Review Article

Screening young athletes for prevention of sudden cardiac death: Practical recommendations for sports physicians

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Regular intensive exercise in athletes increases the relative risk of sudden cardiac death (SCD) compared with the relatively sedentary population. Most cases of SCD are due to silent cardiovascular diseases, and pre-participation screening of athletes at risk of SCD is thus of major importance. However, medical guidelines and recommendations differ widely between countries. In Italy, the National Health System recommends pre-participation screening for all competitive athletes including personal and family history, a physical examination, and a resting 12-lead electrocardiogram (ECG). In the United States, the American College of Cardiology and the American Heart Association recommend a pre-participation screening program limited to the use of specific questionnaires and a clinical examination. The value of a 12-lead ECG is debated based on issues surrounding cost-efficiency and feasibility. The aim of this review was to focus on (i) the incidence rate of cardiac diseases in relation to SCD; (ii) the value of conducting a questionnaire and a physical examination; (iii) the value of a 12-lead resting ECG; (iv) the importance of other cardiac evaluations in the prevention of SCD; and (v) the best practice for pre-participation screening.

Physical training has several cardiovascular benefits. However, in rare cases, intensive exercise may be associated with sudden cardiac death (SCD). Such counterintuitive events are widely publicized because of the public profile of these elite athletes and capture the hearts of society as a nation. Moreover, because athletes are considered to represent the healthiest segment of society, questions are raised among the general public regarding the perceived risk of the competition. The community of sports physicians must respond to these concerns by providing data on the actual prevalence of SCD among young (12–35 years) athletes, and where possible, make recommendations for its prevention.

Epidemiology
Incidence rate of sudden cardiac death

The incidence rate of SCD is widely debated (Table 1) and largely unknown (Harmon et al., 2011; Maron et al., 2014a). There is a great variability in estimates ranging from 1/917 000 in US high school athletes to 1/3 000 in black African-American basketball players, corresponding to 0.1 to 33.3/100 000 athletes (Harmon et al., 2011, 2014). The mode of cardiac event collection (numerator) may be unreliable because data are often obtained from insurance claims data, review of death certificates, retrospective surveys. Many reports have relied on media reports, which may fail to detect up to 80% of deaths (Harmon et al., 2011). In many instances, it is also uncertain whether the data also include aborted cardiac arrests. The estimation of the denominator (e.g., general population, sports population, gender distribution) is also a matter of discussion (Holst et al., 2010).

Variability in the incidence rate between countries and periods

Because of variable incidence rates between countries and time periods, the precise incidence of SCD is unknown. This is due to the methodology used and mainly to inclusion criteria for SCD inclusion (Harmon et al., 2014). For example, the incidence rate may decrease by twofold when studies include postmortem data that establish cardiovascular diagnoses compared with cases where the precise cause of SCD is unknown (Harmon et al., 2011). In the United States (Maron et al., 2009), the incidence rate was 0.6 SCD/100 000 athletes vs 1/100 000 in France (Marijon et al., 2011), 1.2/100 000 in Denmark (Holst et al., 2010), 2.1/100 000 in the Veneto region of Italy (Corrado et al., 2011), and 2.6/100 000 in Israel (Steinvil et al., 2011). In Italy, after
enforcement of mandatory screening, the annual incidence rate declined over time from 3.6/100 000 in 1979–1980 to 0.4/100 000 in 2003–2004 (Holst et al., 2010). According to Maron et al. (2014a), the high incidence rate in Veneto in 1979–1980 was largely attributable to specific cases of familial arrhythmogenic cardiomyopathy cases. In Israel, the comparison of a 12-year period pre-cardiac screening and a 12-year period after implementation of screening showed no statistical difference in the incidence rates (Steinvil et al., 2011). In the United States, the incidence rate of SCD was 2.2-fold higher in 1994–2006 compared with 1980–1993. The increase in the United States was more probably caused by increased media attention and more robust search strategies than to a true acceleration in the occurrence of these events (Maron et al., 2014a).

In summary, incidence rates have a fourfold variation between countries. However, taking into account the more recent studies, the probable incidence range of SCD is between 1 and 2.5/100 000 athletes.

### Incidence rate in athletes and in nonathletes

The incidence rate in athletes and in nonathletes is also subject of controversy. The incidence rate was on average 3–5-fold higher in athletes than in nonathletes (Corrado & McKenna, 2007; Toresdahl et al., 2014), 2.5–3.3-fold higher in athletes competing in Division I than in Division III (Harmon et al., 2011) and 3.7-fold more common in basketball than in cross-country running (Harmon et al., 2011). Exercise serves as a trigger on underlying, predominantly silent, cardiovascular diseases (Maron et al., 2007, 2009; Corrado et al., 2011; Harmon et al., 2011; Marjon et al., 2011). In Italy, the incidence rate in athletes became lower than in nonathletes (0.5 SCD/100 000 vs 0.8 in nonathletes) after implantation of screening. Conversely, without any electrocardiogram (ECG) screening strategy, Harmon et al. (2011) reported no difference in US national collegiate athletes vs the general population: 2.6 SCD/100 000 athletes (17–23 years) vs 2.5 SCD/100 000 in nonathletes of similar age (15–24 years). The greatest difference between athletes vs nonathletes was reported in a Danish study, which found that athletes were 3.3-fold lower risk than nonathletes (Holst et al., 2010). However, it was difficult to draw any solid conclusion from this study because of the small number of reported cases of SCD (n = 15).

In conclusion, most of the studies have reported a higher risk (3–5-fold) of SCD in athletes compared with nonathletes. SCD is more common in men and some athlete subgroups. African-American/black athletes and basketball players appear to be at higher risk (Harmon et al., 2014).

### Incidence rate according to age

Mortality rates in college athletes appear to exceed those of high school student-athletes. In adolescent groups, the risk of SCD is higher at the end of the age range because of longer exposure to training and greater media reporting of deaths in higher profile college athletes compared with high school athletes (Maron et al., 2014b) and increased incidence of inherited disorders after puberty (Bille et al., 2006; Maron et al., 2009). In adults between 20 and 35 years of age, the risk is 100 times higher than

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### Table 1. Incidence rate (IR) of sudden cardiac death for 100 000 athletes-years in different countries: comparison between athletes (IRat) and nonathletes (IRnonat), male and female, white and black people, and different divisions in basketball

<table>
<thead>
<tr>
<th>Authors</th>
<th>Country</th>
<th>Studied period</th>
<th>Age years</th>
<th>Category</th>
<th>Total</th>
<th>IRat/100 000</th>
<th>Sex ratio</th>
<th>Total</th>
<th>IRnonat/100 000</th>
<th>Total</th>
<th>IRat/nonat</th>
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<tr>
<td>Corrado et al., 2007</td>
<td>Italy</td>
<td>1979–2004</td>
<td>12–35</td>
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<td>15–24</td>
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<td>2.3</td>
<td>2.3</td>
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<td></td>
<td></td>
<td></td>
<td>Cross country</td>
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<td>Holst et al., 2010</td>
<td>Denmark</td>
<td>2000–2006</td>
<td>12–35</td>
<td>White</td>
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<td>1.2</td>
<td>–</td>
<td>0.8</td>
<td>3.8</td>
<td>0.2</td>
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<td>10–35</td>
<td>White</td>
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<td>20</td>
<td>1.0</td>
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<td>0.6</td>
<td>8.4</td>
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<td>10–40</td>
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<td>2.6</td>
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<td>USA</td>
<td>2009–2011</td>
<td>College</td>
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<td>1.1</td>
<td>5.7</td>
<td>1.5</td>
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during adolescence because of the increased incidence of coronary artery disease (Corrado et al., 2005; Myerburg & Vetter, 2007; Chevalier et al., 2009).

**Incidence rate according to sex and ethnicity**

Whatever the age, males are 2–20 times at greater risk (Table 1) than females (Harmon et al., 2011; Marijon et al., 2011; Berdowski et al., 2013; Toresdahl et al., 2014). The potential reasons could be that participation in competitive sports is higher in males, men often achieve more intense training loads, and men have a higher incidence and/or phenotypic expression of cardiac diseases like cardiomyopathies or premature coronary artery diseases.

Overall, 2 SCD/100 000 young athletes is considered a reasonable estimate (Harmon et al., 2011). Some athlete subgroups appear to be at a higher risk, specifically men, African-American/black athletes, and basketball players where the incidence rate may increase up to 33.3 SCD/100 000 athletes. Running, swimming gymnastics, rugby, tennis were also reported to have a higher incidence of SCD than other less popular sports (Bille et al., 2006).

**Causes of sudden cardiac death**

A heterogeneous variety of mostly congenital/genetic diseases (≈ 20) are responsible for these events (Maron et al., 2014a). Few autopsy studies have reported data concerning SCD in relation with physical activity. In athletes aged 8–39, Maron et al. (2007) found that SCD was mainly (44%) caused by hypertrophic cardiomyopathy (HCM) plus indeterminate left ventricular hypertrophy (LVH) considered as possible HCM, anomalous coronary artery (17%), myocarditis (6%), arrhythmogenic cardiomyopathy (ACM; 4%), dilated cardiomyopathy (DCM), mitral valve prolapse, and commotio cordis. A pathologically normal heart at autopsy after presumed cardiac death is often presumed to be related to electrical disease such as inherited cardiac ion channel defects, i.e., channelopathies, Brugada, long and short QT, and polymorphic ventricular tachycardia. In Maron’s study, such deaths accounted for only 3% of cases, but in other studies, it accounts for a considerably greater proportion of deaths. Other causes include spontaneous aortic dissection/rupture complicating Marfan syndrome, dilated aortic root, atherosclerotic coronary disease, myocardial bridging, and aortic stenosis. In athletes aged 11–35, Corrado et al. (1998) found that the most common causes of SCD were ACM (22%), atherosclerosis coronary disease (18%), and anomalous origin of the coronary artery (12%). Two to 19% of young athletes who die suddenly had no evidence of structural heart disease (Corrado et al., 2011; Maron et al., 2014b). In US national collegiate athletes (17–23 years), Harmon et al., (2014) found that the most common causes of 45 cases of SCD was structural normal heart or negative autopsy (31%) followed by coronary artery abnormalities (14%), DCM (3.8%), myocarditis (3.8%), aortic dissection (3.8%), and LVH + HCM (3.8%).

In conclusion, HCM + LVH and anomalous coronary artery are the main causes of SCD. The high rate of ACM found in Veneto was probably caused by a specific difference, probably genetic, of the studied population. Atherosclerotic coronary disease is also relatively common in Veneto whereas HCM is relatively rare. Other differences may be based on review of autopsies performed by local coroners or medical examiners. Maron’s cohort is likely limited by ascertainment bias as his registry exists within the Hypertrophic Cardiomyopathy Center, while Corrado’s study has the advantage of specialized cardiac pathology and mandatory reporting of SCD.

**Prevention of sudden cardiac death**

Because sports can reveal underlying severe cardiac disease, pre-participation screening (PPS) has an important role in prevention of SCD in competitive athletes. The main goal of the cardiovascular PPS is to detect a cardiac disease that can be worsened by intensive sports practice or result in a SCD.

Scientific committees such as the American College of Cardiology, the American Heart Association (AHA), and the European Society of Cardiology (ESC), and sports associations such as the International Olympic Committee (IOC) Medical Commission, Fédération Internationale de Football Association (FIFA) and others recommend a PPS program to provide medical clearance for participation in competitive sports.

All recommendations include questionnaires relating to family and personal history, and a physical examination. The necessity of a systematic resting 12-lead ECG is a matter of a major scientific debate between North-American and European recommendations (Myerburg & Vetter, 2007; Wheeler et al., 2010; Borjesson & Dellborg, 2011; Shephard, 2011; Maron, 2012; Sharma, 2012; Maron et al., 2014a). Indeed, based mainly on the results of the mandatory Italian PPS program, the ESC recommends that the first PPS for competitive sports in subjects aged 12–35 includes a resting ECG. This ECG must be repeated every 2 years (Corrado et al., 2014). In 2014, at the AHA session, 1 266 audience members from 86 countries voted for athlete screening: 60% believed that screening programs should include an ECG (Colbert, 2014). However, American Associations still do not recommended an ECG (Maron et al., 2014a) based on several concerns including feasibility, cost-efficiency, prospect of high false positive results, and the lack of physicians qualified to interpret ECGs. In professional sports, medical guidelines are stricter. For
example, FIFA includes a systematic 12-lead ECG and an echocardiogram in the Pre-Competition Medical Assessment.

Questionnaire consultation and physical examination
Medical history questionnaires

Medical history questionnaires address primarily symptoms relating to cardiac disease and a family history. The short questionnaire of the AHA (Maron et al., 2014a) is composed of 14 items, while the longer questionnaire published in the Lausanne Recommendations of the IOC and ESC (Bille et al., 2006) is composed of 36 items. At the discretion of the examiner, a positive response in 1 or more of the items may be judged sufficient to trigger a referral for cardiovascular examination.

Family history

Family history focuses on (i) premature/unexpected SCD in at least one first-degree relative before the age of 50, and (ii) inherited cardiac diseases like cardiomyopathies (CM), Marfan syndrome, short or long QT syndrome, and severe arrhythmias. Any family history of SCD before the age of 50 years requires an appropriate cardiac evaluation (Drezner et al., 2012b) because of the prevalent genetic transmission of HCM, long QT, ACM, Marfan syndrome, and related vascular disorders including familial bicuspid aortic valve (Battle et al., 2011).

In 87 families presenting a case of sudden cardiac arrest (SCA) studied by Drezner et al. (2012b), 40% were identified as having at least one significant family history that was present before the child’s SCA, 27% had a family member that had suffered SCD before the age of 50, and 19% had unexplained syncope or a diagnosis of epileptic seizures. Once again, some warning symptoms were misinterpreted by medical providers.

Wilson et al. (2008) studied 1 074 British junior athletes and found nine athletes with disease associated to SCD. None of them had a significant family history although a 2.9% incidence of SCD was found in the family history of the remaining 1065 studied athletes.

Family history is thus an important element in SCD prevention and can be ascertained by careful history taking (Maron et al., 2014a). However, warning symptoms are often disregarded. Thus, there is clearly a need to improve the education of the public, parents, and children regarding SCA (Drezner et al., 2012b).

Personal history

Personal history focuses on five determinant symptoms related to exercise: (i) syncope or near syncope, (ii) exertional chest pain, (iii) shortness of breath, (iv) palpitation, and (v) abnormal dyspnea or fatigue. The questionnaire also assesses previous history of cardiovascular diseases.

In 50–80% of the cases, SCD is the first clinical manifestation of underlying cardiovascular disease of young athletes who succumb to SCD (Drezner et al., 2012b). Questionnaires focus on warning symptoms that could precede SDC. Fatigue was found to be the most common symptom (44%), followed by near-syncope (30%) in the 87 families of children and young adults (5–29 years) with SCA (Drezner et al., 2012b): 72% reported at least one cardiovascular symptom first occurred, on average, 30 months before. However, for 24%, the syncope remained undiagnosed as a cardiac disorder before SCA.

Symptoms are rarely pathognomonic of any cardiovascular diseases. For example, the vast majority of syncope, seizures, and palpitations are not associated with SCD. Only syncope with abrupt collapse, occurring during exercise, without warning signs may correspond to either structural cardiac disease or a primary arrhythmia syndrome (Drezner et al., 2012b).

In the nine athletes with disease associated to SCD studied by Wilson et al. (2008), none had a significant personal history. However, they found that sportsmen may complain about serious symptoms that were unrelated to any cardiac diseases. The most frequent symptoms were “more breathless than team mates” (9.8%), “chest pain” (6.5%), and “dizziness during exercise” (6.4%).

In summary, the likelihood of discovering significant cardiovascular diseases through personal history is low.

Physical examination

Physical examination focuses on abnormal cardiac auscultation results such as heart murmur diastolic or systolic > 2/6, fixed by respiration and reinforced after exercise, systolic click, irregular heart rhythm, and/or asymmetric artery pulses specially between arms and legs (aorta coarctation), bilateral brachial blood pressure, musculo-skeletal, and ocular features suggestive of Marfan syndrome.

A systolic murmur is the main finding of the physical examination in HMC. It indicates a left ventricular outflow obstruction. It should be audible at rest in 25% of individuals and in 50% by performing the Valsalva maneuver or in the standing position (Maron et al., 2007). In 5615 US high school athletes (Fuller et al., 1997), 175 (3.2%) of auscultation abnormalities were reported. Of them, 43 murmurs (25%) corresponded to some minor valvulopathies, and only one to severe cardiovascular disease: an aortic regurgitation.

Overall, the physical examination for preparticipation screening is relatively poor for detecting disease related to SCD, except in some rare diseases such as aortic coarctation and Marfan syndrome where differences in femoral pulse and physical stigmata are often present. In coronary disease, ion channelopathies, and Wolff-Parkinson-White, the physical examination is usually normal (Maron et al., 2014a).
Conclusion

There is a general agreement that questionnaires and physical examination should be useful. However, their effectiveness to detect diseases is debated as many cardiovascular diseases remain silent and are difficult to diagnose (Drezner et al., 2012b).

For Maron et al. (1996), screening history and physical examination led to an accurate diagnosis in 1–3% of athletes. For Wilson et al. (2012a), screening history and physical examination abnormalities were present in 22%, but only 3% of the athletes had a documented cardiac disease. The limitations of the history and physical examination to detect cardiac diseases that increase the risk of SCD are clear. However, athletes may become symptomatic overtime, justifying that history and clinical examination remain of major importance in the PPS of athletes (Wilson et al., 2012a).

As warning symptoms are often disregarded and misinterpreted by medical providers, it is suggested, as recommended by Drezner et al. (2012b), to create comprehensive questionnaires to improve detection of children at risk of SCA; to improve education of the sports physicians conducting these evaluations; and to determine the sensitivity and specificity of screening with personal and family history questions for future recommendations.

Standard 12-lead resting ECG

Diagnostic value of resting ECG

ECG is abnormal in 85–96.5% of patients with cardiomyopathies (CM): HCM or ACM being the leading causes of SCD (Corrado et al., 2005; Maron et al., 2007). The main ECG abnormalities observed in CM are atrial enlargement, Q wave, QRS axis deviation, ST segment depression, deep T-wave inversion, and complete bundle-branch block (Table 2), showing a sensitivity of 96% and a specificity of 52% (Corrado et al., 2013). Their absence will exclude almost all cases of HCM (Basavarajaiah et al., 2008). A normal ECG has an estimated negative predictive value between 90% (Rowin et al., 2012) and 98% (Pelliccia et al., 2008; Gati et al., 2013). Adding ECG to history and physical examination increased the number of discovered cardiac abnormalities from 5–13 in a group of 1 473 US college athletes (Malhotra et al., 2011). ECG is thus considered a valuable screening tool because of its high negative predictive value and its low cost (Bille et al., 2006).

However, ECG cannot detect all causes of SCD (Table 3). For example, it cannot detect Marfan syndrome. It has a very low diagnostic value in valvular diseases, catecholaminergic polymorphic ventricular tachycardia, and abnormal coronary artery origin or atherosclerotic coronary disease (Maron et al., 2007). Over a 10-year period, Maron et al. (2014a) estimated that out of 64 cardiovascular deaths at least 40% would likely have been “false negative” findings, not reliably suspected by a 12-lead ECG.

ECG interpretation

When athletes’ ECGs are interpreted using older criteria, there is a high false positive rate, however, using more modern criteria the false positive rate of ECG can be lowered to 2–7.5% (Gati et al., 2013).

Pelliccia et al. (2000) have shown that in 40% of 1 005 highly trained athletes, the classical ECG patterns would
be considered abnormal for the general population. Indeed, training may induce ECG adaptations that may be diagnosed as false positive ECG readings (Maron et al., 2007; Corrado et al., 2011). Corrado et al. (2011) proposed a list of common and uncommon ECG changes related to high levels of training. Weiner et al. (2011) showed that the new proposed criteria improve the ECG specificity by 70%, decreasing the risk of false positive ECG readings by almost 3-fold. Uberoi et al. (2011) using the same new criteria, improved ECG specificity up to 95% in 658 athletes. In 2013, normal and abnormal findings in athletes were proposed by an international consensus panel of experts in sports cardiology and described as “The Seattle criteria” (Drezner et al., 2013a,b,c,d).

Corrado et al. (2013) proposed the addition of isolated voltage criteria for right ventricle hypertrophy as training-related changes and four minor ECG changes unrelated to training: isolated left and right axis deviation, with or without right and left atrial enlargement. Gati et al. (2013) investigated 579 athletes with these criteria. They did not find any underlying structural cardiac disease. The exclusion of these criteria reduced the false positive rate from 13% to 7.5% and improved specificity from 90% to 94% with a minimal reduction in sensitivity (91–89.5%). In white athletes, refined criteria improved specificity from 73.8% to 94.1% without compromising the sensitivity of the ECG in detecting pathology (Sheikh et al., 2014).

Influence of ethnicity on athletes’ ECG patterns

Athletes of black ethnicity exhibit a higher incidence of abnormal ECG patterns (Chandra et al., 2012, 2014; Wilson et al., 2012b; Sheikh et al., 2014). Magalski et al. (2008) studied 1959 elite American football players. Marked abnormal ECGs were threefold more common in black than in white players and diffuse T wave inversion > 2 mm 13-fold more common in black than in white players. Papadakis et al. (2011) studied inverted T waves in 904 black athletes compared with both sedentary healthy black controls and to black patients with HCM. T wave inversions were present in 83% of the HCM patients, 77% being in the lateral leads. Few athletes (4.1%) exhibited T wave inversion in the lateral leads, most of them being confined in contiguous anterior leads. The authors concluded that domed ST segment with T wave inversion in leads V1–V4 can represent a frequent (18–24%) ethnic variant of “athlete’s heart” in black athletes. It was proposed as a pattern of early repolarization syndrome (Corrado et al., 2011). Conversely, T wave inversions in lateral leads represent mostly the initial expression of underlying cardiomyopathy and merit further evaluation and regular follow-up.

Zeller et al. (2010) recognized the difficulty in providing medical clearance for athletes with marked ECG repolarization abnormalities after the death of a young asymptomatic black African footballer following 60 min of strenuous exercise. Fifteen days before, resting ECG demonstrated diffuse T wave inversion in V3–V6. Cardiopulmonary exercise testing and echocardiography results, performed by an experienced echocardiographer, were normal. The autopsy revealed hypertrophic left posterior wall of 19 mm, which was not in accordance with the echocardiography. The histological examination revealed mild fibrosis of the septum without myofiber disarray and without any signs of ACM. In conclusion, in the case of T wave inversion in lateral leads, cardiac magnetic resonance (CMR) is recommended, even in the case of normal echocardiography results (Zeller et al., 2010; Papadakis et al., 2011).

Necessity to improve athletes’ ECG classification

There are now ECG systems/tools that specifically interpret athlete ECGs using modern ECG interpretation criteria. They improve the ability to accurately distinguish normal from abnormal findings from 70% up to 94% when used by primary care residents, attending physicians, sports medicine physicians, and even cardiologists (Exeter et al., 2014). However, some limitations concerning the automatic ECG readings have been underlined for athlete ECG interpretation. For example, software calculation may overestimate QT intervals that need to be controlled manually with the tangent method (Postema et al., 2008; Uberoi et al., 2011). There is still a need to increase the number of physicians adequately trained in the interpretation of the athlete’s ECG (Corrado et al., 2005; Bille et al., 2006; Battle et al., 2011; Sharma, 2012; Sheikh et al., 2014) and trained to use standardized ECG criteria tools (Drezner, 2012; Drezner et al., 2012a; Chandra et al., 2014).
Cost of adding ECG to history and physical examination

For Corrado et al. (2005), the main value of adding ECG is to increase the detection of cardiac abnormalities. For example, out of 22 detected CMH only 5 had a positive history and physical examination. For Malhotra et al. (2011) eight asymptomatic athletes were detected by ECG vs five symptomatic detected by history and physical examination out of 1 473 athletes. ECG was performed at an overall cost per diagnosis similar to that of history and physical examination alone: on average $69 000 per diagnosis. It was similar to many other medical diagnoses or therapies with the advantage of identifying and treating disease in a young population. The authors concluded that adding an ECG appears to compare favorably to the cost of other programs.

For Menafoglio et al., 2014, adding ECG to history and physical examination is performed at a reasonable cost in both Switzerland and North Carolina. Indeed, the number of false positive ECGs is low when using modern and selective ECG criteria.

The Italian pre-participation screening involves nearly 6 million athletes of all ages annually, representing about 10% of the overall Italian population with a huge decrease of SCD – 89% over 25 years (Corrado et al., 2005). Wheeler et al. (2010) calculated that the addition of ECG saved 2.06 life-years per 1 000 athletes at an incremental cost of $89 per athlete and yielded a cost-effectiveness ratio of $42 900 per life-year saved.

In some countries, echocardiography cost following an abnormal ECG is a real financial problem (Gati et al., 2013). For example, in the United States, the cost of echocardiography may be between $550 and 3 300 vs €410 in the UK and €100 in France. A 20-year program of yearly ECG screening of 8.5 million young competitive athletes would cost between $10.6 and 14.4 million per life saved (Halkin et al., 2012).

In conclusion, there is a need for further research to improve standardized ECG criteria to reduce the number of false positive ECG. There is also a need for further longitudinal studies to determine if history, physical examination, and ECG could be repeated less often: for example, every 2 years for history and physical examination, every 3 years for ECG. Males could justify more intensive, targeted screening programs than females (Toresdahl et al., 2014). The objective would be to lower directly or indirectly the cost-effectiveness of nationwide screening programs (Chandra et al., 2014).

Results of pre-participation screening
Prevalence of cardiac abnormalities

Prevalence of cardiac abnormalities reported after PPS including resting ECG in young (< 35 years) people are presented in Table 4. Wolff-Parkinson-White is the most common abnormality discovered in screening studies, followed by long QT and cardiomyopathies. The highest HCM prevalence was found by Wilson et al. (2012b). In this study, black athletes were highly present.

Likelihood of finding an arterial hypertension and a left ventricular hypertrophy were also high. In these cases, LVH was induced by arterial hypertension. Indeed, in 50% of the athletes, LVH was reduced within a few months either after diet in overweight athletes, or/and after medical treatment for hypertension, principally calcium channel blockers.

### Results of pre-participation screening

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Wolff-Parkinson-White is the most common abnormality discovered in screening studies, followed by long QT and cardiomyopathies. The highest HCM prevalence was found by Wilson et al. (2012b). In this study, black athletes were highly present.</td>
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### Table 4. Number of cardiac diseases found after athlete screening in 12 studies

<table>
<thead>
<tr>
<th>n</th>
<th>M%</th>
<th>Cat</th>
<th>Ethnicity</th>
<th>CI</th>
<th>MC</th>
<th>LVH</th>
<th>WPW</th>
<th>QT</th>
<th>VA</th>
<th>AHT</th>
<th>Val</th>
<th>IAC</th>
<th>Brug</th>
</tr>
</thead>
<tbody>
<tr>
<td>33 735</td>
<td>85</td>
<td>A</td>
<td>Ita</td>
<td>19</td>
<td>621</td>
<td>34</td>
<td>6</td>
<td>44</td>
<td>37</td>
<td>121</td>
<td>168</td>
<td>133</td>
<td>?</td>
</tr>
<tr>
<td>5615</td>
<td>60</td>
<td>HS</td>
<td>Ca?</td>
<td>13–19</td>
<td>22</td>
<td>0</td>
<td>3*</td>
<td>1</td>
<td>0</td>
<td>15</td>
<td>20</td>
<td>43</td>
<td>0</td>
</tr>
<tr>
<td>3500</td>
<td>75</td>
<td>E</td>
<td>98%</td>
<td>Ca</td>
<td>20.5</td>
<td>15</td>
<td>0</td>
<td>53 †</td>
<td>6</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>2745</td>
<td>100</td>
<td>A</td>
<td>66%</td>
<td>Ca</td>
<td>14–35</td>
<td>12</td>
<td>4</td>
<td>112 †</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>2017</td>
<td>71</td>
<td>S</td>
<td>34%</td>
<td>Ca</td>
<td>14–18</td>
<td>5</td>
<td>1</td>
<td>1 †</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>1959</td>
<td>100</td>
<td>EF</td>
<td>67%</td>
<td>Ba</td>
<td>31%</td>
<td>Ca</td>
<td>23</td>
<td>0</td>
<td>0</td>
<td>6 †</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1220</td>
<td>96</td>
<td>S</td>
<td>Ca?</td>
<td>23</td>
<td>2</td>
<td>2</td>
<td>8 †</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1220</td>
<td>100</td>
<td>AP</td>
<td>66%</td>
<td>Wa</td>
<td>22.6</td>
<td>7</td>
<td>4</td>
<td>13 †</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>1074</td>
<td>100</td>
<td>J</td>
<td>Ca</td>
<td>15.8</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>1070</td>
<td>75</td>
<td>A</td>
<td>98%</td>
<td>Ca</td>
<td>19.7</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>733</td>
<td>57</td>
<td>ES</td>
<td>Ca?</td>
<td>12.3</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>508</td>
<td>61</td>
<td>S</td>
<td>68%</td>
<td>Ca</td>
<td>19</td>
<td>3</td>
<td>2</td>
<td>2 †</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>0</td>
</tr>
</tbody>
</table>

Left ventricular thickness: *≥ 11 mm; †≥ 12 mm; ≥ 13 mm.A, amateur; AHT, arterial hypertension; AP, amateur and professional; Ba, black; Brug, Brugada; Ca, Caucasian; Cat, athlete category; CI, contraindication to sports; E, elite; EF, elite football players; ES, elite school of sports; HS, high school; IAC, interatrial communication; Ita, Italian; J, junior; LVH, left ventricular hypertrophy; M, male; MC, myocardiopathy; QT, long QTc; S, student athletes; VA, ventricular arrhythmia; Val, valvulopathy; Wa, West-Asian, Arabic; WPW, Wolff-Parkinson-White; ?, unspecified or unknown.
Further evaluation in the case of pre-participation screening abnormality

The main goal of the PPS is to detect a potential cardiac disease that can contraindicate intensive sport practice. Thus, further cardiovascular exams are needed in the case of cardiac symptoms, family history of SCD and/or uncommon ECG findings.

The choice of examinations must be adapted to the symptoms and/or ECG abnormalities. In all the cases, participation in intensive sports must not be allowed for the duration of the cardiovascular investigations.

The 2D, M-mode and tissue Doppler echocardiography

Echocardiography has a major place in sports cardiology. Indeed, it is a noninvasive tool that can be repeated easily. It is indicated in cases of pathological murmur, hypertension, abnormal dyspnea and/or fatigue, and palpitations. Some authors (Uberoi et al., 2011; Corrado et al., 2013; Drezner et al., 2013a) have given a list of criteria for the further evaluation of ECG abnormalities (Fig. 1, Table 5).

Intensive training can induce myocardial morphological and functional adaptations. Limitations concerning these adaptations have been already discussed (Battle et al., 2011; Corrado et al., 2011, 2013; Uberoi et al., 2011). Echocardiography may be inconclusive in detecting anomalous coronary artery origin. In rare cases, 3–5% of differential diagnoses with cardiac diseases, like HCM, ACM, or sometimes DCM are difficult. In these cases, the use of other exams like stress test with gas analysis and/or CMR is necessary.

Maximal stress test

A maximal stress test is interesting to study cardiovascular, heart rate, and blood pressure adaptations, as well as the occurrence of arrhythmias in the case of palpitations, unexplained dyspnea, or some ECG abnormalities like T wave inversion. It can also be of value to study the disappearance or worsening of resting arrhythmias and/or of high degree of atrio-ventricular block. A cardiopulmonary exercise test provides information about the physical capacity of the athlete. It can sometimes be helpful in the case of abnormal morphological and/or functional echocardiographic parameters to distinguish between athlete’s heart and HCM, DCM, or valvular diseases. Athletes with HCM or valvular diseases may have low peak oxygen consumption, and/or low oxygen pulse, irrespective of symptomatic status or magnitude of HCM (Sharma et al., 2000).

![Fig. 1. Main ECG patterns in athletes that either require or not further cardiac investigation. CMR, cardiac magnetic resonance; WPW, Wolff-Parkinson-White.](image-url)
### Table 5. Twelve lead ECG criteria requiring further cardiac investigations in athletes (Corrado et al., 2010, 2013; Battle et al., 2011; Ubberoi et al., 2011; Drezner et al., 2013a; b; Gati et al., 2013; Zaidi et al., 2013; Chandra et al., 2014; Sheikh et al., 2014)

<table>
<thead>
<tr>
<th>Heart frequency</th>
<th>Bradycardia &lt; 30 bpm or pauses ≥ 3 s</th>
</tr>
</thead>
<tbody>
<tr>
<td>P wave</td>
<td>Amplitude &gt; 2.5 mm and/or duration &gt; 120 ms*</td>
</tr>
<tr>
<td></td>
<td>In V1–V2, &gt; 1 mm in depth, &gt; 40 ms in duration*</td>
</tr>
<tr>
<td></td>
<td>Atrial fibrillation, flutter, supraventricular tachycardia</td>
</tr>
<tr>
<td>PR interval</td>
<td>PR &lt; 120 ms and delta wave at the beginning of QRS and sometimes inverted T waves = Wolff-Parkinson-White.</td>
</tr>
<tr>
<td></td>
<td>Second degree block without Wenckebach phenomenon</td>
</tr>
<tr>
<td>Q wave</td>
<td>Complete atrio-ventricular block ≥ 3 mm in depth or &gt; 40 ms duration in any lead except in III, VR and V1</td>
</tr>
<tr>
<td>QRS complex</td>
<td>Delta wave</td>
</tr>
<tr>
<td></td>
<td>LBBB &gt; 120 ms</td>
</tr>
<tr>
<td></td>
<td>Left and right axis deviation &lt; -30° &gt; 120°*</td>
</tr>
<tr>
<td></td>
<td>R wave in V1 &gt; 7 mm*</td>
</tr>
<tr>
<td></td>
<td>R/S &gt; 1 in V1–V2*, R/S &lt; 1 in V5–V6*</td>
</tr>
<tr>
<td></td>
<td>Brugada Type 1</td>
</tr>
<tr>
<td></td>
<td>Epsilon wave</td>
</tr>
<tr>
<td>ST segment</td>
<td>Depression &gt; 0.5 mm in V4,V5,V6, I, VL</td>
</tr>
<tr>
<td></td>
<td>Depression &gt; 1 mm in any lead</td>
</tr>
<tr>
<td>Inverted T wave</td>
<td>Before puberty in any lead except III, VR, V1, V2, V3</td>
</tr>
<tr>
<td></td>
<td>Post-puberty and adult in any lead except III, VR, V1</td>
</tr>
<tr>
<td></td>
<td>Except V2, if IRBBB</td>
</tr>
<tr>
<td></td>
<td>Except V2 and V3 in black athletes</td>
</tr>
<tr>
<td>QTc</td>
<td>&gt; 470 ms in male, &gt; 480 ms in female</td>
</tr>
<tr>
<td></td>
<td>&lt; 340 ms in any athlete</td>
</tr>
<tr>
<td>Ventricular premature beat</td>
<td>≥ 2 premature ventricular beats</td>
</tr>
</tbody>
</table>

*If isolated or in association with other criteria, no need for further investigation.ECG, electrocardiogram; IRBBB, incomplete right bundle-branch block; LBBB, left bundle-branch block; QTc, corrected QT duration (Bazet formula); WPW, Wolff-Parkinson-White.

### SCD in athletes

Electrophysiological study

Electrophysiological study is useful to study severe ventricular arrhythmias. It is recommended for the risk evaluation of Wolff-Parkinson-White pattern on resting ECG. It is also used for ablation of arrhythmogenic (atrial or ventricular) substrate like pre-excitation pathways with short anterograde refractory period, which could degenerate into ventricular fibrillation and SCD (Mangold et al., 2013; Pappone et al., 2014).

The signal-averaged ECG

The signal-averaged ECG is a special ECG recording that can detect delayed electrical potentials which represent an arrhythmogenic substrate. Currently, this examination is helpful especially in the diagnosis of the ACM (Marcus et al., 2010). It can thus be proposed in the case of negative T waves observed in right precordial leads.

Pharmacological and genetic tests

When a genetic disease is suspected, the first step is to draw a pedigree (Cirino & Ho, 2013). First-degree family cardiovascular evaluation is proposed. It involves mainly a resting ECG and echocardiography. It concerns essentially HCM, ACM, long or short QT, and Brugada syndrome. In the case of suspicion of Brugada syndrome, a pharmacological provocation test (flecainide/a ajmaline) may be proposed. In the case of long QT, an isoproterenol test may be proposed (Shimizu & Kamakura, 2001). Genetic tests may be proposed to: (i) clarify the diagnosis in a person who has or is suspected to have inherited heart disease; (ii) identify the cause of heart disease in a family; (iii) to predict which family members are at risk of developing the heart disease; (iv) to provide important counseling and options for family planning; and (v) identify postmortem SCD (Ubberoi et al., 2011; Drezner et al., 2012b; Cirino & Ho, 2013). The tests can be positive, negative, or inconclusive. Only positive tests have a diagnostic value to support a clinical diagnosis. Indeed, negative tests cannot rule out a cardiac disease (Charron, 2012).

### CMR imaging

With late gadolinium enhancement imaging and high-resolution 3D imaging technique, CMR imaging has turned out to be the method of choice to assess the diagnosis of HCM (Schnell et al., 2015), DCM, ACM, myocarditis, and to detect, as a cardiac CT scan, anomalous coronary artery origins or pathway (Elliott et al., 2000; Moon et al., 2004). It can detect fibrosis and scar within the spectrum of HCM (Battle et al., 2011; Mangold et al., 2013). CMR visualizes more precisely than echocardiography the right atrium and right ventricle for ACM detection (Ubberoi et al., 2012), the thickness of the apical zone, and any asymmetrical thickness. It can measure with a high precision the cardiac mass after training and deconditioning and functional parameters with good inter- and intra-observer reliability (Mangold et al., 2013; Chan et al., 2014).
Conclusions

Regular physical training has proven health benefits. However, vigorous and competitive physical exercise may be associated with a small risk of SCD in athletes, especially in male adolescents and young adults. Most cases of SCD are due to silent arrhythmogenic cardiovascular diseases. Although the prevalence of these diseases is low, the incidence of SCD is high enough to justify screening. The question remains: how should athletes be screened?

Scientific committees and sports associations recommend a pre-participation screening program to provide medical clearance to participate in sport; however, the methodology varies between the United States and Europe.

To improve accuracy and lower the cost of interpretation of the ECGs, we propose (i) to focus on athlete subgroups more at risk of SCD, specifically men, professional and elite athletes, African-American/black athletes, football and basketball players; (ii) to repeat yearly family history taking, physical examinations, and resting ECG in professional and elite athletes and every 2 years in other athletes; (iii) to use refined ECG (Sheikh et al., 2014) (iv) to conduct longitudinal studies to determine if family history taking, physical examinations, and resting ECG could be repeated only every 3–5 years in recreational athletes (Myerburg & Vetter, 2007; Carré et al., 2009).

Key words: Black athlete, cardiomyopathy, electrocardiogram, echocardiography, pre-participation screening.

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Author contributions

J. C. C. and F. C. drafted the manuscript and prepared the tables and figures; I. M. and J. J. G. edited and revised the manuscript; J. C. C., I. M., J. J. G. and F. C. approved the final version of the manuscript.

References


