) with most T-wave inversions in HCM patients (76.9%) involving the lateral leads. During follow-up one BA survived cardiac arrest and two athletes (one BA, one WA) were diagnosed with HCM. All three exhibited T-wave inversions in the lateral leads.

Conclusions T-wave inversions in leads V1–V4 appear to represent an ethnic variant of 'athlete's heart'. Conversely, T-wave inversions in the lateral leads may represent the initial expression of underlying cardiomyopathy and merit further evaluation and regular surveillance.

Keywords Athlete's heart • Echocardiography • Electrocardiography • Ethnicity • Hypertrophic cardiomyopathy

Introduction

Participation in regular, intensive exercise is associated with repolarization changes affecting the ST-segment and T-wave morphology.[1,2] Certain electrical anomalies occasionally overlap with those observed in cardiomyopathies.[3,4] Data from Caucasian athletes [white athletes (WAs)] suggest that 3–4% of athletes exhibit T-wave inversions but their precise significance remains controversial.[1,2,5] Whereas, some authorities regard T-wave inversions to represent physiological variants, a recent longitudinal study reported sudden cardiac deaths (SCDs) from cardiomyopathy in a small proportion of athletes harbouring such repolarization changes.[6]

Limited studies in American football players reveal that athletes of African/Afro-Caribbean origin [black athletes (BAs)] exhibit a greater prevalence of T-wave inversions than WAs.[7,8] In the

*Corresponding author. Tel: +44 208 7255939, Fax: +44 208 7253328, Email: ssharma21@hotmail.com

absence of detailed investigation and longitudinal follow-up, it is uncertain whether T-wave inversions in BAs represent benign ethnic variants of physiological cardiovascular adaptation or potential harbingers of life-threatening cardiac disease. The issue is complicated further because BAs frequently exhibit left ventricular hypertrophy (LVH) which, in the context of co-existent repolarization anomalies, poses significant challenges in differentiating physiological LVH from hypertrophic cardiomyopathy (HCM).[9] This conundrum is of particular significance since exercise-related SCD secondary to HCM in the USA is reportedly higher in BAs.[10] Moreover, a growing number of scientific and sporting bodies recommend/mandate preparticipation cardiac evaluation utilizing 12-lead ECG criteria denoting abnormal results, solely derived from WAs.[11,12] Extrapolation of such criteria to BAs raises the possibility of unnecessary investigation and anxiety, false diagnoses, and potential disqualification from sport.

This study aimed to identify the prevalence and significance of T-wave inversions in highly trained male BAs to facilitate the differentiation between 'black athlete's heart' and HCM.

Methods

Setting

The SCD of several athletes has led many sporting organizations to implement preparticipation evaluation to aid the identification of athletes at risk. Neither the UK nor France offers state-funded cardiovascular preparticipation evaluation. In the UK, the charitable organization Cardiac Risk in the Young subsidizes cardiovascular evaluations for several elite sporting organizations that self-fund evaluations for recruits competing at regional, national, or international level. In France, athletes competing at national or international level are legally obliged to undergo cardiovascular evaluation comprising annual ECG and at least one echocardiogram in their career.

Athletes

Between 1996 and 2010, 2745 male athletes aged 14–35 years were evaluated in the UK and France. Athletes competed at regional, national, or international level. All athletes underwent at least one preparticipation evaluation comprising of a health questionnaire relating to training activity, presence of cardiac symptoms, family history of cardiomyopathy or premature ($\leq$40 years) SCD and drug history, cardiovascular examination, 12-lead ECG, and 2D echocardiography. Black ethnicity was determined through self-reported questionnaires.

Twenty-two athletes were excluded based on blood pressure readings $>$140 mmHg systolic and/or $>$90 mmHg diastolic. The final cohort comprised of 904 BAs and 1819 WAs.

Black controls

The charitable organization Cardiac Risk in the Young also offers cardiovascular evaluation for conditions predisposing to SCD to all young individuals who wish to be tested irrespective of their athletic status. Evaluations are performed throughout the UK and comprise of a health questionnaire, cardiovascular examination, and 12-lead ECG, identical to that performed in athletes. As part of recruitment of healthy black controls (BCs) for this study, we offered all black individuals attending for evaluation an on site 2D echocardiogram.

Between 2006 and 2010, a total of 7326 individuals were assessed. Selection criteria for inclusion as a control in our study included: black ethnicity, male sex, age 14–35 years, sedentary life style defined as $\leq$2 h of organized physical activity per week, absence of cardiac symptoms, drug history and family history of cardiomyopathy, or premature ($\leq$40 years) SCD as well as a structurally normal heart. The final cohort comprised of 119 consecutive, black, sedentary individuals.

Hypertrophic cardiomyopathy patients

Between 2001 and 2010, 155 consecutive patients with HCM were assessed in three specialist cardiomyopathy clinics in South London. These clinics serve populations consisting of a high proportion of individuals of African/Afro-Caribbean descent, reaching as high as 30% in some areas, compared with the average UK national black population of only 2%. Most patients with HCM were diagnosed either following primary care referrals for symptoms, identification of a cardiac murmur or an abnormal ECG or during cardiovascular evaluation in the context of a family history of HCM or SCD, whereas others were referred from district hospitals for specialist opinion.

Hypertrophic cardiomyopathy was defined as LVH with a maximal end-diastolic left ventricular wall thickness (max-LVWT) $\geq$15 mm in the absence of a cardiac or systemic cause, or a max-LVWT $<$15 mm in the context of electrocardiographic repolarization anomalies and identification of HCM in a first-degree relative. Only patients of African/Afro-Caribbean (black) ethnicity were included. Patients subject to therapeutic interventions potentially affecting repolarization patterns, such as septal myomectomy or pacemaker dependent patients, were excluded. A total of 52 patients with HCM fulfilled all inclusion criteria.

Electrocardiography

Standard 12-lead ECGs were performed using a GE Marquette Hellige (Milwaukee, WI, USA) or Philips Pagewriter Trim III (Bothel, WA, USA), as described elsewhere.[13] ST-segment shift and T-wave inversions were considered to represent repolarization abnormalities. ST-segment shift was considered significant if $\geq$0.1 mV in $\geq$2 contiguous leads. T-wave inversion of ≥ -0.1 mV in $\geq$2 leads was considered significant, (excluding AVR, V1 + lead III in isolation). Biphasic T-wave inversion was counted as abnormal if the negative deflection of the T-wave exceeded ≥ -0.1 mV. The distribution of T-wave inversions was classified into three groups: (i) T-wave inversions confined to the anterior leads (V1–V4), (ii) T-wave inversions involving the inferior leads (II, III, AVF), and (iii) T-wave inversions involving the lateral leads (I, AVL, V5, V6). Deep T-wave inversions were defined as a T-wave deflection ≥ -0.2 mV. Left ventricular hypertrophy was identified using the Sokolow–Lyon criterion.[14] Left atrial enlargement was defined as a bi-phasic P-wave in lead V1 where the negative portion was $\geq$0.1 mV deep and $\geq$0.04 s in duration, while Q-waves were considered pathological if $\geq$0.04 s in duration or $\geq$25% of the height of the ensuing R-wave. Left QRS-axis deviation was defined as a frontal axis of -30° to -90°.

All ECGs were read independently by the two senior authors (S.S. and F.C.) in the UK and France, respectively, who are highly experienced in sports cardiology and HCM.

Echocardiography

Two-dimensional echocardiography was performed using either an Accuson Computed Sono-graph 128XP/10c (San Jose, CA, USA), GE Vivid I (Tirat, Israel), Philips Sonos 7500, Philips iE33 or Philips CPX50 (Bothel, WA, USA). Standard views were obtained and cavity and wall thickness measurements were performed using established guidelines.[15] Left atrial diameter and left ventricular internal diameter were measured from the parasternal long-axis view using the two-dimensional images. Left ventricular wall thickness was

measured in the two-dimensional parasternal short-axis view, at the levels of the mitral valve and papillary muscles; the greatest measurement was defined as the max-LVWT. Left ventricular mass (LVM) was calculated with the formula of Devereux.[16] Two-dimensional continuous- and pulsed-Doppler imaging were performed using standard parasternal and apical views.[17] The systolic pulmonary artery pressure was estimated using the simplified Bernoulli equation ($4V^2_{max}$ + right atrial pressure), where V_{max} is the maximal velocity of the tricuspid regurgitant jet measured using continuous-wave Doppler in the four-chamber view.[18] In the absence of a raised jugular venous pressure during cardiovascular examination in any of the athletes, the right atrial pressure was assumed to be 5 mmHg. A cardiologist blinded to the athlete's identity reviewed all scans.

Further evaluation and follow-up

Athletes with significant T-wave inversions ± ST-segment depression and those exhibiting a max-LVWT >12 mm were invited for further clinical evaluation including upright exercise stress testing ± cardiopulmonary testing,[19–22] 24–48 h Holter,[23] cardiac magnetic resonance imaging with gadolinium injection[24,25] and evaluation of first-degree relatives, to check for the broader phenotype of underlying cardiomyopathies, in particular HCM and arrhythmogenic right ventricular cardiomyopathy (ARVC).

Several athletes underwent repeat cardiac evaluations in accordance with the policies of their sporting organizations irrespective of baseline results.

Ethical approval/consent

In the UK, ethical approval was granted by the National Research Ethics Service, Essex 2 Research Ethics Committee. In France, the study was approved by the French Ministry of health and youth. Written consent was obtained from individuals aged ≥16 years and from a parent/guardian for those aged <16 years.

Statistical analysis

Statistical analyses were performed using SPSS software, version 16 (Chicago, IL, USA). Variables were tested for normality using the Kolmogorov–Smirnov test. Values were expressed as mean ± standard deviation (SD) or percentages, as appropriate. Group differences were tested using Student's *t*-test or one-way ANOVA (Sidak test for *post hoc* analysis) and Mann–Whitney *U* or Kruskal–Wallis (Dunn's test for *post hoc* analyses) tests for normally and non-normally distributed variables, respectively. χ^2 test or Fisher's exact test was used as appropriate to test group differences of proportions.

Univariate analyses were performed to determine variables (ethnicity, age, body surface area, hours of training/week, systolic and diastolic blood pressure, mLVWTd, and left atrial size) associated with T-wave inversions and ST-segment elevation among athletes. Binary logistic regression analyses were used to determine the independence of the above associations. The goodness of fit was evaluated using the Hosmer–Lemeshow test. Significance was defined as a two-tailed *P*-value of <0.05 throughout.

Results

Athletes

None of the athletes reported sinister cardiac symptoms, such as angina, breathlessness disproportionate to the amount of exercise being performed, palpitations, dizziness, or syncope during exertion, causing concern to the screening physician or family history of cardiomyopathy or premature SCD and none took regular medication.

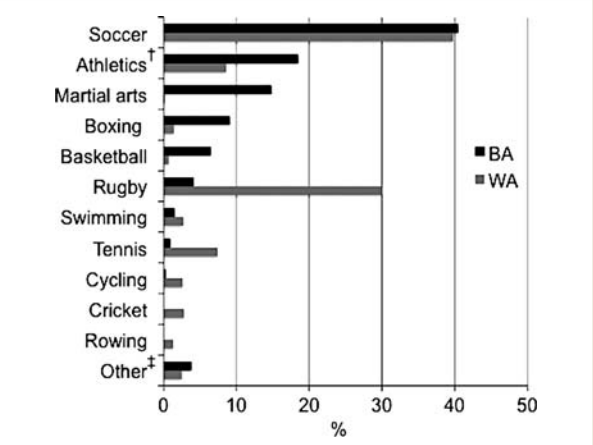

Figure 1 Sporting disciplines expressed as percentage (%) of the total black athlete (black bars) and white athlete (grey bars) cohort, respectively. †Track and field events. ‡<1% of the total cohort. White athletes: biathlon, *n* = 15; speed skating, *n* = 10; Gaelic football, *n* = 7; badminton, *n* = 5. Black athletes: weight lifting, *n* = 6; American football, *n* = 5; gymnastics, *n* = 5; fencing, *n* = 5.

Athletes competed in a total of 25 sporting disciplines (*Figure 1*). Black athletes exercised more than WAs (15.2 ± 6.1 vs. 13.1 ± 6.2 h/week, $P < 0.001$). Black athletes were older (95% aged >16 years old), had higher body surface area and higher systolic blood pressure compared with WAs (*Table 1*).

Black controls

Black sedentary individuals were younger and had lower body surface area but exhibited a higher systolic blood pressure compared with BAs (*Table 1*).

Patients with hypertrophic cardiomyopathy

Detailed demographic, clinical, echocardiographic, and electrocardiographic characteristics of black patients with HCM are reported in *Table 2*.

Prevalence and distribution of repolarization changes

Black athletes vs. white athletes

Both ST-segment elevation and T-wave inversions (including deep T-wave inversions) were commoner in BAs compared with WAs (*Table 3*). T-wave inversions in BAs were predominantly observed in the anterior leads (12.7%) (*Figure 2A* and *2B*) with only 4.1% of BAs exhibiting T-wave inversions in the lateral leads. ST-segment depression was rare in both ethnic groups.

Table 1 Comparison of demographic and echocardiographic parameters between black athletes, white athletes and black controls

Parameter	Black athletes, $n = 904$	White athletes, $n = 1819$	Black controls, $n = 119$	*P*-value
Age (years)	22.5 ± 5.0	17.4 ± 4.1	18.6 ± 6.0	<0.001[a,b,c]
BSA (m^2)	1.92 ± 0.20	1.87 ± 0.24	1.87 ± 0.24	<0.001[a,b]
Systolic BP (mmHg)	116.5 ± 13.1	111.8 ± 11.0	121.7 ± 8.4	<0.001[a,b,c]
Ao (mm)	30.2 ± 3.3	29.5 ± 3.3	28.2 ± 3.1	<0.001[a,b]
LA (mm)	35.4 ± 4.5	34.7 ± 4.7	33.0 ± 4.8	0.002[a,b]
LVED (mm)	52.6 ± 4.4	52.6 ± 4.3	47.9 ± 3.4	<0.001[b,c]
max-LVWT (mm)	10.6 ± 1.6	10.0 ± 1.2	9.2 ± 1.4	<0.001[a,b,c]
LVM (g)	203.4 ± 50.6	188.3 ± 44.1	155.2 ± 34.9	<0.001[a,b,c]
LVM/BSA (g/m^2)	103.7 ± 25.1	98.5 ± 21.8	84.0 ± 14.8	<0.001[a,b,c]
E-wave (m/s)	0.8 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	<0.001[a,b]
A-wave (m/s)	0.5 ± 0.2	0.4 ± 0.1	0.5 ± 0.1	0.34
E/A	2.1 ± 0.9	2.2 ± 0.8	2.2 ± 0.6	0.004[a]

A-wave, late diastolic mitral valve peak inflow peak velocity; Ao, aortic root; BP, blood pressure; BSA, body surface area; E-wave, early diastolic mitral valve peak inflow velocity; FS, fractional shortening; LA, left atrium; LVED, left ventricular cavity diameter in end-diastole; LVM, left ventricular mass; max-LVWT, maximal left ventricular wall thickness in end-diastole.
[a]Statistically significant between black athletes and white athletes.
[b]Statistically significant between black athletes and black controls.
[c]Statistically significant between white athletes and black controls.

Black athletes vs. black sedentary individuals vs. black patients with HCM

There were no differences in the prevalence of ST-segment elevation between BAs and BCs; however, both the athletes and controls exhibited a significantly higher prevalence of ST-segment elevation compared with individuals with HCM (63.2% BAs vs. 65.5% BCs vs. 9.6% HCM, $P < 0.001$) (*Figure 3A*). In contrast, ST segment depression was virtually absent in athletes and controls but was common in individuals with HCM (0.4% BAs vs. 0% BCs vs. 50% HCM, $P < 0.001$).

Individuals with HCM exhibited a higher prevalence of T-wave inversions (including deep T-wave inversions) compared with athletes and controls (22.8% BAs vs.10.1% BCs vs. 82.7% HCM, $P < 0.001$) (*Figure 3A*). There were also significant differences in the distribution of T-wave inversions between the groups; BAs had a higher prevalence of T-wave inversions in the anterior leads compared with BC and HCM patients (12.7% BAs vs. 4.2% BCs vs. 3.8% HCM, $P = 0.006$), whereas individuals with HCM had a higher prevalence of T-wave inversions in the lateral leads (4.1% BAs vs. 3.4% BCs vs. 76.9% HCM, $P < 0.001$). All groups revealed a similar prevalence of T-wave inversions in the inferior leads (6% BAs vs. 2.5% BCs vs. 1.9% HCM, $P = 0.21$) (*Figure 3B*).

ST-segment morphology

Several ST-segment morphologies were noted in BAs including convex ST-segments, concave/saddle-shaped and high take-off patterns (*Figure 2C*). The convex ST-segment pattern was more prevalent in BAs compared with BCs and WAs (38.4 vs. 6.7 vs. 2.7%, $P < 0.001$). Most (64.3%) T-wave inversions in the anterior leads in BAs were preceded by convex ST-segment elevation (*Figure 2B*).

Echocardiography

Both BAs and WAs exhibited greater max-LVWT and cavity size compared with BCs. Black athletes exhibited greater max-LVWT compared with WAs. In absolute terms, 112 (12.4%) BAs exhibited LVH (max-LVWT >12 mm) compared with only 29 (1.6%) WAs. The max-LVWT did not exceed 16 mm in any athlete (*Figure 4*). Athletes with LVH had normal or increased left ventricular cavity size and normal indices of diastolic function.

None of the athletes with T-wave inversions in the anterior precordial leads exhibited right ventricular hypokinesia, regional wall motion abnormalities or aneurismal bulging of the right ventricle indicative of ARVC and none had a pulmonary artery pressure of ≥30 mmHg or evidence of an intra-cardiac shunt on colour-flow echocardiography.

Exercise stress testing, Holter monitor, cardiac magnetic resonance imaging, and familial evaluation in athletes

All 350 athletes with T-wave inversions and/or LVH on echocardiography were invited to undergo further investigations to exclude the broad phenotype of HCM. Of the 350 athletes, 233 (66%) were investigated comprehensively with the full complement of tests including exercise testing, 24–48 h Holter monitor, and cardiac magnetic resonance imaging. The remaining 34% either failed to attend ($n = 62$, 18%), attended only for some of the investigations ($n = 20$, 6%), or moved clubs and could not be traced ($n = 35$, 10%).

All athletes achieved a peak-VO_2 >120% predicted. Thirteen athletes exhibited ≥100 ventricular or supra-ventricular extrasystoles over 24 h, which did not exceed >0.5% of the total heartbeats. Only one BA exhibited asymmetric septal hypertrophy

Table 2 Demographic, clinical, echocardiographic, and electrocardiographic characteristics of black patients with HCM

	Black HCM patients ($n = 52$)
Demographic and clinical characteristics (%)	
Age of diagnosis (years)	48.1 ± 17.1
Gender (males)	61.5
Family history of HCM/SCD	34.6
Patients on treatment	51.9
β-Blockers	26.9
Calcium antagonists	26.9
Amiodarone	7.7
Diuretics	17.3
Disopyramide	3.8
Intracardiac defibrillator *in situ*	5.8
Echocardiographic characteristics	
Ao (mm)	31.3 ± 3.7
LA (mm)	40.9 ± 7.3
LVED (mm)	44.0 ± 6.1
max-LVWT (mm)	17.4 ± 4.9
LVM (g)	279.6 ± 106.5
E-wave (m/s)	0.70 ± 0.18
A-wave (m/s)	0.67 ± 0.18
E/A	1.11 ± 0.44
SAM (%)	23.1
LVOT gradient ≥30 mmHg (%)	23.1
LVH pattern (%)	
ASH	25
Concentric	44.2
Apical	28.8
No hypertrophy	1.9
Electrocardiographic characteristics (%)	
LVH (Sokolow and Lyon)	53.8
LA enlargement	44.2
Pathological Q-waves	11.5
Left-axis deviation	11.5
Inverted T-waves	82.7
T-wave inversions in V1–V4	3.8
T-wave inversions in inferior leads	1.9
T-wave inversions in lateral leads	76.9
Deep T-wave inversions	69.2
ST-segment elevation	9.6
ST-segment depression	50

Where applicable results are expressed as mean ± standard deviation. A-wave, late diastolic mitral valve peak inflow peak velocity; Ao, aortic root; ASH, asymmetric septal hypertrophy, BP, blood pressure; BSA, body surface area; E-wave, early diastolic mitral valve peak inflow velocity; FS, fractional shortening; HCM, Hypertrophic cardiomyopathy; LA, left atrium; LVED, left ventricular cavity diameter in end-diastole; LVH, left ventricular hypertrophy; LVM, left ventricular mass; LVOT, left ventricular outflow tract; max-LVWT, maximal left ventricular wall thickness in end-diastole; NYHA, New York Heart Association; SAM, systolic anterior motion of the anterior mitral valve leaflet; SCD, sudden cardiac death.

(15 mm) on cardiac magnetic resonance imaging. None of the athletes revealed evidence of gadolinium enhancement. We had the opportunity to investigate first-degree relatives in only 33 (9.4%) athletes and identified HCM in one parent.

Determinants of repolarization changes in athletes

Univariate analyses demonstrated a significant association between ST-segment elevation and ethnicity, age, body surface area, hours of training/week, left atrial size, and max-LVWT. Multivariable analysis revealed that black ethnicity was the strongest independent predictor with BAs being four times more likely to exhibit ST-segment elevation compared with WAs (OR 3.95; 95% CI 2.73–5.75, $P < 0.001$). The only other predictor was the hours of training/week (OR 1.03, 95% CI 1.00–1.06, $P = 0.03$).

Univariate analysis demonstrated significant association between T-wave inversions and ethnicity, age, hours of training/week, systolic blood pressure, and max-LVWT. After adjustment for all variables, black ethnicity was the strongest independent predictor with BAs being almost six times more likely to exhibit T-wave inversions compared to WAs (OR 5.56; 95% CI 3.55–8.70, $P < 0.001$). The only other predictor identified was max-LVWT (OR 1.18; 95% CI 1.02–1.35, $P = 0.02$).

Clinical significance of repolarization changes

Of all 2723 athletes, follow-up data were available in 1243 (46%) athletes who underwent ≥2 cardiac evaluations either as part of the standard preparticipation evaluation programme or on-going clinical surveillance based on the presence of marked repolarization changes and/or LVH. During a mean follow-up of 69.7 ± 29.6 months, three athletes were diagnosed with HCM.

Athlete 1 (black soccer player) was diagnosed following an abnormal ECG showing deep T-wave inversions and ST-segment depression in the inferior and lateral leads in the context of asymmetric septal hypertrophy and a non-dilated LV cavity on echocardiography and cardiac magnetic resonance imaging (*Figure 5*). Athlete 2 (black soccer player) exhibited T-wave inversions in the inferior and lateral leads with mild concentric LVH on echocardiography and cardiac magnetic resonance imaging (*Figure 5*). These features were initially considered to represent 'athlete's heart' based on a peak-VO_2 >120% of maximum predicted and the absence of the broad HCM phenotype. The athlete was retrospectively diagnosed with HCM after successful resuscitation from ventricular fibrillation arrest during a football match. Athlete 3 (white triathlete) also exhibited T-wave inversions in the inferior and lateral leads but had a structurally normal heart on echocardiography and cardiac magnetic resonance imaging (*Figure 5*). The athlete demonstrated high peak-VO_2 and normal Holter recording but was diagnosed with HCM following identification of the apical form of HCM in his mother and subsequent confirmation with gene testing which identified a myosin-binding protein C mutation in both individuals.

Table 3 Electrocardiographic characteristics of black and white athletes

Parameter	Black athletes, $n = 904$ (%)	White athletes, $n = 1819$ (%)	Black controls, $n = 119$ (%)	*P*-value BAs vs. WAs	*P*-value BAs vs. BCs
Sinus bradycardia[a]	47.1	60.7	20.2	<0.001	<0.001
First-degree AV block	11.2	3.6	2.5	<0.001	0.003
QRS duration (ms)	88 ± 13	96 ± 10	89 ± 9	<0.001	0.42
QTc (ms)	393 ± 26	404 ± 20	400 ± 18	<0.001	0.005
Partial RBBB	24.7	12.3	5.0	<0.001	<0.001
RBBB	0.3	1.2	0	0.03	0.53
Left-axis deviation	1.1	0.6	2.5	0.10	0.20
Right-axis deviation	0.1	0.9	0	0.01	0.72
Pathological Q-waves	0.9	0.4	0	0.152	0.31
LA enlargement	8.6	2.8	5.9	<0.001	0.17
RA enlargement	6.3	0.3	2.5	<0.001	0.066
LVH	23.2	36.8	39.5	<0.001	<0.001
RVH	13.3	2.6	4.2	<0.001	<0.001
Inverted T-waves	22.8	3.7	10.1	<0.001	0.003
T-wave inversions in V1–V4	12.7	1.9	4.2	<0.001	0.007
T-wave inversions in inferior leads	6	1.5	2.5	<0.001	0.12
T-wave inversions in lateral leads	4.1	0.3	3.4	<0.001	0.70
Deep T-wave inversions	12.1	1	1.7	<0.001	0.002
ST-segment elevation	63.2	26.5	65.5	<0.001	0.61
ST-segment depression	0.4	0	0	0.01	0.47

Where applicable results are expressed as mean ± standard deviation. AV, atrioventricular; LA, left atrium; LVH, left ventricular hypertrophy; RA, right atrium; RBBB, right bundle branch block; RVH, right ventricular hypertrophy.
[a]Heart rate <60 b.p.m.

Other significant findings in athletes

Nineteen athletes (0.7%) exhibited structural or electrical abnormalities, excluding HCM: Wolff–Parkinson–White ($n = 4$), long-QT syndrome ($n = 3$), Brugada syndrome ($n = 1$), bicuspid aortic valve ($n = 3$), patent foramen ovale ($n = 3$), atrial septal defect ($n = 2$), ventricular septal defect ($n = 1$), mitral valve prolapse ($n = 1$), and cor-triatriatrum ($n = 1$).

Discussion

Cross-sectional studies in black US football players have revealed a high prevalence of repolarization changes that occasionally overlap with the phenotype observed in HCM.[7,8] This study attempted to elucidate the significance of repolarization changes in 904 BAs competing in 25 different sporting disciplines by comparing repolarization changes in BAs, with those observed in sedentary black individuals and black individuals with HCM, to facilitate differentiation between expressions of ethnicity alone, ethnic variation in physiological adaptation to exercise, and quiescent cardiac pathology. In contrast with other studies, this is the first study where all BAs were assessed with 2D echocardiography and a significant proportion of BAs, with a range of repolarization phenotypes, underwent more comprehensive evaluation and follow-up, in an attempt to provide a clinical perspective for ECG repolarization changes in BAs.

Black athletes demonstrated a high prevalence of repolarization changes; almost 25% exhibited T-wave inversions and two-thirds showed ST-segment elevation.

Ethnic differences in repolarization changes in elite athletes

Anterior leads

Black athletes exhibited a greater prevalence of T-wave inversions confined to the anterior leads compared with BCs, indicating that anterior T-wave inversions probably represent an ethnic response to physiological adaptation to exercise rather than an effect of ethnicity alone. In contrast, T-wave inversions confined to the anterior leads were uncommon in HCM. Further support that anterior T-wave inversions represent physiological adaptation comes from previously reported observations by our group demonstrating regression of anterior T-wave inversions in BAs as early as 6 weeks after cessation of exercise.[26] Although, T-wave inversions in the anterior leads are also the hallmark of ARVC,[27] our athletes with T-wave inversions did not fulfil any other criteria for ARVC during subsequent investigation. The high prevalence of T-wave inversions in the anterior leads in BAs, the co-existence of preceding ST-segment elevation in a large proportion, and the

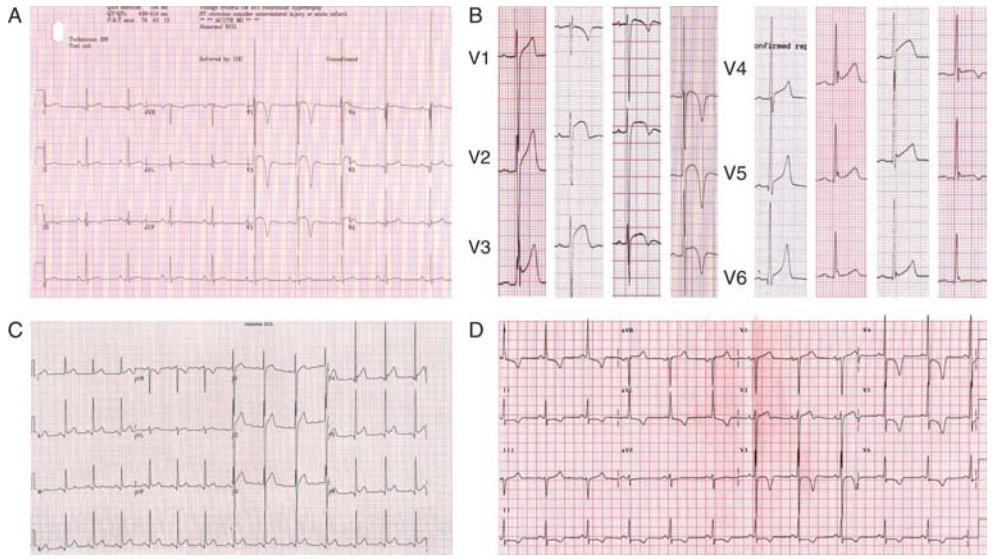

Figure 2 ECG examples demonstrating common repolarization changes in black individuals. (*A*) black long-distance runner with convex ST-segment elevation and deep T-wave inversions in leads V1–V3, (*B*) examples of common ST-segment morphologies in leads V1–V3 and V4–V6 in black athletes, (*C*) black sedentary individual with widespread ST-segment elevation of the concave/saddle-shaped and high take-off pattern, (*D*) black hypertrophic cardiomyopathy patient with ST-segment depression and deep T-wave inversions in the lateral leads.

demonstration of regression with detraining suggests that such repolarization changes are unlikely to represent ARVC.

Inferior leads

The prevalence of T-wave inversions in the inferior leads was similar in all groups. Isolated inferior T-wave inversions in the athletic groups commonly involved leads III and AVF, which in the authors' experience of 14 years of preparticipation evaluation, do not represent a malignant phenotype.

Lateral leads

T-wave inversions in the lateral leads were present in a similar proportion of black individuals irrespective of athletic activity (3–4%), implying that such ECG patterns may reflect ethnic variation in most BAs. However, the majority of patients with HCM and all 3 athletes diagnosed with the disorder during follow-up exhibited T-wave inversions in the lateral leads (*Figure 2D*), indicating that such ECG repolarization patterns should be viewed with caution in any athlete, since a proportion may represent HCM.

Our conclusion relating to the potentially sinister nature of lateral T-wave inversions is further supported by the study of Pelliccia *et al.*[6] where all athletes with marked repolarization abnormalities who were diagnosed with a cardiomyopathy during subsequent follow-up exhibited T-wave inversions in the lateral leads.

ST-segment shift

ST-segment elevation was highly prevalent in all black individuals irrespective of athletic training suggesting an ethnicity-related effect.[28,29] More detailed inspection of the morphology of the ST-segments revealed that although the concave/saddle-shaped patterns (*Figure 2B* and *C*) simulating acute pericarditis were common in both groups, convex ST-segment elevation in leads V1–V4 (*Figure 2A* and *B*) that often mimic acute anterior myocardial infarction or the Brugada phenotype, were six-fold commoner in the athletes, indicating a physiological response to training.

Clinical implications

Based on current recommendations, the identification of marked repolarization changes on an athlete's ECG is an indication for further investigation.[11] Extrapolation of ECG criteria derived from WAs would affect a considerable proportion of the elite BAs population. If consideration is given to the presence of T-wave inversions alone, almost 25% of our BAs cohort would fall within the grey zone warranting further investigations and potentially face unfair disqualification.

Following the observations in this study, the investigators would consider anterior T-wave inversions confined to leads V1–V4, especially when associated with convex ST-segment elevation, to represent an ethnically determined, physiological response to exercise. In contrast, BAs exhibiting T-wave inversions in the lateral leads or ST-segment depression warrant comprehensive cardiovascular evaluation and continued clinical surveillance, since such anomalies may represent initial or incomplete expressions of HCM. Applications of these criteria could reduce the number of BAs with repolarization changes requiring further investigations to as low as 4% and would represent major cost savings in countries with a large proportion of elite BAs.

Limitations

The follow-up period was relatively short considering event rates in HCM are low and the authors did not have complete follow-up

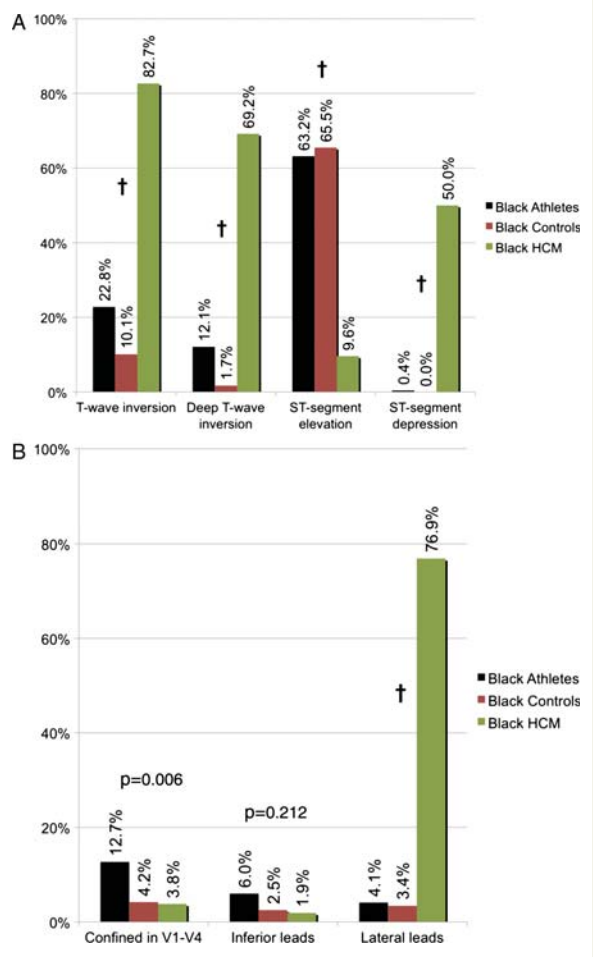

Figure 3 (*A*) Histogram demonstrating the prevalence of repolarization changes as percentage (%) of the total cohort in black athletes, black controls, and black hypertrophic cardiomyopathy patients groups. (*B*) Histogram demonstrating the distribution of T-wave inversions as percentage (%) of the total cohort in the three groups. $^{\dagger}P < 0.001$ when comparing the three groups.

data, including evaluation of first-degree relatives, in a significant number of athletes. However, follow-up data was available in a substantial number of athletes ($n = 1243$) to enable relatively accurate conclusions, especially when one takes into consideration the practical difficulties associated with motivating apparently well athletes to attend clinical institutions in the absence of perceived benefit relating to exercise performance.

The diagnosis of HCM was established only in athletes with repolarization changes and/or LVH who exhibited fatal arrhythmias, familial disease, or asymmetric septal hypertrophy with a non-dilated left ventricle. However, HCM is heterogeneous with respect to its phenotypic expression and therefore milder/more benign forms of the disorder may not have been identified. Although it is plausible that athletes without repolarization anomalies on their ECG or athletes with T-wave inversions confined in the anterior leads and those with T-wave inversions in the inferior leads may harbour quiescent disease, our follow-up findings did not provide any indicators to support this statement.

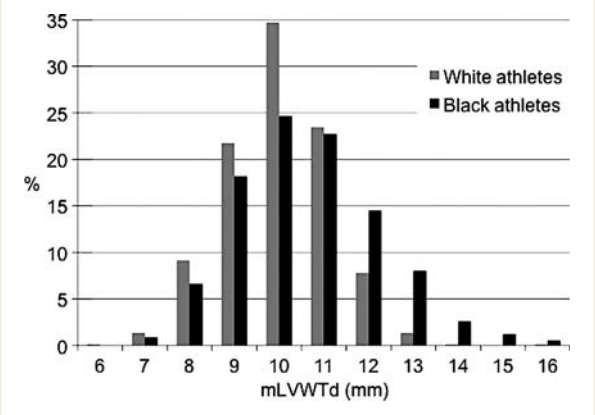

Figure 4 Histogram demonstrating the distribution of maximal left ventricular wall thickness at end-diastole (mLVWTd) as percentage (%) of the total black athlete (black bars) and white athlete (grey bars) cohort, respectively.

The authors recognize that misuse of performance-enhancing substances is associated with LVH and repolarization changes, however, most athletes studied were part of national and international squads and underwent regular testing for the presence of such substances.

Only 52 patients with HCM were included in the study, limiting the conclusions that can be deduced relating to the qualitative characteristics of black individuals with HCM. However, this number is relatively large when one considers that only 2–3% of the UK population is of African/Afro-Caribbean origin. The definition of HCM (LVH in the absence of a cardiac or systemic cause) *per se* marred a conclusive diagnosis of HCM in many affected black individuals since over 50% aged >40 years old have hypertension which is also a recognized cause of LVH.[30,31] Our predicament is supported by a multicentre American study involving 1986 HCM patients where only 8% were black.[32]

Finally, we were unable to utilize genetic testing to aid the differentiation of athlete's heart from HCM outside the context of familial disease, as per guidelines.[33]

Conclusion

The current study observed a striking association of T-wave inversions in contiguous lateral leads with a potentially fatal cardiomyopathy but event-free episodes in athletes with T-wave inversions confined to leads V1–V4, suggesting that T-wave inversions in leads V1–V4, commonly associated with convex ST-segment elevation in BAs, are likely to represent an ethnic variant of 'athlete's heart'. Conversely, T-wave inversions in the lateral leads may represent the initial expression of HCM and merit further cardiovascular evaluation and regular follow-up.

The relatively low event rate in HCM and short follow-up period of our athletes necessitates a larger, multicentre study of longer duration to validate our conclusions.

LA (mm)	IVSd (mm)	LVPWd (mm)	LVED (mm)	LVM (g)	E/A	Athlete
42	15	12	48	302	1.8	1
36	14	14	46	256	2.4	2
34	11	9	49	175	2.4	3

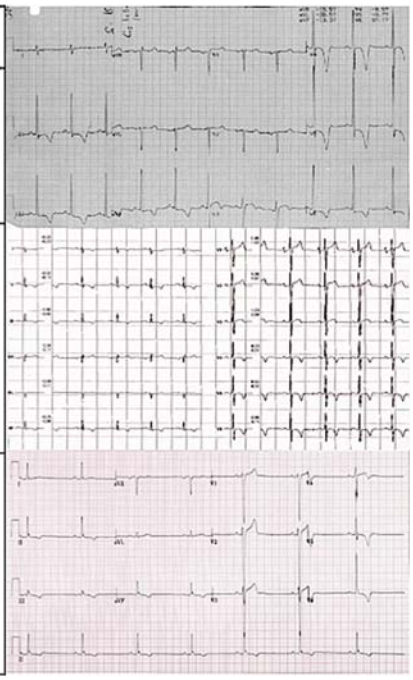

Figure 5 12-lead electrocardiograms and echocardiographic data of all three athletes diagnosed with hypertrophic cardiomyopathy during subsequent follow-up. Abbreviations: A, late diastolic mitral valve inflow peak velocity; E, early diastolic mitral valve peak inflow velocity; IVSd, maximal left ventricular septal wall thickness in end-diastole; LA, left atrium; LVED, left ventricular cavity diameter in end-diastole; LVM, left ventricular mass; and LVPWd, maximal left ventricular posterior wall thickness in end-diastole.

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References

1. Papadakis M, Basavarajaiah S, Rawlins J, Edwards C, Makan J, Firoozi S, Carby L, Sharma S. Prevalence and significance of T-wave inversions in predominantly Caucasian adolescent athletes. *Eur Heart J* 2009;**20**:1728–1735.
2. Pelliccia A, Maron BJ, Culasso F, Di Paolo FM, Spartaro A, Biffi A, Caselli G, Piovano P. Clinical significance of abnormal electrocardiographic patterns in trained athletes. *Circulation* 2000;**102**:278–284.
3. Ryan MP, Cleland JGF, French JA, Joshi J, Choudhury L, Choinowska L, Michalak E, Al-Mahdawi S, Nihoyannopoulos P, Oakley CM. The standard electrocardiogram as a screening test for hypertrophic cardiomyopathy. *Am J Cardiol* 1995;**76**: 689–694.
4. Marcus FI. Prevalence of T-wave inversion beyond V1 in young normal individuals and usefulness for the diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia. *Am J Cardiol* 2005;**95**:1070–1071.
5. Sharma S, Whyte G, Elliott P, Padula M, Kaushal R, Mahon N, McKenna WJ. Electrocardiographic changes in 1000 highly trained junior elite athletes. *Br J Sports Med* 1999;**33**:319–324.
6. Pelliccia A, Di Paolo FM, Quattrini FM, Basso C, Culasso F, Popoli G, De Luca R, Spataro A, Biffi A, Thiene G, Maron BJ. Outcomes in athletes with marked ECG repolarisation abnormalities. *N Engl J Med* 2008;**358**:152–161.
7. Choo JK, Abernethy WB III, Hutter AM Jr. Electrocardiographic observations in professional football players. *Am J Cardiol* 2002;**90**:198–200.
8. Magalski A, Maron BJ, Main ML, McCoy M, Florez A, Reid KJ, Epps HW, Bates J, Browneet JE. Relation of race to electrocardiographic patterns in elite American football players. *J Am Coll Cardiol* 2008;**51**:2250–2255.
9. Basavarajaiah S, Boraita A, Whyte G, Wilson M, Carby L, Shah A, Sharma S. Ethnic differences in left-ventricular remodeling in highly-trained athletes. Relevance to differentiating physiologic left ventricular hypertrophy from hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2008;**51**:2256–2262.
10. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes. Analysis of 1866 deaths in the United States, 1980–2006. *Circulation* 2009;**119**:1085–1092.
11. Corrado D, Pelliccia A, Bjørnstad HH, Vanhees L, Biffi A, Borjesson M, Panhuyzen-Goedkoop N, Deligiannis A, Solberg E, Dugmore D, Mellwig KP, Assanelli D, Delise P, van-Buuren F, Anastasakis A, Heidbuchel H, Hoffmann E, Fagard R, Priori SG, Basso C, Arbustini E, Blomstrom-Lundqvist C, McKenna WJ, Thiene G. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol: consensus statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur Heart J* 2005;**26**:516–520.
12. Bille K, Figuiras D, Schamasch P. Sudden cardiac death in athletes. The Lausanne recommendations. *Eur J Cardiovasc Prev Rehabil* 2006;**13**:859–875.
13. Rawlins J, Carre F, Kervio G, Papadakis M, Chandra N, Edwards C, Whyte GP, Sharma S. Ethnic differences in physiological cardiac adaptation to intense physical exercise in highly trained female athletes. *Circulation* 2010;**121**:1078–1085.

14. Sokolow M, Lyon TP. The ventricular complex in left ventricular hypertrophy obtained by unipolar precordial and limb leads. *Am Heart J* 1949;**37**:161–186.
15. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise J, Solomon S, Spencer KT, Sutton MST, Stewart W. Recommendations for chamber quantification. *Eur J Echocardiogr* 2006;**7**:79–108.
16. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 1986;**57**:450–458.
17. Lewis JF, Spirito P, Pellicia A, Maron BJ. Usefulness of Doppler echocardiographic assessment of diastolic filling in distinguishing "athlete's heart" from hypertrophic cardiomyopathy. *Br Heart J* 1992;**68**:296–300.
18. Chan KL, Currie PJ, Seward JB, Hagler DJ, Mair DD, Tajik AJ. Comparison of 3 Doppler ultrasound methods in the prediction of pulmonary artery pressure. *J Am Coll Cardiol* 1987;**9**:549–554.
19. Bruce RA. Exercise testing of patients with coronary artery disease. Principles and normal standards for evaluation. *Ann Clin Res* 1971;**3**:323–332.
20. Frenneaux MP, Counihan PJ, Caforio AL, Chikamori T, McKenna WJ. Abnormal blood pressure response during exercise testing in hypertrophic cardiomyopathy. *Circulation* 1990;**82**:1995–2002.
21. Sharma S, Elliott PM, Whyte G, Mahon N, Virdee MS, Mist B, McKenna WJ. Utility of metabolic exercise testing in distinguishing hypertrophic cardiomyopathy from physiologic left ventricular hypertrophy in athletes. *J Am Coll Cardiol* 2000;**36**:864–870.
22. Gimeno JR, Tome-Esteban M, Lofiego C, Hurtado J, Pantazis A, Lambiase P, Mist B, Mckenna WJ, Elliott PM. Exercise-induced ventricular arrhythmias and risk of sudden cardiac death in patients with hypertrophic cardiomyopathy. *Eur Heart J* 2009;**30**:2599–2605.
23. Monseratt L, Elliot PM, Gimeno JR, Sharma S, Penas-Lado M, McKenna WJ. Non-sustained ventricular tachycardia in hypertrophic cardiomyopathy: an independent risk marker of sudden death in young patients. *J Am Coll Cardiol* 2003;**42**:873–879.
24. Grothues F, Smith GC, Moon JCC, Bellenger NG, Collins P, Klein HU, Pennell DJ. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. *Am J Cardiol* 2002;**90**:29–34.
25. Grothues F, Moon JC, Bellenger NG, Smith GS, Klein HU, Pennell DJ. Interstudy reproducibility of right ventricular volumes, function and mass with cardiovascular magnetic resonance. *Am Heart J* 2004;**147**:218–223.
26. Rawlins J, Mills P, Sharma S. ECG repolarisation abnormalities in an African descent athlete: pathologic or physiologic finding? In: Pelliccia A (ed.), *Sports Cardiology Case Book*. London, England: Springer-Verlag London Limited; 2009. p85–91.
27. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA, Calkins H, Corrado D, Cox MGPJ, Daubert JP, Fontaine G, Gear K, Hauer R, Nava A, Picard MH, Protonotarios N, Saffitz JE, Yoerger Sanborn DM, Steinberg JS, Tandri H, Thiene G, Towbin JA, Tsatsopoulou A, Wichter T, Zareba W. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. *Circulation* 2010;**121**:1533–1541.
28. Powel SJ. Unexplained electrocardiograms in the African. *Brit Heart J* 1959;**21**:542–548.
29. Seriki O, Smith AJ. The electrocardiogram of young Nigerians. *Am Heart J* 1966;**72**:153–157.
30. Cappuccio FP, Cook DG, Atkinson RW, Strazzullo P. Prevalence, detection, and management of cardiovascular risk factors in different ethnic groups in south London. *Heart* 1997;**78**:555–563.
31. Agyemang C, Bhopal R. Is the blood pressure of people from African origin adults in the UK higher or lower than that in European origin white people? A review of cross-sectional data. *J Hum Hypertens* 2003;**17**:523–534.
32. Maron BJ, Carney KP, Lever HM, Lewis JF, Barac I, Casey SA, Sherrid MV. Relationship of race to sudden cardiac death in competitive athletes with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2003;**41**:974–980.
33. Garratt CJ. for the Heart Rhythm UK Familial Sudden Death Syndromes Statement Development Group. Clinical indications for genetic testing in familial sudden cardiac death syndromes: an HRUK position statement. *Heart* 2008;**94**:502–507.