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Prevalence and significance of T-wave inversions in predominantly Caucasian adolescent athletes

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Aims Athletic activity is associated with electrocardiographic T-wave inversions in some adults, resembling those observed in cardiomyopathy. The prevalence and significance of T-wave inversions in adolescent athletes, the group most vulnerable to exercise-related sudden death from cardiomyopathy, is unknown.

Methods and results This study evaluated 1710 adolescent athletes and 400 healthy controls. Subjects with T-wave inversions underwent intensive cardiac investigations to identify a potential cause. There was no significant difference in the overall prevalence of T-wave inversions between athletes and controls (4 vs. 3%; $P = 0.46$). T-wave inversions in leads V1–V3 were largely confined to athletes and controls aged <16 years. Only 0.1% of athletes aged ≥16 years exhibited T-wave inversions beyond V2. T-wave inversions in the inferior and/or lateral leads and deep T-wave inversions occurred infrequently in athletes (1.5 and 0.8%, respectively) and were associated with a high prevalence of left ventricular hypertrophy or congenital cardiac anomalies. Despite intensive investigations, no athlete was diagnosed with a cardiomyopathy.

Conclusions T-wave inversions in V1–V3 are relatively common in athletes <16 years and probably represent the juvenile electrocardiogram pattern. In adolescent athletes, T-wave inversions beyond V2 if ≥16 years, T-wave inversions in the inferior/lateral leads and deep T-wave inversions in any lead are unusual, warranting further investigations for underlying cardiomyopathy.

Keywords Athelete's heart • Adolescent • Electrocardiography • T-wave inversion • Pre-participation

Introduction

Regular participation in intensive physical training is associated with an increase in cardiac dimensions[1,2] and pronounced cardiac vagal tone.[3] These physiological responses that are fundamental to generating and sustaining a high cardiac output for prolonged periods collectively constitute the athlete's heart and are commonly reflected on the surface electrocardiogram (ECG) in the form of high-voltage QRS complexes, sinus bradycardia, and repolarization changes.[4,5] Certain repolarization anomalies, specifically T-wave inversions, are rare in athletes but are common manifestations in individuals with hypertrophic cardiomyopathy (HCM)[6] and arrhythmogenic right ventricular cardiomyopathy (ARVC)[7] which collectively account for over one-third of all sudden cardiac deaths (SCDs) in young athletes.[8,9]

The prevalence of T-wave inversions in adult athletes is 3–4%.[5,7,10] However, neither the prevalence nor the significance of T-wave inversions in adolescent athletes have been studied in depth. Adolescent athletes and even younger children participating in competitive sport are of particular interest since they are the most vulnerable cohort at risk of exercise-related SCD from underlying cardiomyopathies.[11,12] The interpretation of the ECG in young, asymptomatic adolescent athletes can be challenging, since they often exhibit T-wave inversions in the right precordial leads (V1–V3), similar to ARVC, which are considered to represent the normal juvenile ECG pattern and large magnitude QRS complexes resembling those observed in HCM, secondary to thin chest walls.[4]

In the pre-participation screening era, accurate differentiation between ECG patterns related to physical maturation or

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physiological ventricular remodelling secondary to exercise, from HCM or ARVC, is crucial. The aim of this study was to identify the prevalence of T-wave inversions and their relationship to structural heart disease, with view to improving the identification of young athletes at risk of sudden death during sport, as well as minimizing the number of adolescent athletes subjected to unnecessary investigations following an initial pre-participation screening ECG.

Methods

Setting

The death of several professional sports persons from structural or electrical cardiac defects has led to discussions relating to pre-participation cardiovascular evaluation of all athletes for the identification of potentially sinister cardiovascular disorders prior to selection for competition. Owing to financial constraints, the UK, as with many other countries in the developed world, does not offer a state-funded cardiovascular evaluation of athletes; however, some sporting organizations provide independent, self-funded cardiovascular evaluation for all junior recruits competing (or expected to) at regional or national level. For the past 12 years, the Centre of Sports Cardiology at the Olympic Medical Institute which is funded by the charitable organisation Cardiac Risk in the Young (CRY) has been responsible for performing cardiovascular evaluations for a variety of elite sporting organizations. In some sporting organizations such as the British lawn tennis association, premier rugby league, premier league football, the national swimming, and boxing squad, cardiac evaluation is a mandatory pre-requisite prior to on-going competition. However, in other circumstances, e.g. basketball and field and track athletics, the cardiovascular evaluation of all athletes in any given club/team is performed at the jurisdiction of the club coach or doctor. The senior author (S.S.) has been responsible for conducting and supervising all screenings since 1996.

Between April 1996 and April 2008, 1710 post-pubertal adolescent athletes and 400 healthy controls underwent a cardiac evaluation, comprising of a health questionnaire relating to training activity, presence of cardiac symptoms, family history of cardiomyopathy, or premature ($\leq$40 years old) SCD and drug history, cardiovascular examination including blood pressure measurement, 12-lead ECG, and two-dimensional transthoracic echocardiography. None of the athletes were excluded on the basis of poor echocardiographic windows or unacceptable ECG tracings. Criteria for puberty were the onset of menstruation in females, and voice changes in males.

Based on responses ascertained from the health questionnaire, none of the subjects had prior symptoms suggestive of underlying cardiac disease, family history of cardiomyopathy, or premature SCD, and none of the athletes were taking any relevant medication, including performance-enhancing drugs. All subjects were normotensive with a systolic blood pressure reading of $\leq$120 mmHg and diastolic of $\leq$80 mmHg. Athletes and controls with significant T-wave inversions were investigated further with exercise tolerance testing, 48 h Holter monitor, and cardiac magnetic resonance (CMR) imaging, in an attempt to identify the broader phenotype of HCM or ARVC. All first-degree relatives of adolescents with significant T-wave inversions were invited for cardiovascular screening to check specifically for phenotypic evidence of a familial cardiomyopathy.

Ethical approval for the study was granted by Harrow Research Ethics Committee to the charity Cardiac Risk in the Young, Centre of Sports Cardiology. Written consent for cardiac evaluation was obtained from individuals aged $\geq$16 years and from a parent or guardian for those aged $<$16 years.

Athletes

All athletes competed at regional or national level and represented a variety of sport disciplines, including football (soccer), $n = 445$ (26%); tennis, $n = 393$ (23%); rugby, $n = 240$ (14%); swimming, $n = 171$ (10%); rowing, $n = 72$ (4%); cycling, $n = 50$ (3%); athletics $n = 48$ (3%); hurling, $n = 45$ (3%); triathlon, $n = 42$ (2.5%); netball, $n = 41$ (2.5%); badminton, $n = 40$ (2%); basketball, $n = 38$ (2%); boxing, $n = 34$ (2%); fencing, $n = 26$ (1.5%); and speed skating, $n = 25$ (1.5%). Of the 1710 athletes, 1414 (83%) were males and 1645 (96%) were Caucasian. The mean age and body surface area (BSA) were 16 $\pm$ 1.7 years (range 14–18) and 1.78 $\pm$ 0.25 m^2 (range 1.10–2.25), respectively. The amount of training per athlete averaged 11 $\pm$ 4.5 h/week (range 8–23).

Controls

The control group was derived from a database of cardiac screening performed at various secondary education schools. The authors selected 400 consecutive subjects who were of similar age, gender, and ethnicity to the athletic population, to enable appropriate comparisons between the two groups. Subjects were selected to fulfil the following criteria: (i) sedentary life style defined as $<$2 h of organized physical activity per week, (ii) age between 14 and 18 years old, who were post-pubertal, (iii) of similar gender to the athletic population, 330 (83%) males, and (iv) of similar ethnicity to the athletic population; 385 (96%) Caucasians. Although BSA was not part of our selection criteria, the controls were of similar BSA to the athletic population (1.76 $\pm$ 0.22 m^2).

12-Lead electrocardiogram

A standard 12-lead ECG was performed during quiet respiration in a supine position using a Marquette Hellige recorder (Milwaukee, USA). The electrodes were placed carefully to ensure consistency, and ECGs were recorded at a paper speed of 25 mm/s. Heart rate and QRS axis were calculated. P-, Q-, R-, S-, and T-wave voltages; ST-segments; QRS duration; PR interval; and QT-interval were measured in each lead using callipers and a millimetre ruler as described elsewhere.[13] The QT-interval was corrected for the heart rate (QTc) using the Bazzet's formula.[14]

Left ventricular hypertrophy (LVH) was identified using the Sokolow–Lyon criterion.[15] T-wave inversions in two or more leads were considered significant, other than in leads V1 and III. Deep T-wave inversion was defined as a negative T-wave of $-$0.2 mV or more in any lead.

Echocardiography

Two-dimensional echocardiography was performed by a cardiologist or a senior cardiac physiologist, using an Accuson Computed Sonograph 128XP/10c (San Jose, CA, USA) or a GE Vivid I (Tirat, Israel), both with 3 MHz transducer. Standard views were obtained as previously described.[16] Standard chamber measurements were performed as suggested by current guidelines.[17] Two-dimensional continuous- and pulsed-Doppler, as well as colour tissue-Doppler imaging were performed using standard parasternal and apical views. Left ventricular wall thickness was measured from two-dimensional short-axis views at end-diastole and the greatest measurement within the left ventricular wall was defined as the maximal wall thickness. 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.[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. All scans were reviewed by a cardiologist experienced in 'athlete's heart' and cardiomyopathy.

Criteria for consideration of the diagnosis of hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy

Echocardiographic criteria for HCM were the presence of LVH, with a left ventricular wall thickness of >12 mm (based on previous studies in adolescents),[19] in association with a relatively non-dilated left ventricular cavity (<54 mm), in end-diastole and one or more of: (i) impaired diastolic function,[20] (ii) enlarged left atrial diameter (>45 mm),[21] (iii) the presence of systolic anterior motion of the anterior mitral valve leaflet and associated left ventricular outflow tract obstruction or an intra-cavity gradient, and (iv) a family history of HCM in a first-degree relative.

Owing to the inherent limitations of two-dimensional echocardiography in the assessment of the right ventricle, we considered an echocardiogram to be consistent with phenotypic features of ARVC[22] in the presence of (i) regional wall motion abnormalities in the right ventricle, (ii) impairment of the right ventricular systolic function, or (iii) aneurysmal dilation of the right ventricular cavity.

Exercise tolerance testing, 48 h Holter monitor and cardiac magnetic resonance imaging

Athletes and controls with T-wave inversions underwent an exercise stress test, 48 h Holter monitoring, and CMR scan with gadolinium enhancement.[23–25]

All subjects exercised to volitional exhaustion using the standard Bruce protocol.[26] Signals from a 12-lead ECG were displayed continuously and recorded at 1 min intervals, looking specifically for the development of arrhythmias or ischaemic changes. Blood pressure was measured by auscultation over the brachial artery at 1 min intervals during the test and for the first 3 min after the test using a mercury sphygmomanometer. A systolic blood response of >25 mmHg from baseline to peak exercise was considered normal.[26]

Ambulatory ECG monitoring was analysed for any evidence of supra-ventricular and/or ventricular arrhythmias.[27,28] Athletes were encouraged to continue their usual daily activities, including exercise during the recordings.

Cardiac magnetic resonance imaging was performed with a Siemens Sonata 1.5 T (Erlangen, Germany) using steady-state, free precession breath-hold cines (TE/TR 1.6/3.2 ms, flip angle 60°) in long-axis planes and sequential 7 mm short-axis slices (3 mm gap) from the atrioventricular ring to the apex. Late gadolinium enhancement images were acquired 10 min after intravenous gadolinium-DTPA (Schering, 0.1 mmol/kg) in identical short-axis planes using an inversion-recovery gradient echo sequence. Inversion times were adjusted to null normal myocardium (typically 320–440 ms; pixel size 1.7 × 1.4 mm). Late gadolinium enhancement images were phase swapped to exclude artefact. Ventricular volumes and function were measured for both ventricles using standard techniques[29,30] and analysed using semi-automated software (CMR tools, Cardiovascular Imaging Solutions, London, UK). All volumes and masses were indexed for age, gender, and BSA.

Assessment of first-degree relatives

First-degree relatives of all athletes and controls exhibiting significant T-wave inversions were invited to undergo cardiovascular screening. A total of 140 relatives responded to our invitation and were subjected to a health questionnaire, relating to the presence of cardiac symptoms, past medical history, drug history and a review of the family history for cardiomyopathy or premature (≤40 years old) SCD, and cardiovascular examination including blood pressure measurement, 12-lead ECG, and two-dimensional transthoracic echocardiography, to assess the possibility of familial cardiomyopathy.

Statistical analysis

Means and standard deviations (SDs) or medians and 25th–75th percentile values, where appropriate, were calculated for continuous variables. Group differences were examined using *t*-test and Mann–Whitney *U* test for parameters with normal and non-normal distributions, respectively. Chi-square or Fisher's exact test was used to test group differences of proportions. Binary logistic analysis was used to investigate the presence of an independent association between age, gender, anthropometric parameters (height, weight, BSA), type of sport (dynamic, mixed), duration (years), and intensity (hours per week) of exercise and the presence of T-wave inversion in adolescent athletes. The goodness of fit was evaluated using the Hosmer–Lemeshow test. Significance was defined as $P < 0.05$ throughout, and *P*-values were adjusted for multiple testing, where appropriate, using the Bonferroni correction. Statistical analysis was performed using SPSS software, version 14 (SPSS Inc., Chicago, IL, USA).

Results

12-Lead electrocardiogram

Electrocardiographic characteristics of adolescent athletes and controls are reported in *Table 1*.

Prevalence and distribution of T-wave inversions

There was no significant difference in the overall prevalence of T-wave inversions between adolescent athletes and sedentary individuals (4 vs. 3%; $P = 0.46$) (*Figure 1*). Deep T-wave inversions were exceedingly rare in both groups, being present in only 14 (0.8%) of the athletes (range −0.2 to −0.6 mV) and none of the control group.

The prevalence and distribution of T-wave inversions in the anterior pre-cordial leads was similar in athletes and sedentary adolescents, being present in 2.5 and 3%, respectively ($P = 0.49$). The majority of T-wave inversions in the anterior pre-cordial leads were confined to leads V1–V2, with only 0.8% of adolescent athletes and 0.5% of controls exhibiting T-wave inversions extending beyond the lead V2 (*Figure 2*). In contrast, the prevalence of T-wave inversions in the inferior and/or lateral leads differed significantly between the two groups, with a small but substantial number of athletes 25 (1.5%), but none of the controls exhibiting T-wave inversions in the inferior and/or lateral leads ($P = 0.03$).

Table 1 Electrocardiographic characteristics of adolescent athletes and controls

	Athletes ($n = 1710$)	Controls ($n = 400$)	*P*-value
Sinus bradycardia (heart rate <60 b.p.m.)	1368 (80%)	80 (20%)	<0.001
Sinus arrhythmia	940 (55%)	40 (10%)	<0.001
Nodal rhythm	5 (0.3%)	0	0.61
Wandering pacemaker	3 (0.2%)	0	0.92
First-degree AV block	77 (4.5%)	2 (0.5%)	<0.001
Second-degree AV block Mobitz type 1	2 (0.1%)	0	0.49
PR interval (ms)	155 ± 22 (100–245)	138 ± 17 (100–205)	<0.001
QRS duration (ms)	93 ± 12 (54–129)	88 ± 7 (65–114)	<0.001
Incomplete RBBB	513 (30%)	36 (9%)	<0.001
Complete RBBB	9 (0.6%)	0	0.30
QRS axis (degrees)	78 ± 18 (−20 to+124)	72 ± 19 (−1 to+100)	<0.001
QTc (ms)	392 ± 27 (346–450)	375 ± 29 (314–445)	<0.001
Sokolow–Lyon voltage criterion for LVH	770 (45%)	88 (22%)	<0.001
ST-segment elevation	770 (45%)	80 (20%)	<0.001
Tall T-wave (≥1 mV)	393 (23%)	24 (6%)	<0.001
T-wave inversion	67 (4%)	12 (3%)	0.46
Deep T-wave inversion (−0.2 or more, mV)	14 (0.8)	0	0.14

Where applicable, results are expressed as mean ± standard deviation with the range in parentheses. Abbreviations: AV, atrioventricular; LVH, left ventricular hypertrophy; RBBB, right bundle branch block.

T-wave inversions in relation to age, gender, body size, type, duration, and intensity of training

T-wave inversions in the anterior precordial leads, extending beyond the lead V2, were almost confined (85%) to individuals aged <16 years; of the 819 athletes aged ≥16 years, only 2 (0.2%) male athletes exhibited T-wave inversions beyond V2 when compared with 11 of the 891 (1.2%) athletes aged <16 years ($P = 0.04$). None of the controls aged ≥16 years exhibited T-wave inversions in the anterior precordial leads extending beyond V2.

None of the 296 female athletes exhibited T-wave inversions in the inferior and/or lateral leads or deep T-wave inversions and only 1 (0.3%) exhibited T-wave inversions in the right pre-cordial leads extending beyond lead V2.

Based on the univariable analysis, there was no significant association between age, gender, height, weight, BSA, type of sport, duration, and intensity of training with the presence of T-wave inversions in our cohort of adolescent athletes (*Table 2*).

Significance of T-wave inversions

Echocardiography

Most athletes and all the controls with T-wave inversions in the anterior precordial leads exhibited a structurally normal heart; none exhibited echocardiographic features of ARVC. None of the athletes with T-wave inversions in the anterior precordial leads had a pulmonary artery pressure of ≥30 mmHg or evidence of an intra-cardiac shunt. Although there was no correlation between T-wave inversions and left ventricular chamber size, athletes with T-wave inversions in the inferior and/or lateral leads had a high prevalence of LVH and congenital cardiac anomalies, i.e. of the 25 athletes, 10 (40%) had LVH and 2 (8%) had a congenital cardiac abnormality (mitral valve prolapse, ($n = 1$) and atrial septal defect, ($n = 1$)).

All athletes exhibiting LVH in this study were males ($n = 26$; 1.5%). The maximum wall thickness recorded ranged from 13 to 15 mm. All athletes with LVH were considered to have athlete's heart rather than HCM based on an enlarged left ventricular cavity, normal indices of diastolic function, and a left atrial diameter within normal limits.

Exercise tolerance testing, 48 h Holter monitor and cardiac magnetic resonance imaging

All 67 athletes and 12 controls with T-wave inversions underwent cardiopulmonary exercise stress testing, 48 h Holter monitor, and CMR, and none exhibited phenotypic evidence of HCM or ARVC.[31] With respect to the 48 h Holter monitor, six athletes and two controls with T-wave inversions exhibited ≥100 ventricular or supraventricular extrasystoles per 24 h, which did not exceed >0.5% of the total heart beats.

Assessment of first-degree relatives

From 67 athletes and 12 controls with T-wave inversions, we evaluated 140 relatives. None of the relatives exhibited phenotypic evidence of an underlying familial cardiomyopathy.

Other significant findings in adolescents screened

A total of 11 athletes (0.6%) exhibited electrical or structural abnormalities: long-QT syndrome ($n = 3$), Brugada syndrome ($n = 1$), Wolff-Parkinson White syndrome ($n = 4$), bicuspid

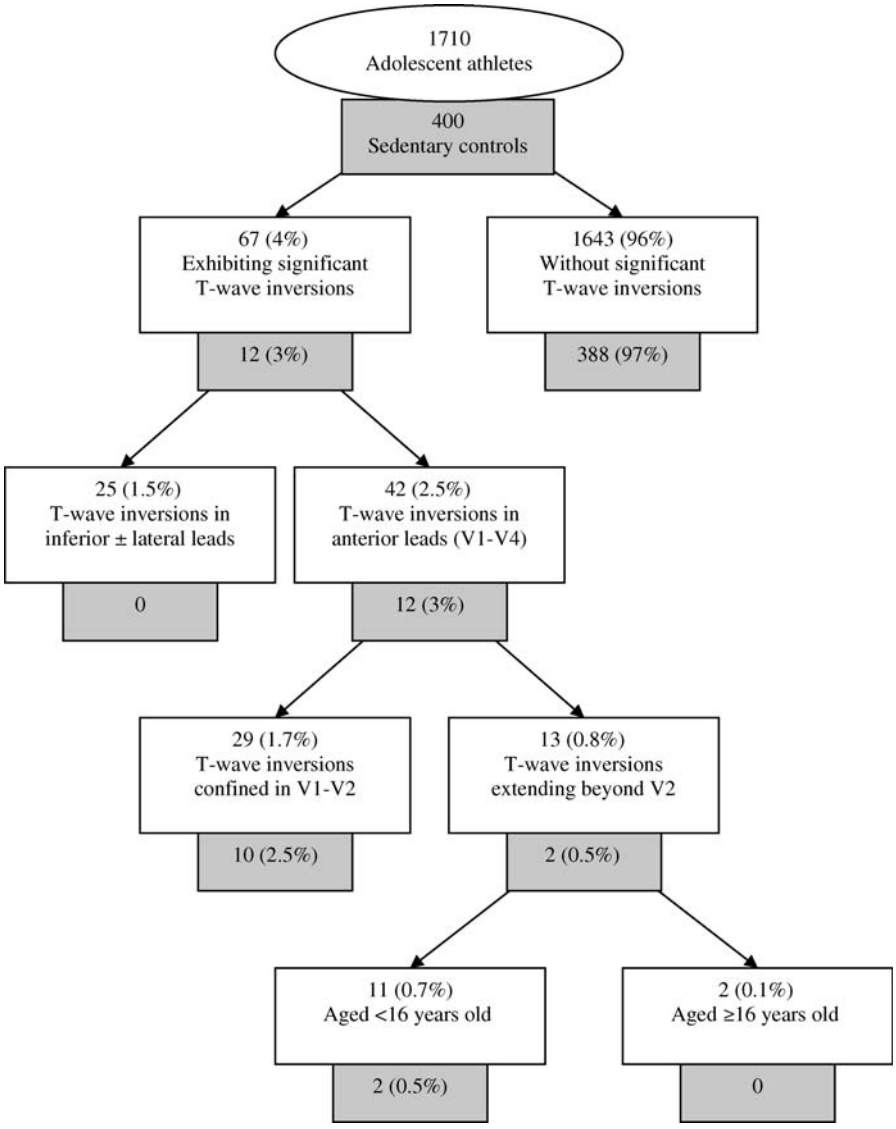

Figure 1 Diagrammatic representation of the prevalence and distribution of significant T-wave inversions in adolescent athletes (white boxes) and controls (grey boxes). Numbers in brackets express percentages (%) of each cohort.

aortic valve ($n = 2$), and cor triatriatum ($n = 1$). Only 1 (0.3%) of the 400 control subjects had an anatomical abnormality, specifically mitral valve prolapse with mild mitral regurgitation.

Discussion

T-wave inversions are regarded to be representative of the normal spectrum of cardiovascular adaptation in a minority of highly trained adult athletes. They are also, however, commonly encountered in HCM and ARVC, and it is well established that most affected individuals exhibit T-wave inversions at the time of diagnosis.[7,32,33]

Deaths from HCM and ARVC in sport are fortunately rare but are most prevalent in adolescent athletes who may exhibit T-wave inversions as part of the juvenile ECG pattern or physiological cardiac remodelling. Paradoxically, the prevalence and, more importantly, the significance of these repolarization anomalies, in this particularly vulnerable cohort of athletes, have never been evaluated in detail and magnifies the risk of a false diagnosis or conversely erroneous reassurance.

This study of over 1700 highly trained, predominantly Caucasian, athletes identified T-wave inversions in 4% of athletes, all of whom underwent intensive clinical investigations. Based on the observations of the distribution and magnitude of T-wave inversions in relation to age and gender in this study, the investigators attempt to devise a practical algorithm for selecting which asymptomatic adolescent athletes require further investigation following the initial 12-lead ECG outside the context of familial HCM or ARVC.

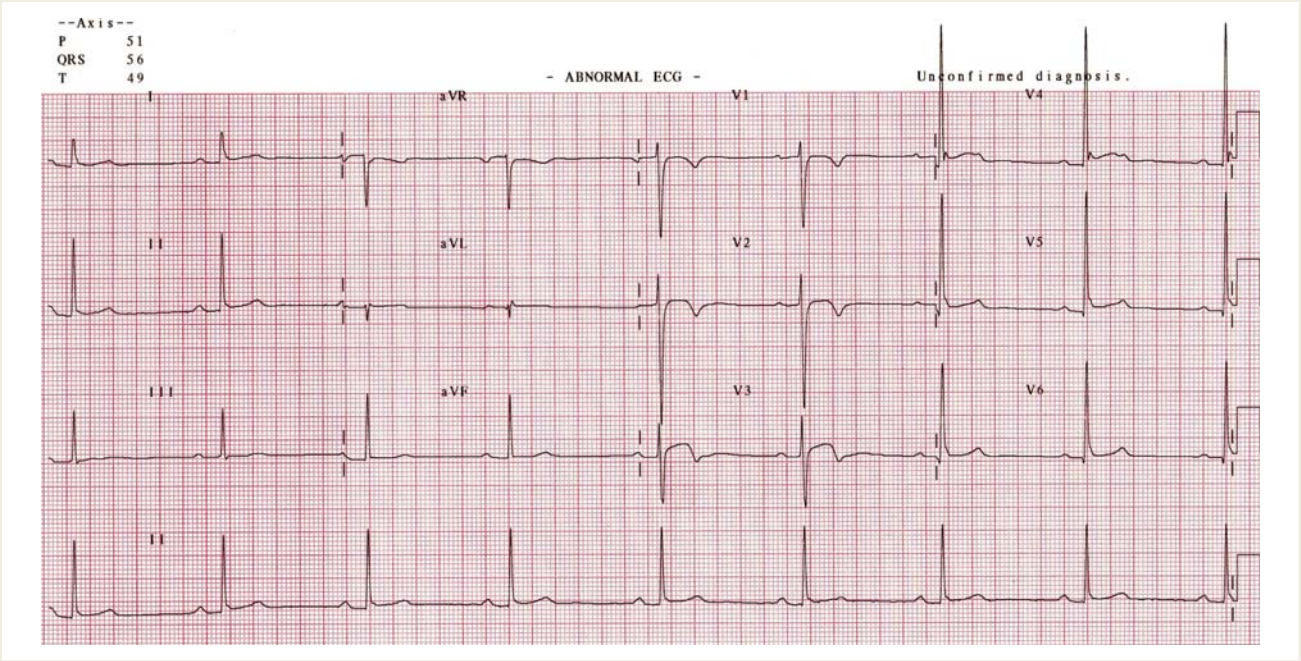

Figure 2 Electrocardiogram of a 15-year-old football player demonstrating sinus bradycardia, Sokolow–Lyon criterion for LVH and ST-segment elevation, associated with T-wave inversions in leads V1–V3. Extensive cardiac investigations, including two-dimensional echocardiogram, exercise tolerance testing, 48 h Holter monitor, cardiac magnetic resonance imaging, and family screening, did not reveal any phenotypic evidence suggestive of a diagnosis of ARVC or HCM.

Table 2 Univariate predictors of the presence of T-wave inversion in the ECG of adolescent athletes

	OR (95% CI)	*P*-value
Age (per year increment)	1.02 (0.85–1.23)	0.829
Female vs. male	0.83 (0.42–1.64)	0.591
Height (per cm increment)	0.99 (0.96–1.01)	0.341
Weight (per kg increment)	1.00 (0.99–1.02)	0.703
Body surface area (per 0.1 m^2 increment)	1.00 (0.88–1.13)	0.996
Type of sport (dynamic vs. mixed)	1.03 (0.60–1.75)	0.919
Duration of sport (per year increment)	0.98 (0.82–1.17)	0.828
Intensity of sport (per h/week increment)	1.00 (0.91–1.09)	0.949

Abbreviations: OR, odds ratio; CI, confidence interval.

Athletes with T-wave inversions in the anterior pre-cordial leads

In adolescent athletes, almost 70% of T-wave inversions in the anterior precordial leads were identified in leads V1–V2 and did not differ significantly when compared with controls. T-wave inversions extending beyond V2 were rare (0.8%) and almost confined to athletes aged <16 years old. Based on the plethora of normal investigations in both athletes and controls, we suspect that these T-wave inversions reflect the juvenile ECG pattern. On the contrary, T-wave inversions beyond V2 were identified only in two athletes aged ≥16 years. Although, the investigators were unable to identify any structural heart disease or the broader phenotype of ARVC[31] in these athletes, given the rarity of T-wave inversions in the anterior precordial leads beyond V2 in athletes aged ≥16 years, the difficulties in diagnosing ARVC in the concealed phase and the potential implications associated with the disorder, i.e. sudden death,[22,31,34] the authors cannot consider T-wave inversions beyond V2 to represent a normal variant in any athlete aged ≥16 years, without detailed investigation.

Athletes with T-wave inversions in the inferior and/or lateral leads

T-wave inversions in the inferior and/or lateral leads were present in a small (1.5%) number of athletes and were associated with a high prevalence of LVH on echocardiography or a structural abnormality of the heart. Our findings indicate that all adolescent athletes with T-wave inversions in the inferior and/or lateral leads should undergo echocardiography and further investigations, if indicated. Gender is particularly relevant to our recommendation since none of the females in our study exhibited T-wave inversions in the inferior and/or lateral leads, indicating that the presence of these repolarization anomalies are highly likely to represent a pathological myocardial substrate in the young female population.

Differences between adult and adolescent athletes in relation to T-wave inversions

The prevalence of T-wave inversions in predominantly Caucasian, adolescent athletes does not appear to differ significantly from previous reports of 3–4% in adult athletes.[5,7,10] However, deep

T-wave inversions are much commoner in adult counterparts, having been documented in almost 3% of adult athletes[5] compared with just 0.8% in our study of adolescent athletes. The low prevalence of deep T-wave inversions in adolescents compared with adult athletes is probably reflective of differences in physical maturity, duration, and intensity of training between the two groups. Based on the observations of a very low frequency of deep T-wave inversions in adolescent athletes, the investigators would recommend echocardiography in all adolescent athletes exhibiting deep T-wave inversions.

Clinical applications

Cardiovascular screening in predominantly Caucasian athletes, utilizing 12-lead ECG, has been shown to be effective in reducing deaths from HCM and ARVC[35–37] and has recently been adopted by major scientific and sporting organizations.[38,39] In the current era, it is probable that junior athletes participating in competitive sport at regional, national, or international level, in many European countries will be subjected to regular cardiovascular screening. Extrapolation of data derived from adult athletes for defining an abnormal ECG could be associated with an increased number of false-positive results, unnecessary investigations, and unwarranted anxiety.

In this study the application of the ESC guidelines for an abnormal ECG derived from adult athletes would have resulted in 4% of our adolescent athletes requiring further investigations, based on the presence of significant T-wave inversions.[38] By adjusting the ECG criteria based on this large study of highly trained adolescent athletes, the number of false-positive ECGs should be reduced to a minimum, leading to a more efficient and cost-effective cardiovascular pre-participation screening in this cohort. Based on the experience of this study, the investigators favour further cardiovascular evaluation in adolescent athletes exhibiting: (i) T-wave inversions in the anterior pre-cordial leads beyond lead V2 in athletes aged $\geq$16 years, (ii) T-wave inversions in the inferior and/or lateral leads, and (iii) deep T-wave inversions in any lead. Application of these criteria would reduce the number of adolescent athletes requiring further investigation, based on the presence of T-wave inversions, in our cohort to 2%, following the initial ECG.

This study exhibits some important limitations that warrant mention. Despite intensive investigations, this study failed to identify any individual with HCM or ARVC. The investigators suspect that this was due to the relatively low number of athletes studied when one considers the prevalence of either disorder in the general population (0.2 and 0.1%, respectively), since great emphasis was placed in selecting the most elite athletic population, i.e. those competing at regional or national level. Moreover, the incidence and prevalence of both disorders, based on phenotypic manifestation, is probably considerably lower in the paediatric population when compared with adults since it is well recognized that gene carriers for HCM may not exhibit the phenotype until early adulthood and the natural history of ARVC is not fully understood.[40,41] In this regard, the investigators concede that this cross-sectional study may have failed to identify some athletes harbouring HCM or ARVC gene mutations who had not yet developed the disease phenotype, as suggested by a recent longitudinal study in Italian athletes.[42] However, the purpose of the study was to identify the prevalence and immediate significance of T-wave inversions in adolescent athletes and the investigators believe that the findings from the current study provide important clinical foundations in relation to screening of adolescent athletes. All athletes with T-wave inversions are under annual follow-up to evaluate the long-term significance of the aforementioned electrical anomalies. Finally, the investigators did not have the opportunity of evaluating the effects of ethnicity on the 12-lead ECG, and therefore the results of this study should be applied with caution to non-Caucasian athletes.

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