Prevalence of Cardiomyopathy in Italian Asymptomatic Children With Electrocardiographic T-Wave Inversion at Preparticipation Screening

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Background—T-wave inversion on a 12-lead ECG is usually dismissed in young people as normal persistence of the juvenile pattern of repolarization. However, T-wave inversion is a common ECG abnormality of cardiomyopathies such as hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy, which are leading causes of sudden cardiac death in athletes. We prospectively assessed the prevalence, age relation, and underlying cardiomyopathy of T-wave inversion in children undergoing preparticipation screening.

Methods and Results—The study population included 2765 consecutive Italian children (1914 male participants; mean age, 13.9 ± 2.2 years; range 8–18 years) undergoing preparticipation screening including an ECG. Of 229 children (8%) who underwent further evaluation because of positive findings at initial preparticipation screening, 33 (1.2%) were diagnosed with cardiovascular disease. T-wave inversion was recorded in 158 children (5.7%) and was localized in the right precordial leads in 131 (4.7%). The prevalence of right precordial T-wave inversion decreased significantly with increasing age (8.4% in children < 14 years of age versus 1.7% in those ≥ 14 years; P < 0.001), pubertal development (9.5% of children with incomplete versus 1.6% with complete development; P < 0.001), and body mass index below the 10th percentile (P < 0.001). Incomplete pubertal development was the only independent predictor for right precordial T-wave inversion (odds ratio, 3.6; 95% confidence interval, 1.9–6.8; P < 0.001). Of 158 children with T-wave inversion, 4 (2.5%) had a diagnosis of cardiomyopathy, including arrhythmogenic right ventricular cardiomyopathy (n = 3) and hypertrophic cardiomyopathy (n = 1).

Conclusions—The prevalence of T-wave inversion decreases significantly after puberty. Echocardiographic investigation of children with postpubertal persistence of T-wave inversion at preparticipation screening is warranted because it may lead to presymptomatic diagnosis of a cardiomyopathy that could lead to sudden cardiac death during sports. (Circulation. 2012;125:529-538.)

Key Words: arrhythmogenic right ventricular dysplasia ■ athletes ■ cardiomyopathy, hypertrophic ■ child ■ electrocardiography

T-wave inversion is a normal feature of a 12-lead ECG in children. Inversion of the T wave in the right precordial leads occurs in infants > 48 hours of age and persists during childhood because of right ventricular (RV) dominance with a repolarization polarity directed posteriorly. During the first decade of life, changes in electric predominance from the RV to the left ventricle (LV) result in a gradual reversal of T-wave polarity, which progresses from left to right precordial leads as children grow older and leads after puberty to the adult ECG pattern, characterized by a negative T wave limited to V1. T-wave inversion in leads V1 to V2/V3 may occasionally be observed in postpubertal adolescents as persistence of the normal children’s pattern. This ECG pattern, known as persistence of the juvenile pattern of repolarization, is traditionally considered nonspecific and not associated with an increased cardiovascular risk. On the other hand, T-wave inversion in ≥ 2 adjacent leads is the most common ECG abnormality of cardiomyopathies such as hypertrophic cardiomyopathy (HCM) and arrhythmogenic RV cardiomyopathy (ARVC), which are recognized leading causes of sudden cardiac death (SCD).

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On the other hand, T-wave inversion in ≥ 2 adjacent leads is the most common ECG abnormality of cardiomyopathies such as hypertrophic cardiomyopathy (HCM) and arrhythmogenic RV cardiomyopathy (ARVC), which are recognized leading causes of sudden cardiac death (SCD).
in young people and athletes. These heart muscle diseases are genetically determined and show an age-related phenotype. Because early clinical manifestations of such cardiomyopathies usually occur after puberty, the persistence of right precordial T-wave inversion (beyond V1) in the postpubertal age raises the problem of the differential diagnosis between a benign juvenile pattern of repolarization and a developing heart muscle disease.

Identification by preparticipation screening (PPS) and disqualification of adolescents and young adults with ARVC and HCM from competitive sports activity have been demonstrated to reduce on-field mortality significantly.

The aim of the present study was to prospectively assess the prevalence, age relation, and underlying heart diseases of T-wave inversion on resting ECGs in a large series of children undergoing PPS.

**Methods**

**Study Population**

The study population included 2765 consecutive children who underwent PPS at the Center for Sports Medicine of Padova, Italy, from January 2007 to June 2009.

All individuals were white; there were 1914 male (70%) and 851 female (30%) participants with a mean age of 13.9 ± 2.2 years (median, 14 years; range, 8–18 years). They were engaged in a variety of sports disciplines reported in Table 1.

**Screening Protocol**

All children underwent PPS according to the Italian protocol. The initial cardiovascular evaluation included family and personal history, physical examination (with determination of blood pressure), and ECG. Additional examinations such as echocardiography were reserved for athletes who had positive findings at the first screening. Athletes diagnosed with clinically relevant cardiovascular abnormalities were managed according to available guidelines.

**Medical History**

Family history was considered positive when a close relative had experienced a premature heart attack or sudden death (<55 years of age in male and <65 years in female subjects) or in the presence of a family history of cardiomyopathy, Marfan syndrome, long-QT syndrome, short-QT syndrome, Brugada syndrome, severe arrhythmias, coronary artery disease, or other disabling cardiovascular diseases. Personal history was considered positive in cases of chest pain or discomfort, syncope or near syncope, and irregular heart beat or palpitations on exertion and in the presence of shortness of breath or fatigue out of proportion to the degree of physical effort.

**Physical Examination**

Positive physical findings included musculoskeletal and ocular features suggestive of Marfan syndrome; diminished and delayed artery pulses; midsystolic or end-systolic clicks; a second heart sound, single or widely split and fixed with respiration; marked heart murmurs (any diastolic and systolic grade ≥2/6); irregular heart rhythm; and brachial blood pressure >140/90 mm Hg (on >1 readings). According to the design of the present study, physical examination included the assessment of anthropometric characteristics and degree of pubertal development. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Subjects with BMI below the 10th percentile were considered underweight. Stage of pubertal development was assessed according to the Tanner staging system based on external primary and secondary sex characteristics, with stage 1 corresponding to infantile and stage 5 corresponding to complete puberty.

**12-Lead ECG**

A standard ECG was performed in all subjects in the supine position during quiet respiration with a Cardioline Delta 60 Plus recorder. ECGs were recorded at a paper speed of 25 mm/s and at a standard gain of 1 mV/cm. ECG parameters, including heart rate; P wave; PR interval; QRS axis, duration, and morphology; T-wave voltages and polarity; ST-segment displacement; and QT interval (corrected according to the Bazzett formula), were analyzed and measured by 3 experienced physicians; discrepancies were solved by consensus.

ECG abnormalities were interpreted by use of the Davignon normative values for ages 8 to 16 years and according to the criteria recommended by the section of Sport Cardiology of the European Association of Cardiovascular Prevention and Rehabilitation for subjects >16 years.

T-wave inversion was diagnosed in the presence of a negative T wave ≥1 mm in ≥2 contiguous leads. Athletes with T-wave inversion associated with pectus excavatum or completed right bundle-branch block were excluded. ECG alterations were classified according to the criteria recommended by the section of Sport Cardiology of the European Association of Cardiovascular Prevention and Rehabilitation and divided in the following 2 groups: group 1, those with common and training-related ECG changes, and group 2, those with uncommon and training-unrelated ECG abnormalities.

**Further Clinical Evaluation**

Children with a positive history, abnormal physical examination, or group 2 ECG abnormalities underwent further clinical evaluation. All children with T-wave inversion underwent additional study by echocardiography, 24 hour-Holter ECG monitoring, and maximal exercise testing. Technical equipment, protocols, and references values for such testing have been reported in detail elsewhere.

Diagnosis of ARVC and HCM was based on recognized clinical and echocardiographic criteria. According to the

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### Table 1. Type of Sports Practiced by the 2765 Athletes

<table>
<thead>
<tr>
<th>Type of Sport</th>
<th>n (%)</th>
</tr>
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<tbody>
<tr>
<td>Soccer</td>
<td>1057 (38.2)</td>
</tr>
<tr>
<td>Volleyball</td>
<td>571 (20.6)</td>
</tr>
<tr>
<td>Basketball</td>
<td>456 (16.5)</td>
</tr>
<tr>
<td>Skating</td>
<td>134 (4.8)</td>
</tr>
<tr>
<td>Swimming</td>
<td>112 (4.0)</td>
</tr>
<tr>
<td>Martial arts</td>
<td>86 (3.1)</td>
</tr>
<tr>
<td>Tennis</td>
<td>75 (2.7)</td>
</tr>
<tr>
<td>Rugby</td>
<td>55 (2.0)</td>
</tr>
<tr>
<td>Artistic gymnastics</td>
<td>53 (1.9)</td>
</tr>
<tr>
<td>Athletics</td>
<td>47 (1.7)</td>
</tr>
<tr>
<td>Fencing</td>
<td>33 (1.2)</td>
</tr>
<tr>
<td>Hockey</td>
<td>16 (0.6)</td>
</tr>
<tr>
<td>Skating</td>
<td>14 (0.5)</td>
</tr>
<tr>
<td>Horse-riding</td>
<td>12 (0.4)</td>
</tr>
<tr>
<td>Cycling</td>
<td>8 (0.3)</td>
</tr>
<tr>
<td>Baseball</td>
<td>8 (0.3)</td>
</tr>
<tr>
<td>Diving activities</td>
<td>6 (0.2)</td>
</tr>
<tr>
<td>Triathlon</td>
<td>6 (0.2)</td>
</tr>
<tr>
<td>Others</td>
<td>16 (0.6)</td>
</tr>
</tbody>
</table>
recently revised International Task Force criteria. ARVC was diagnosed in the presence of major and minor criteria encompassing genetic, ECG, arrhythmic, morphofunctional, and histopathological factors and classified as definitive when 2 major criteria, 1 major and 2 minor criteria, or 4 minor criteria from different groups were fulfilled; ARVC was defined as borderline in the presence of 1 major and 1 minor criteria or 3 minor criteria. According to these International Task Force criteria, echocardiographic diagnosis of ARVC relied on RV wall motion abnormalities (akinesia, dyskinesia, or aneurysm) plus RV dilatation (RV outflow tract ≥32 mm in the parasternal long-axis view and ≥36 mm in the parasternal short-axis view) and/or RV dysfunction (fractional area change ≥33%).

The diagnosis of HCM was based on demonstration of hypertrophied, nondilated LV with a wall thickness ≥13 mm in the absence of another systemic or cardiac disease that is capable of producing that magnitude of wall thickening (systemic hypertension, aortic valve stenosis, etc.).

In the presence of mild LV hypertrophy (13–15 mm), the distinction between HCM and athlete’s heart was based on echocardiographic and clinical features such as the distribution of thickening of the LV wall, the dimension of the LV cavity, the type of sport played, and the results of deconditioning.

### Statistical Analysis

Results are expressed as range and mean±SD. Regression analysis was performed to assess the relationship between prevalence of T-wave inversion and age. Univariate binary logistic analysis was used to identify variables that were significantly associated with right precordial T-wave inversion. Significantly associated variables (P<0.15) were integrated into multivariable analysis by use of binary logistic analysis to identify independent predictors of the presence of right precordial T-wave inversion in children. A 2-tailed value of P<0.05 was considered statistically significant. Statistics were analyzed with SPSS version 17 (SPSS Inc).

### Results

One or more ECG alterations were identified in 1314 of 2765 children (47%). ECG changes were classified as group 1 in 1119 children (40%) and group 2 in 195 (7%). A total of 229 children (8%) were referred for further investigation, 34 (1.2%) because of positive medical history and/or abnormal physical examination and 195 (7%) with group 2 ECG abnormalities, including 158 (5.7%) with T-wave inversion (Table 2). Additional clinical evaluation led to a diagnosis of heart disease in 33 children (1.2%; Figure 1).

### T-Wave Inversion

The prevalence and localization of T-wave inversion are shown in Figure 2. T-wave inversion was detected in 158 children (5.7%) and was localized as follows: right precordial leads (V1–V3) in 131 (4.7%), inferior leads (II/III/aVF) in 24 (0.9%), and lateral precordial leads (V4–V6/aVL) in 3 (0.1%).

### Right Precordial T-Wave Inversion

T-wave inversion in right precordial leads was observed in 88 of 1914 male (4.6%) and in 43 of 851 female (5%) participants (P=0.15). There was a statistically significant decreasing prevalence of right precordial T-wave inversion with increasing age in both male (R²=0.84, P<0.001) and female (R²=0.86, P<0.001) participants (Figure 3). With a cutoff value of 14 years (ie, the median age of study population), T-wave inversion in right precordial leads was recorded in 105 of 1244 children (8.4%) <14 years of age versus 26 of 1521 children (1.7%) ≥14 years of age (P<0.001). At 14 years of age, 241 of 281 male (86%) and 108 of 119 female (91%) participants showed Tanner stage 5. All male participants ≥17 years of age and all female participants ≥16 years of age had reached a complete pubertal development.

The prevalence of right precordial T-wave inversion was significantly higher in children with incomplete (Tanner stage 4 or less) versus complete (Tanner stage 5) pubertal development (104 of 1087 [9.5%] versus 27 of 1678 [1.6%]; P<0.001) and in children with a BMI below the 10th percentile (33 of 296 [11%] versus 98 of 2469 [4%]; P<0.001). There was no statistically significant relation between right precordial T-wave inversion and specific sports.

Table 3 shows univariate and multivariable predictors for right precordial T-wave inversion. Univariate predictors were
incomplete pubertal development (odds ratio, 6.5; 95% confidence interval, 4.2–9.9; \( P < 0.001 \)), age \( \leq 14 \) years (odds ratio, 5.3; 95% confidence interval, 3.4–8.2; \( P < 0.001 \)), and BMI below the 10th percentile (odds ratio, 2.4; 95% confidence interval, 1.7–3.2; \( P < 0.001 \)). On multivariable analysis, incomplete pubertal development remained the only independent predictor (odds ratio, 3.6; 95% confidence interval, 1.9–6.8; \( P < 0.001 \)).

### Inferolateral T-Wave Inversion

There was no statistically significant correlation between T-wave inversion in inferolateral leads and any clinical variables such as age, sex, pubertal development, BMI, and type of sport.

### Cardiovascular Diagnosis and Sport Eligibility

Of the 229 children who underwent further additional cardiovascular evaluation because of positive history, abnormal physical examination, and group 2 ECG changes, 196 (7%) showed no cardiovascular diseases and were considered eligible for sports participation. Thirty-three (1.2%) were diagnosed as having HCM (Figures 2 and 5). All received a complete restriction from competitive sports.

### Other Cardiovascular Disorders

The following cardiovascular disorders were identified in the remaining 29 children: mitral valve prolapse (n=16), atrial septal defect (n=3), ventricular preexcitation (Wolff-Parkinson-White syndrome; n=6), long-QT syndrome (n=2), short QT syndrome (n=1), and Brugada syndrome.
There was no statistically significant relation between specific sports and specific forms of cardiovascular disease. The 16 children with mitral valve prolapse had an echocardiographically trivial mitral valve regurgitation and no significant ventricular arrhythmias on 24-hour Holter ECG monitoring and maximal exercise testing. Three of them (13, 14, and 17 years of age) had a T-wave inversion in inferior leads. They received no sports restriction.

The 3 children with atrial septal defect had a mild shunt and received no sports restriction. The 6 children with ventricular preexcitation underwent transesophageal electrophysiological study for risk stratification: 3 of them had an antegrade effective refractory period of the accessory pathway >240 ms and received a temporary sports restriction until they underwent successful radiofrequency catheter ablation, and the remaining 3 children had an antegrade effective refractory period of the atrioventricular accessory pathway >240 ms and received no sports restriction.

A child with a family history of SCD and ajmaline-induced “coved-type” ST-segment elevation in leads V1 and V2, consistent with Brugada syndrome, was deemed ineligible for competitive sports activity.

Two children with long-QT interval (QTc, 510 and 530 milliseconds) and 1 child with short-QT interval (QTc, 300 ms) were detrained for a 6-month period without significant changes in their QTc interval and received complete competitive sports restriction. Both children with long-QT interval showed mutations of the KCNQ1 gene consistent with long-QT syndrome type 1 and were treated with β-blockers.

Discussion

ECG changes are common in athletes and usually reflect the structural and electric remodeling of the heart as an adaptation to regular physical exercise (athlete’s heart).29,30 However, T-wave inversion may be the expression of an underlying heart disease capable of causing SCD during sports.11,31–37

| Table 3. Univariate and Multivariable Predictors for T-Wave Inversion in Right Precordial Leads |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Variables                       | OR   | 95% CI    | P       | OR   | 95% CI    | P       |
| Incomplete pubertal development | 6.5  | 4.2–9.9   | <0.001  | 3.6  | 1.9–6.8   | <0.001  |
| Age <14 y                       | 5.3  | 3.4–8.2   | <0.001  | 1.7  | 0.9–3.3   | 0.1     |
| BMI below the 10th percentile   | 2.4  | 3.2–1.7   | <0.001  | 1.5  | 0.9–2.1   | 0.09     |
| Male sex                        | 1.1  | 0.8–1.6   | 0.15    | 1.1  | 0.8–1.7   | 0.55     |

OR indicates odds ratio; CI, confidence interval; and BMI, body mass index.

| Table 4. Clinical and Instrumental Findings in 4 Children With T-Wave Inversion and Cardiomyopathy |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Clinical Findings               | HCM             | Definitive ARVC | Borderline ARVC | Borderline ARVC |
| Age, y                          | 15              | 14              | 15              | 17              |
| Sex                             | Male            | Male            | Female          | Male            |
| Pubertal development (Tanner stage) | Complete (5)   | Complete (5)   | Complete (5)   | Complete (5)   |
| Type of sport                   | Soccer          | Soccer          | Soccer          | Soccer          |
| Family history                  | Positive        | Negative        | Negative        | Negative        |
| Physical examination            | Negative        | Negative        | Negative        | Negative        |
| Symptoms                        | No              | No              | No              | No              |
| Resting ECG                     | T-wave inversion in I–aVL; Q wave in inferior leads | T-wave inversion in V1–V2 | T-wave inversion in V1–V3 | T-wave inversion in V1–V3 |
| Echocardiographic findings      | Maximal septal thickness 31 mm | RV posterobasal (subtricuspid) akinesia; RVOT dilatation (37 mm at PLAX view, 39 mm at PSAX view) | RV anterolateral akinesia; RVOT dilatation (30 mm at PLAX view, 32 mm at PSAX view) | RVOT akinesia: RVOT dilatation (31 mm at PLAX view, 35 mm at PSAX view) |
| SAECG                           | Negative        | Positive        | Negative        | Negative        |
| 24-h (12-lead) ECG Holter monitoring | No arrhythmias | 2782 PVBs and nonsustained VT (4 beats, 170 bpm, LBBB/superior axis pattern) | 357 PVBs (LBBB/inferior axis pattern) | 389 PVBs (LBBB/inferior axis pattern) |
| Maximal exercise testing        | No ST-segment ischemic changes; no arrhythmias | No ST-segment ischemic changes; coupled PVBs at maximal exercise | No ST-segment ischemic changes; no arrhythmias | No ST-segment ischemic changes; no arrhythmias |

HCM indicates hypertrophic cardiomyopathy; ARVC, arrhythmogenic right ventricular cardiomyopathy; RV, right ventricular; RVOT, right ventricular outflow tract; PLAX, parasternal long-axis view; PSAX, parasternal short-axis view; SAECG, signal-averaged ECG; PVB, premature ventricular beat; VT, ventricular tachycardia; and LBBB, left bundle-branch block.
This study was designed to prospectively assess the prevalence of T-wave inversion, the relation to age and sex, and the presence of an underlying cardiomyopathy in a large cohort of children undergoing PPS. The major findings were the following: (1) In this age group, T-wave inversion was documented in 5.7% of cases and was localized predominantly in the right precordial leads; (2) right precordial T-wave inversion significantly decreased with increasing age and pubertal development; and (3) T-wave inversion reflected an underlying cardiomyopathy in 2.5% of cases (4 of 158).

T-Wave Inversion
Inverted T-waves beyond lead V1 are common in children. By studying the ECGs of 50 healthy children from 2 weeks to 15 years of age, Lepeschkin et al demonstrated that the T-wave is inverted on the right side of the chest, upright on the left side, and biphasic in the precordial lead transition. This transition is more to the left in children than in grown-ups. After pubertal development, the T wave is usually inverted in lead V1 and upright in leads V2 to V6. When T-waves remain inverted beyond lead V1 in children >14 years of age, the ECG pattern is generally deemed the result of the persistence of the juvenile pattern of repolarization of no clinical significance. On the other hand, the presence of T-wave inversion beyond lead V1 is a typical ARVC feature with a sensitivity of 87% among patients fulfilling the International Task Force criteria.25,38 Because early clinical manifestation of ARVC usually occurs after puberty, the persistence of right precordial T-wave inversion (beyond V1)
in the postpubertal age raises the problem of a differential diagnosis between a benign juvenile pattern of repolarization and a developing ARVC. This is particularly important in young competitive athletes.

The concern arises as to the specificity of the juvenile T-wave pattern for ARVC because it has been reported to occur in a sizeable proportion of healthy children. It is unclear what the prevalence of the juvenile T-wave pattern is in a child who has a normal heart and how often the persistence of the juvenile pattern of repolarization is associated with a cardiomyopathy. A review of the literature shows that the prevalence of T-wave inversion varies according to the age of the study population. Suarez and Suarez reported the following prevalence of precordial T-wave inversion in children <12 years of age: lead V2 in 45% to 65% of children, lead V2 to V4 in 30% to 40%, and beyond lead V4 in 5% to 20%. In individuals 12 to 18 years of age, the prevalence of T-wave inversion decreased to 10% to 20% in lead V2 and to 5% in lead V3, with no patients showing T-wave inversion beyond lead V3. In an older healthy population 19 to 45 years of age, the prevalence of the juvenile pattern of right precordial T-wave inversion was only 13% in lead V2 and 3% in lead V4.

The traditional idea that ST-T-wave abnormalities are more common in trained athletes than in a sedentary population may be explained by the high prevalence of early repolarization changes in the athlete’s heart, with J-point–ST-segment elevation often followed by a terminal negative T wave, which simulates T-wave inversion. The true prevalence of T-wave inversion in competitive athletes overlaps that of nonathletes of the same age and sex, ranging from 2.7% in the series of top-level athletes (mean age, 22.3±12.5 years) reported by Pelliccia et al to 4% in the junior elite athletes (mean age, 16±1.7 years) reported by Papadakis et al.

Recent studies revealed that athletes of Afro-Caribbean origin exhibit a greater prevalence of T-wave inversion than white competitors. Papadakis et al reported that T-wave inversion, confined predominantly to anterior leads (V1–V4), are more common in black than in white athletes (22.8% versus 3.7%, respectively).

In the present study, T-wave inversion was found in 5.7% of our large cohort of 2765 children and was localized in the right precordial leads in 4.7%. This relatively greater prevalence of T-wave abnormalities is explained by the expected higher rate of physiological right precordial T-wave inversion in our study population, which included a sizeable proportion of prepubertal children. The prevalence of right precordial T-wave inversion decreased significantly with increasing age (8.4% in those <14 years of age compared with 1.7% of children ≥14 years of age), complete pubertal development, and greater BMI. Incomplete pubertal development was the only independent predictor of right precordial T-wave inversion.

In our large series of children, T-wave inversion in the inferior-lateral leads was an uncommon finding, not exceeding 1% (0.9% in inferior leads and 0.1% in lateral leads). This low prevalence of T-wave inversion in inferolateral leads was similar to that (1.5%) previously reported by Papadakis et al. Unlike right precordial T-wave inversion, we did not find any correlation between inferolateral T-wave inversion and sex, age, anthropometric characteristic, and pubertal development.

**T-Wave Inversion and Cardiomyopathy**

In the Papadakis et al study, the prevalence of right precordial T-wave inversion beyond V2 in athletes ≥16 years of age was 0.1%, and despite intensive cardiovascular evaluation, no athletes were diagnosed with cardiomyopathy. Our study confirmed and extended these previous observations by showing that T-wave inversion in children with complete pubertal development, although uncommon, may reflect an early cardiomyopathy. Indeed, a cardiomyopathy was diagnosed in 4 children with T-wave inversion: ARVC in 3 with T-wave inversion in the right precordial leads and HCM in 1 with T-wave inversion in the lateral leads.

The discrepancy between the previous and present studies may be explained by the differences in the study population and study design. Our study included a larger cohort of 2765 children who had a greater likelihood to be affected by cardiomyopathies, the estimated prevalences of which in the general population are 1:500 for HCM and 1:2000 for ARVC. Although the role of genetic factors in the population of the Veneto region of Italy cannot be excluded, the relatively high prevalence of ARVC in our study is reasonably explained by the use of revised International Task Force criteria for ARVC diagnosis, which have increased the sensitivity for early/minor ARVC variants, as indicated by the identification of 2 borderline ARVC cases that would have been missed by the old International Task Force criteria.

We found a relatively low prevalence of HCM in our study population of children with a mean age of ~14 years. This may be explained by the fact that HCM is an inherited heart muscle disease with phenotypic manifestations that are age dependent and occur during adolescence in association with accelerated body growth, with morphological expression usually completed during young adulthood when physical maturity is achieved. Therefore, screening of children is expected to have a low sensitivity for the detection of HCM, which usually develops during a later period of life.

**Implications for Preparticipation Screening**

The present study showed that echocardiographic evaluation of children with persistence of T-wave inversion beyond puberty on PPS allowed identification of ARVC and HCM, which are recognized leading causes of SCD in young competitive athletes. These results have significant implications for PPS, clinical diagnosis, and risk stratification for the prevention of SCD. In this regard, a previous study demonstrated that identification and disqualification of young competitive athletes with ARVC and HCM actually reduce mortality during sports activity.

According to our study findings, echocardiographic study to exclude an underlying cardiomyopathy is warranted for athletes with postpubertal persistence of T-wave inversion in ≥2 contiguous leads on resting ECG regardless of age.
In our study, PPS led to identification of additional ECG-detectable cardiovascular diseases capable of causing SCD such as Wolf-Parkinson-White syndrome, long- and short-QT syndrome, and Brugada syndrome. These conditions have been implicated in most SCDs occurring without postmortem evidence of structural heart abnormalities. Unlike cardiomyopathies, most cardiac ion channel disorders have been discovered only recently, so diagnosis at PPS is being increased over time, and its impact on mortality will be assessed in the near future.

The ECG is traditionally considered a nonspecific and non–cost-effective tool for cardiovascular evaluation of athletes because of the presumed high level of false-positive results. This concept was based on a few studies of small and selected series of highly trained athletes from a limited number of sports disciplines. More recent studies on large cohorts of athletes have disproved the traditional idea that ECG is a nonspecific screening test. In the present study, among 2765 children undergoing PPS, 229 (8%) were referred for additional testing because of positive findings such as positive medical history, abnormal physical examination, or ECG abnormalities. Further clinical workup led to the identification of heart diseases in 33 children (1.2%). Hence, the estimated percentage of false positives (ie, athletes with abnormal PPS findings in the absence of heart disease) was 7%. These figures are in keeping with those from a previous prospective Italian study of 42,386 athletes undergoing PPS, which reported a 9% prevalence of athletes with positive findings requiring further examination and a 2% prevalence of total cardiovascular disorders (≈7% of false-positive results). It is noteworthy that if we had not further investigated athletes with right precordial T-wave inversion owing to incomplete pubertal development, the proportion of false-positives would have been reduced to 3.3% without altering the screening power for detection of cardiomyopathies and thus resulting in a more favorable screening cost-effectiveness.

Our study results demonstrate that athletes diagnosed with heart diseases at PPS were not indiscriminately disqualified from sports competitions. Rather, various heart conditions required different management strategies: (1) follow-up without sports restriction (eg, mitral valve prolapse), (2) return to sports participation after treatment (eg, Wolff-Parkinson-White syndrome), and (3) definitive, complete sports restriction (eg, cardiomyopathies and channelopathies). It is noteworthy that only 8 of 2765 children (0.3%) were diagnosed with cardiomyopathies and channelopathies (Figure 1), which carry a high risk of SCD and mandate disqualification from competitive sports activity.

Study Limitations
Our results were derived from a population of white athletes and should not be generalized to populations of different ethnic origins. There is emerging evidence that racial factors have a significant impact on the physiological adaptation to exercise. In this regard, current data reveal that black athletes, male or female, develop a greater magnitude of LV hypertrophy and a higher prevalence of ECG abnormalities such as increased QRS voltages and T-wave inversion compared with white athletes. As a corollary, the implementation of PPS in countries with a large proportion of black athletes may prove problematic and result in a high number of false-positive tests. Recent data suggest, however, that athletes of Afro-Caribbean origin showing T-wave inversion in the right precordial leads do not have echocardiographic evidence of cardiomyopathy, and subsequent follow-up does not reveal any cardiac morbidity or mortality. This indicates that the higher proportion of ECG abnormalities observed in this athletic population much more often represents ethnic variants rather than cardiac pathology.

According to the study design and the screening protocol, clinical evaluation and follow-up were reserved for the subgroup of children engaged in competitive sports activity who showed positive findings at preparticipation screening. Because of this selection bias, the study results on the prevalence of ECG abnormalities and underlying cardiomyopathy may not be generalized to the general population of children not involved in sports.

Conclusions
ECG abnormalities are relatively common in children undergoing PPS. Most ECG abnormalities reflect the physiological prepubertal ECG repolarization pattern and/or physiological ECG changes related to the cardiac adaptation to physical exercise (athlete’s heart). After complete pubertal development, T-wave inversion in children becomes significantly less common than traditionally believed and may reflect an underlying heart muscle disease such as ARVC and HCM. Our study results suggest that demonstration of postpubertal persistence of T-wave inversion in children engaged in competitive sports activity justifies an echocardiographic investigation that may lead to symptomatic identification of early cardiomyopathy capable of causing SCD during sports.

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Disclosures
None.

References


CLINICAL PERSPECTIVE

T-wave inversion (≥2 contiguous leads) on a 12-lead ECG is usually dismissed in children as a normal “juvenile pattern of repolarization.” However, T-wave inversion is a common ECG abnormality of inherited heart muscle diseases such as hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy, which are leading causes of sudden cardiac death in young competitive athletes. These cardiomyopathies are genetically determined and show an age-dependent phenotypic expression. Because early disease manifestations usually occur after puberty, the persistence of T-wave inversion in the postpubertal age raises the problem of differential diagnosis between a developing heart muscle disease and a benign juvenile pattern of repolarization. The present study was designed to assess prospectively the prevalence, age relation, and underlying cardiomyopathy of T-wave inversion in a large, consecutive series of Italian children (2765) with a mean age of 13.9±2.2 years (range, 8–18 years) undergoing preparticipation screening. In this age group, T-wave inversion, localized predominantly in the right precordial leads, was documented in 5.7% of cases, significantly decreased with increasing age and pubertal development, and most important, reflected an underlying cardiomyopathy such as arrhythmogenic right ventricular cardiomyopathy and hypertrophic cardiomyopathy in 2.5% of cases. These results indicate that after complete pubertal development, T-wave inversion becomes significantly less common than traditionally believed, and its persistence may suggest an underlying heart muscle disease at risk of sudden cardiac death. As a corollary, demonstration of postpubertal persistence of T-wave inversion in children engaged in competitive sports activity justifies an echocardiographic investigation, which may lead to presymptomatic identification of early cardiomyopathy.
Prevalence of Cardiomyopathy in Italian Asymptomatic Children With Electrocardiographic T-Wave Inversion at Preparticipation Screening

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