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REVIEW

Sudden cardiac death in young athletes

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Ingegerd Östman-Smith

Division of Paediatric Cardiology, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Sweden

Abstract: Athletic activity is associated with an increased risk of sudden death for individuals with some congenital or acquired heart disorders. This review considers in particular the causes of death affecting athletes below 35 years of age. In this age group the largest proportion of deaths are caused by diseases with autosomal dominant inheritance such as hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, long QT-syndrome, and Marfan's syndrome. A policy of early cascade-screening of all first-degree relatives of patients with these disorders will therefore detect a substantial number of individuals at risk. A strictly regulated system with preparticipation screening of all athletes following a protocol pioneered in Italy, including school-age children, can also detect cases caused by sporadic new mutations and has been shown to reduce excess mortality among athletes substantially. Recommendations for screening procedure are reviewed. It is concluded that ECG screening ought to be part of preparticipation screening, but using criteria that do not cause too many false positives among athletes. One such suggested protocol will show positive in approximately 5% of screened individuals, among whom many will be screened for these diseases. On this point further research is needed to define what kind of false-positive and false-negative rate these new criteria result in. A less formal system based on cascade-screening of relatives, education of coaches about suspicious symptoms, and preparticipation questionnaires used by athletic clubs, has been associated over time with a sizeable reduction in sudden cardiac deaths among Swedish athletes, and thus appears to be worth implementing even for junior athletes not recommended for formal preparticipation screening. It is strongly argued that in families with autosomal dominant disorders the first screening of children should be carried out no later than 6 to 7 years of age.

Keywords: sudden death, athletes, hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, screening

Introduction

The sudden death of a presumed healthy individual during athletic activity is a devastating event, both for the family and for team members and coaches. Athletic activity is associated with an increased risk of sudden death for individuals with some congenital or acquired heart disorders, but at the same time we know that regular physical activity has a beneficial effect on long-term cardiovascular morbidity and mortality. Thus the overwhelming majority should be encouraged to take part in athletic activity, but we need to develop tools to identify the small number of individuals at an increased risk, preferably before they get involved in organized sports activity. There are various task force reports concerning the general prevention of sudden death (all ages),[1] and prevention of sudden death during athletic activity.[2] In this review I shall focus on school-age

Correspondence: Ingegerd Östman-Smith
Division of Paediatric Cardiology, Queen Silvia Children's Hospital, Smörslottsgatan
416 85 Gothenburg, Sweden
Tel +46-31-3434512
Fax +46-31-3435947
Email ingegerd.ostman-smith@pediat.gu.se

and young adult athletes, since the majority of athletes dying suddenly in relation to sports activity after 35 years of age die as a result of early ischemic heart disease.

How large is the risk of sudden death among young athletes?

The risk of dying suddenly in association with athletic activities has been quoted as ranging from 1 to 3 deaths per 100,000 person years.[3] In a 25-year study from the Veneto region in Italy (1979–2004) the sudden death rate among nonathletes of 12 to 35 years, ranged from 0.77 to 0.81 per 100,000 throughout the period. Before any kind of preparticipation screening was instituted the sudden death rate in athletes 12 to 35 years was 4.19 per 100,000 which, after screening was introduced in 1982, gradually fell to a death rate of 0.87 per 100,000 in the 1993 to 2004 period.[4] Less widely publicized is the particularly high sudden death risk in young athletes. Of 286 cardiovascular sudden deaths in the US the mean age was 17 ± 3 years,[5] and a subsequent largely retrospective registry study found the lowest age of sudden death in an athlete to be 8 years of age.[3] Statistics on deaths directly associated with athletic activity from the Swedish insurance company Folksam, which insures a large proportion of Sweden's organized athletes are shown in Table 1. The insurance company has documented a gradual fall in average nontrauma related sudden deaths per year from the early rate of 9.6 per year from 1986 to 1990. Following media publicity related to excess death in athletes caused by myocarditis the sports organizations issued strong guidance about avoiding training while suffering from infections, and in the period 1998 to 2005 the annual number of deaths per 1.6 million insured fell to 5.9 per year corresponding to 0.6 per 100,000 insured. In 2006 the Swedish Department of Health and Sports Federation issued guidelines on instituting guidelines for cascade screening in families affected by disorders causing sudden death, and additional guidance about which symptoms should be referred for investigations. In the period 2006 to 2009 the number of deaths averaged 3.5 per year (0.22 per 100,000 insured). The age distribution is interesting with the 15- to 19-year age range showing a higher rate of sudden death than any other age group apart from the 60- to 64-year-olds, and comprising 36% of the <35 year deaths (www.media.folksam.se/allt-farre-plotsliga-dodsfall-inom-idrotten).

Table 1 Sudden death in athletes during, or clearly associated with, athletic activity according to deaths reported to the Folksam insurance company 1998–2009 related to population insured (1.6 million)

Age (years)	Number of deaths	Proportion of deaths per 100,000 insured
14 or below	5	0.31 per 100,000
15–19	9	0.56 per 100,000
20–24	3	0.19 per 100,000
25–29	2	0.05 per 100,000
30–34	6	0.09 per 100,000
35–65 and over	43	0.38 per 100,000 and 5-year age range
All ages	68	4,25 per 100,000

Notes: Total mortality equates an annual mortality rate of 0.35 per 100,000 insured athletes. Data from www.media.folksam.se/allt-farre-plotsliga-dodsfall-inom-idrotten.

Which diseases cause most sudden death among young athletes?

The most detailed information on the breakdown of different diagnoses associated with sudden death in athletes comes from a large study on 1866 deaths among athletes in the USA. After excluding deaths due to trauma causing structural injuries and heat stroke, there were 1049 cardiovascular deaths and an additional 65 deaths caused by commotio cordis. Of the 690 with confirmed diagnosis 36.4% were due to definite hypertrophic cardiomyopathy (HCM), 8.3% were diagnosed as pathological left ventricular hypertrophy possibly due to HCM, 17.2% had coronary artery anomalies, 5.9% myocarditis, 4.3% arrhythmogenic right ventricular cardiomyopathy, 3.6% ion channelopathies associated with arrhythmia (among the 359 cardiovascular deaths with unconfirmed etiology there may be a lot more of undiagnosed ion channel disorders since the registry includes a large number of years where "molecular autopsy" was not practiced), 2.8% aortic rupture, 2.5% valvar aortic stenosis, 2.0% dilated cardiomyopathy, and 1.6% Wolff–Parkinson–White syndrome.[3] The data in this registry are however not population-based, but have been compiled from deaths which have elicited media-reports, so that there is a definite possibility of a selection bias. In a population-based study from northern Italy, however, arrhythmogenic right ventricular cardiomyopathy (ARVC) is the commonest cause of sudden death (26%); since after the introduction of compulsory preparticipation screening, a significant number of athletes with HCM have been disqualified from sports, and thus HCM comprises only 2% of the sudden deaths in athletes.[6] The prevalence of ARVC is however clearly higher in northern Italy than in most other countries. The Italian study has a 15% proportion of coronary artery anomalies causing athletic deaths there, in contrast to a series from the UK where only 7% were thought attributable to coronary artery anomalies,

and 34% were attributed to left ventricular hypertrophy or fibrosis not proven to be due to HCM.[7] It is known that a number of performance enhancing drugs such as anabolic steroids, growth hormone analogs, and beta-receptor agonists such as clenbuterol can cause significant generalized cardiac hypertrophy, and some of the cases under this heading might thus be doping-induced.[8] Certainly anabolic steroid misuse has been associated with an increased risk of sudden death, and must be considered among causes of sudden death in athletes.[9,10] The UK series is however also afflicted by selection bias, since it emanates from a tertiary center of pathology used for a second opinion by other pathologists when cause of death is not definitely established. Thus cases of typical valvar aortic stenosis, HCM, dilated cardiomyopathy (DCM), and clear-cut coronary artery malformations are not likely to be referred for a second opinion. Lastly, some patients who have had surgically corrected congenital heart disease may have an increased risk of exercise-induced ventricular tachycardia.[11–13] Apart from the study from the Veneto-region in Italy there is a shortage of population based studies specifically relating to athletes. Mortality related to age-specific population in the diagnoses commonly associated with sudden death has been published,[14] and is summarized in Table 2. These data confirm that in the 8- to 16-year age range HCM is by far the commonest cause of death; however the circumstances of death are not documented in this series. Sudden deaths in 15- to 35-year-olds, not associated with substance abuse but with or without physical activity has a rather stable population incidence of 0.93 per 100,000 in Sweden.[15] In this material, 21% had no structural anomaly and might have been due to ion channelopathies, and coronary artery disease (17.7%), DCM (12.3%), HCM (10.5%), and myocarditis (10.5%) were the most commonly identified diagnoses. The population incidence of sudden death in Japanese school children ranged from 0.40 to 70 per 100,000, with a particularly high incidence in senior high school students, presumably around 15 to 19 years of age.[16] The most frequently identified causes were myocarditis and "idiopathic cardiomyopathy".

In the Folksam insurance company database the most common causes of death in the <35-year-olds were HCM, ARVC, and myocarditis, ie, similar to the American and Italian data, whereas 71% of the above 35-year-olds died from ischemic heart disease (www.kroppsnytt.se/plotsligdodhosidrottare).

Table 2 Population-based annual mortality per 100,000 age-specific population in Sweden according to death certificates 1997–2003

Cardiac diagnosis	8- to 16-year age range	17- to 30-year age range
HCM	0.112	0.055
DCM	0.034	0.151
Aortic stenosis	0.042	0.009
Coronary anomaly	0.017	0.046
Myocarditis	0.024	0.008
Marfan's and/or aortic dissection	0.048	0.290
Sudden death normal heart (R960)	0.050	0.114
Combined mortality (including I 42.8)	0.327	0.689

Notes: Note that during this period ARVC did not have a separate diagnostic code; some unrecognized episodes have entered the R960 category, others might have been entered under DCM diagnostic code. A total of 2 cases over 8 years (0.016 per 100,000) have been entered under the code I42.8 as causing deaths in the 17–30 year age range, and might have been ARVC or other unspecified cardiomyopathy. Data from Östman-Smith I, Wettrell G, Keeton B, et al. Age-and gender-specific mortality rates in childhood hypertrophic cardiomyopathy. *Eur Heart J*. 2008;29(9):1160–1167.[14]

Abbreviations: ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy.

Which sports are particularly associated with sudden death?

In the large study from US team games such as American football (30%), basketball (20%), soccer (6%), and baseball (6%) contributed the largest numbers of deaths compared with track-and-field (5%).[3] In the Swedish insurance company data base, among the <35-year-olds the majority of the deaths were also due to intensive team sports: 44% soccer, 20% ice hockey, and 16% indoor- and ice-based bandy, with only 8% associated with athletics (www.media.folksam.se/allt-farre-plotsliga-dodsfall-inom-idrotten). However, these team sports also have by far the largest numbers of active practitioners, so that in the absence of specific statistics related to numbers of athletes in the sport no definite conclusions can be drawn.

Are there gender and ethnic differences?

In the postpubertal individual, sudden death is more common in men than in women with a 3:1 to 10:1 male preponderance.[15,17,18] In the Swedish insurance data base there is an astounding 33:1 male preponderance of sudden deaths (www.media.folksam.se/allt-farre-plotsliga-dodsfall-inom-idrotten). However in the early vulnerable years, from 8 to 15, at least for sudden deaths associated with HCM, there is no male preponderance, ie, girls share the higher risk in that age band.[14] In US studies of deaths among athletes there was a significantly higher mortality in sudden death in male than in female athletes, and among nonwhite athletes (predominantly blacks) with the higher death rate particularly attributable to HCM and coronary anomalies, whereas the

fraction of deaths reported to be due to ion channelopathies was higher among whites than nonwhites.[3,5]

What kind of preventative strategies can be employed?

Among the diseases causing sudden death after exercise several have autosomal dominant inheritance (HCM, ARVC, Marfan's syndrome, long QT-syndrome), and both DCM and Wolff–Parkinson–White can have a family history.[1] Thus the initiation of cascade screening of all first degree relatives of patients with inherited cardiac disorders should be the responsibility of the physician making the diagnosis in the index patient. However, there is a substantial spontaneous mutation rate for many of these syndromes, and thus a negative family history alone does not exclude any of these diseases. ARVC also presents a particular problem in this regard as female mutation carriers may not only be symptom-free, but may also not show clear diagnostic features even at an age when their sons are symptomatic. Males are much more likely to become symptomatic, but usually develop signs of the disease from 15 years or older, so that a negative early family screening has to be repeated at intervals, just as for HCM.[19,20] A well functioning school health service should be able to pick up individuals with valvar aortic stenosis and coarctation of the aorta, as long as at least one routine physical examination even for children includes a blood pressure measurement in the right arm, as well as auscultation of the heart and back of the chest by a physician. Many patients with Marfans's syndrome could be identified early if the school health assessment included a measurement of arm span (increased in Marfan's syndrome) in all children with a height over the normal range for age, and for all children with pectus excavatum or pectus carinatum.

What is the role of screening?

The WHO criteria for a screening procedure to be justified includes: 1) The disease should be diagnosable at an early stage. 2) Good methods to evaluate disease progress should exist. 3) A treatment that improves prognosis must exist. HCM, ARVC, long QT, Marfan's syndrome, aortic stenosis and coarctation of the aorta all easily fulfil these criteria. Taken together however (see Table 3), the incidence is around 1.82/1000, and in the view of most authors is not high enough to merit a systematic population screening program. However, directed screening to high risk groups is eminently justified, in particular to first degree relatives of patients with inherited heart disorders, but also to individuals engaging in high risk activity such as organized sport.

Table 3 Population incidence of diseases commonly associated with sudden death

Condition	Population incidence
HCM	2/1000
ARVC	0.6–4/1000
Coronary artery anomaly	<10/1000
Wolff–Parkinson–White	1.5–2.5/1000
Patients with complex cardiac reconstruction or conduits	0.85/1000
Coarctation of the aorta	0.25–0.39/1000
Marfan's syndrome	0.2–0.33/1000
Long QT syndrome	0.2/1000 or more
Valvar aortic stenosis	0.09–0.24/1000
Myocarditis	Unknown

Abbreviations: ARVC, arrhythmogenic right ventricular cardiomyopathy; HCM, hypertrophic cardiomyopathy.

Several working parties from the American Heart Association Council and from the European Society of Cardiologists have concluded that preparticipation screening is advisable for individuals engaged in athletic activity,[21,22] but there is a transatlantic disagreement about the form of screening with the American document recommending screening with history and physical examination only, whereas the European document suggests also including a routine ECG-screening, as does the International Olympic Committee.[23] There has been a heated debate about these suggestions, and some poorly documented figures about number of "false positives" of ECG-screening have been bandied about as an argument for not including ECG-screening. For example, based on criteria of ECG-normality in sedentary individuals, a college athlete study is often quoted as showing that ECG has a "false positive rate of 20%", whereas in fact only 11% had ECG-findings as the only positive screening finding.[24] The figure of 20% has also been vigorously rebutted by a large study on 32,652 unselected subjects undergoing preparticipation cardiovascular screening in Italy.[25] This study showed a normal ECG in 88.2%, and some abnormality in 11.8%. However some of these abnormalities were mild and known to be associated with regular physical training (mild prolongation of PR-interval, incomplete right bundle branch block, and early repolarization pattern) accounted for 7 out of the 11.8%). The ECG-abnormalities considered more suggestive of cardiac disease were deep T-wave inversion in at least 2 precordial and/or standard leads (2.3%), increased RS-voltages suggesting LV-hypertrophy (0.8%), complete right bundle branch block (1.0%), left anterior fascicular block (0.5%), left bundle branch block (0.1%), pre-excitation (0.1%), and surprisingly few prolonged QTc (0.03%). Thus only 4.8% had ECG-abnormalities that by themselves indicated further investigations according to the authors.[25] Unfortunately this

study was limited by not having access to the diagnostic tests performed and final diagnosis reached in the ECG-positive individuals. Therefore assessing from this study how many of the 4.8% were false positives, or if there were any important false negatives among the individuals with minor or no ECG-abnormalities, is not possible. Certainly, in other contexts it has been reported that patients with ARVC failed to come out positive in the standard Italian screening protocol.[4] That the Italian screening approach has tangible effects in reducing mortality in athletes has, however, been clearly shown.[4] Fortunately Baggish et al have carried out the first prospective screening study that compared the outcome of screening with history and examination with and without ECG, to the findings on echocardiography that was performed on all subjects (and further diagnostic work-up as indicated).[26] Among 510 college athletes, age 18 or above, there were 11 individuals identified considered at potential risk from sports participation. History and examination alone detected 5 (sensitivity 45.5%; 95% CI 16.8%–76.2%) whereas the addition of ECG detected a further 5 (sensitivity 90.9%; 95% CI 79.1–86.0). The false positive rate for history and examination alone was 5.5%, compared with a false positive rate of 16.9% when ECG was added. After further detailed work-up, 3/11 were disqualified from athletics, and only 1 out of those 3 had been detected with screening without ECG.[26] The authors used standard ECG-criteria for sedentary individuals and commented that their false positive rate would have been lower if a novel ECG algorithm had been developed that would differentiate physiological remodeling from pathologic heart disease in athletes. Simultaneously, a large cost-effectiveness study concluded that addition of ECG to preparticipation screening would save 2.06 additional life-years per 1000 athletes screened, with a cost-effectiveness of $42,900 per life-year saved, whereas screening with history and examination alone saved only 0.56 life-years per 1000 athletes screened, at a cost of US$199,000 per life year saved.[27] The authors concluded that screening based on history, examination, and ECG saved 2.6 life-years per 1000 athletes screened, and that the cost was reasonable, whereas screening with history and examination alone was poor value for money. They also suggested that a higher threshold for ECG-positivity, and that organized mass screening of young athletes, should bring down costs, whereas annual screening of all school students was unlikely to be cost-effective.[27]

More specific criteria for ECG-screening of athletes have indeed recently been suggested by Corrado et al.[28] It is a large document, with many useful ECG illustrations, but occasionally suffers from being written purely from an adult cardiologist's perspective, and includes recommendations about the subsequent cardiological work-up of individuals with suspected cardiac findings. I have therefore tried to summarize their recommendations in Table 4, also taking account of the findings in young athletes reported by Sharma et al.[29] There have been reports that T-wave inversion across several precordial leads is more common in Afro-Caribbean than in Caucasian athletes,[30] which has led some authors to suggest different and laxer criteria for Afro-Caribbean athletes. At the same time the large American review of deaths among athletes showed a considerable excess mortality among Afro-Caribbean athletes caused by HCM,[3] a diagnosis where precordial T-wave changes may precede severe hypertrophy.[31] Certainly, in a large follow-up of Italian athletes who had abnormal T-wave changes on preparticipation screening, but who were cleared for participation as no definite abnormalities were found on standard echocardiography, 1/84 died suddenly during sports activity with a postmortem diagnosis of arrhythmogenic right ventricular cardiomyopathy; of the 81 subjects with follow-up 5/81 (6%) later developed overt cardiomyopathy, and 6/81 other cardiovascular disease, so that in total 11/81 (13.6%) had undetected cardiovascular disease.[32] Furthermore, the ability to detect as many cases of ARVC as possible rests with doing further assessment of all patients with T-wave inversion in leads V_3–V_4. Consequently my recommendation is that all individuals with abnormal T-wave inversion for age should be referred for detailed echocardiography including tissue Doppler assessment of diastolic relaxation and longitudinal systolic function. Some authors have suggested that the normalization of T-wave inversion on exercise means that it is innocent, but that is not necessarily true, as it is seen, for example, in patients with hypertrophic cardiomyopathy due to absence of glycogen synthesase.[33] An ECG-scoring system for assessing the risk of sudden death in patients with HCM has been proposed, which has a sensitivity of 85% for HCM related sudden death, and a specificity of 100%, ie, 0% false positives among a group of 34 athletes. Using this score will certainly have high sensitivity in detecting patients with HCM at risk for sudden death.[34] This score approach might be developed, by including more features suggestive of ARVC, to be used for general athlete screening, but will first need to be tested in a larger group of athletes before being generally adopted for screening. Based on studies from tertiary referral centers researchers have claimed that in the vast majority of patients with HCM, 75% to 95%, have abnormal ECGs, making ECG-screening effective.[2] This is however not correct for young HCM patients <18

Table 4 How to assess ECG abnormalities in the athlete

Innocent physiological findings in athletes	Uncommon ECG abnormalities requiring further investigations
Sinus bradycardia 30–60/min	Left atrial enlargement
First-degree AV block (and transient A block Mobitz type I Wenchebach resolving with exercise)	Pathological Q-waves
Incomplete right bundle branch block (as long as there is not fixed splitting of the second heart sound on auscultation, and no abnormal T-wave inversion in precordial leads)	Inverted T-waves in leads other than III, avR and V1 (V2 T-wave inversion can be accepted in prepubertal athletes)
Early repolarization (elevation of QR-ST junction >1 mm with up-sloping ST and usually concave shape)	ST-segment depression >1 mm
Isolated increase of QRS-voltages (without evidence of atrial hypertrophy or T-wave changes)	Complete right bundle branch block
Infrequent isolated unifocal ventricular ectopics disappearing at heart rates >110/min	Complete left bundle branch block
	Left axis deviation
	Right axis deviation
	Nonspecific intraventricular conduction defect with QRS duration >110 ms
	Pre-excitation with PR interval <0.12 sec
	Prolonged QTc interval male: >440 msec, female: >460 msec
	Short QT-interval QTc < 320 msec
	Brugada-like ECG abnormalities with a ST-elevation ≥2 mm most prominent in right precordial leads characterized by high J-point and down sloping ST, with a "coved" or "saddleback" T-wave
	Frequent or polymorph ventricular ectopics
	Epsilon-waves in right precordial leads

Abbreviation: AV, atrioventricular.

years of age identified through cascade screening, where only around 56% have ECG-abnormalities, if 12-lead QRS amplitude sum >24 mV is counted as a diagnostic abnormality.[35] However, the latest proposal from Corrado et al is that ECG-amplitude voltages should be ignored when screening athletes.[28] The ECG shown in Figure 1 illustrates that this suggestion poses a dilemma. This was a 12-year-old boy who fainted during exercise (ie, high risk for sudden death), and where investigations established that he had obstructive hypertrophic cardiomyopathy. Yet the only abnormality on his ECG was that of voltages: Sokolow–Lyon index of 5.8 mV, limb lead QRS-amplitude sum of 11.7 mV (fulfilling pediatric high-risk criteria in HCM,[36] and a 12-lead amplitude voltage sum of 31.5 mV). Konno et al showed that 12-lead QRS amplitude voltage sum of >24 mV, and a Romhilt–Estes score of ≥4 were the most sensitive ECG measures to identify genetically verified HCM, with a false positive rate of 5%.[37] The comment of Baggish in an author reply "that we need criteria based on data rather than opinion" is still very valid,[38] and we do need a prospective study that actually documents the false positives and false negatives in athletes with these new criteria suggested by Corrado et al,[28] and also includes testing a higher voltage-amplitude cut-off for 12-lead voltages, or using limb-lead amplitude duration product, which has the same normal range in both genders, simplifying its use in screening.[34]

Equally valid is a comment by Yarows that: "As a parent, wouldn't you rather pay $88 once for your high school student to receive effective screening for potential cardiovascular sudden death rather than yearly ineffective and unproven sports physicals. This cost is less than that of a pair of athletic shoes" (referring to the American screening system).[38]

How should screening be performed?

1. There is general consensus that a history should be taken, which includes questions on a family history of unexpected sudden death below 50 years of age, knowledge of a family member with symptomatic heart disease below 50 years of age, and any knowledge of heart muscle disorders, arrhythmia problems or Marfan's or long QT-syndrome. Further, any existence of symptoms such as heavy chest pain, or abnormal breathlessness on exertion, episodes of palpitations, previous episodes of faints or sudden near fainting episodes should be ascertained. Both HCM and DCM, as well as coronary artery malformations, may have exercise-related symptoms that for years are misinterpreted as exercise-induced asthma.

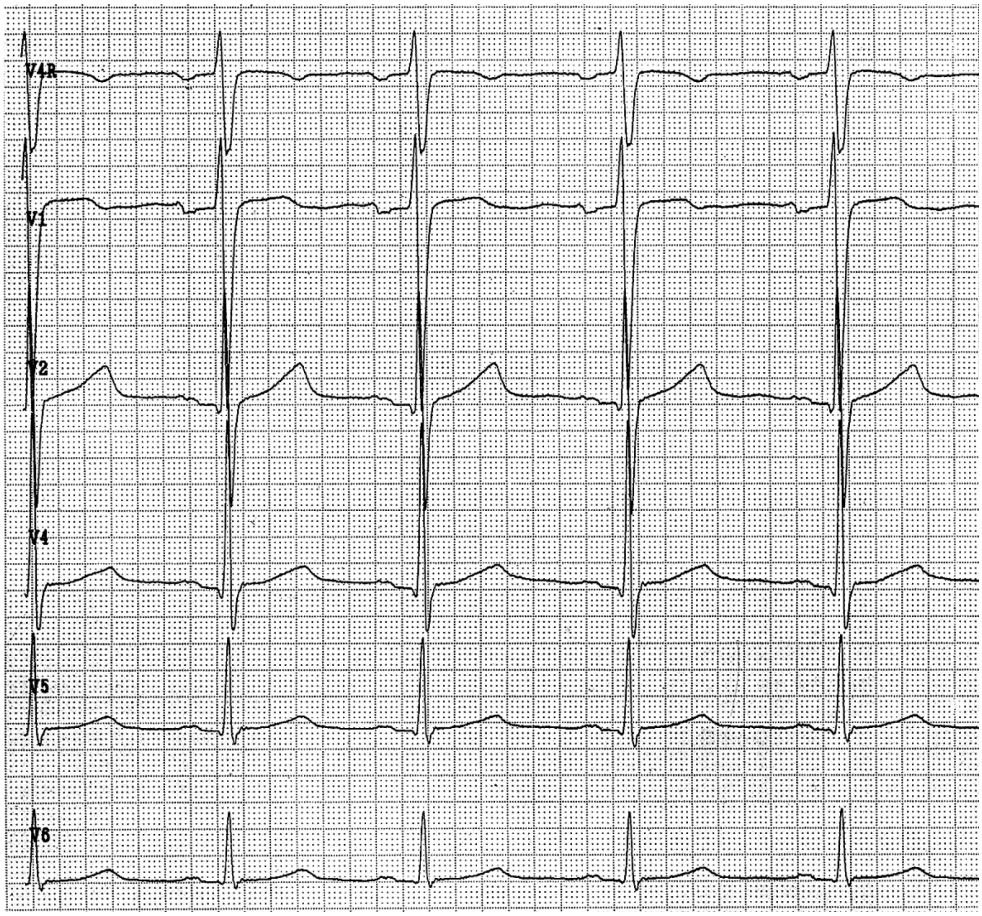

Figure 1 The precordial ECG from a 12-year-old boy with hypertrophic obstructive cardiomyopathy, with syncope on exercise as presenting symptom. The only abnormality is that of large ECG-voltages, and a typical feature is the way R and S-waves from different leads are superimposed on each other at standard magnification with 10 mm/mV. The Sokolow–Lyon index is 5.8 mV, limb lead QRS-amplitude sum is 11.7 mV (fulfilling pediatric high risk criteria in HCM,[36] and the 12-lead amplitude voltage sum is 31.5 mV, also in the high-risk territory.[34]

Any previous findings of heart murmur or elevated blood pressure should be recorded. This could initially be established by a questionnaire, which also allows young athletes to consult their parents for the family history.

2. Physical examination should include listening for cardiac murmurs precordially and over the back, measuring the blood pressure in the right arm, palpating the femoral pulses, and to visually assess possible stigmata of Marfan's syndrome, including measuring span (or sitting height) on all individuals with a height >2 SD for age. Appearances suggestive of Noonan´s syndrome are also relevant, in view of the high correlation with hypertrophic cardiomyopathy.
3. A resting ECG should be taken. If resting ECG shows, eg, very marked sinus bradycardia or ventricular ectopics, it could be combined with a simple instantaneous limited exercise with a repeat ECG after a simple step-test, or repeated sit-ups, to assess how heart rate increases, and how ventricular ectopics repond to a faster sinus rhythm (should disappear at heart rates >110). The best current experience suggests that the ECG should be judged according the criteria in Table 4, and that those positive should be referred to detailed echocardiography before being cleared for participation in sports, or to 24-hour ECG and exercise test in case of suspected rhythm disorders. Some examples of ECG findings in HCM, ARVC, Long QT-syndrome, and Wolff–Parkinson–White are illustrated in Figures 1–4. Individuals with symptoms, and patients with findings suspicious of long (or short) QT or Brugada syndrome ought to be referred promptly to a cardiologist with expertise in these disorders.

At what age should preparticipation screening be commenced?

The task force recommendations (written by adult cardiologists) have been to commence screening "after 12–14 years of age". Considering that a significant number of athlete deaths occur before 15 years of age, and particularly with HCM, in children as young as 8 years of age, see Figure 5[3,14]

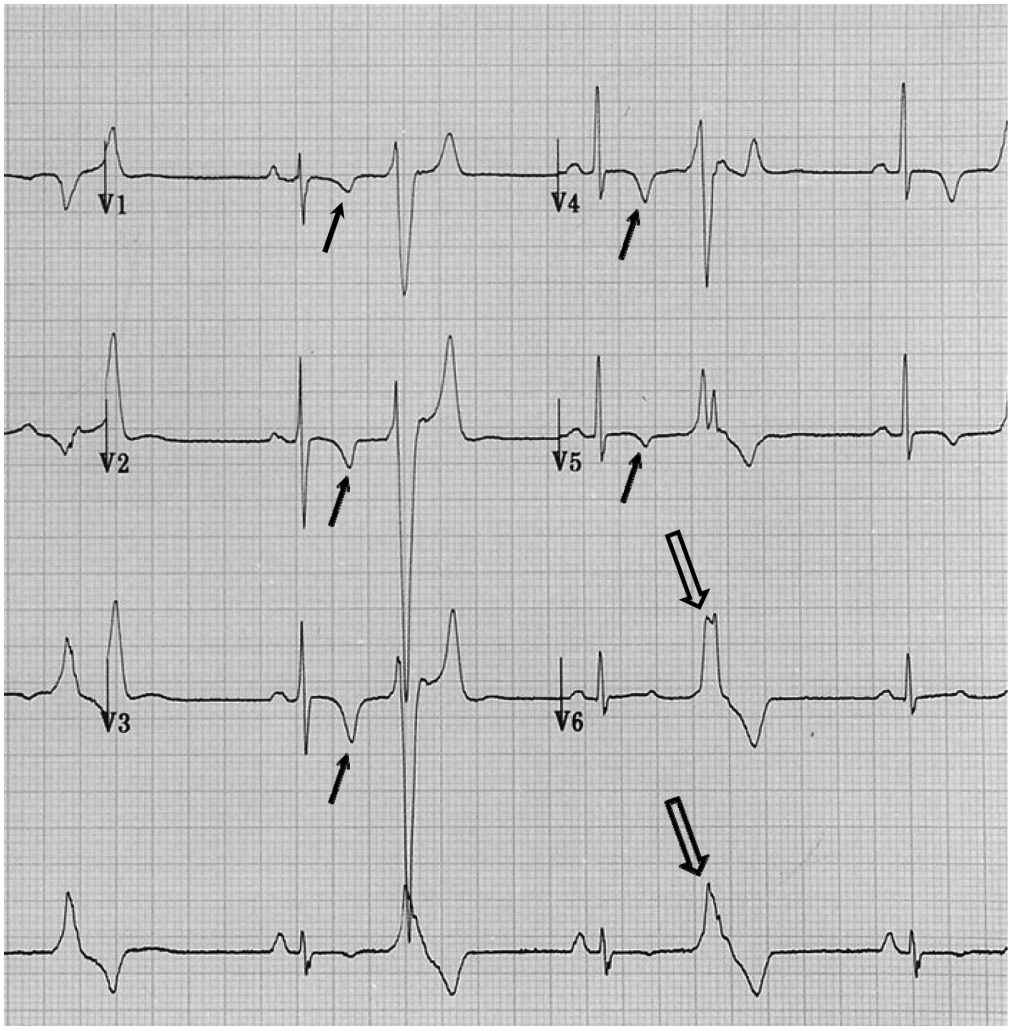

Figure 2 Precordial ECG from a patient with arrhythmogenic right ventricular cardiomyopathy, narrow arrows show inverted T-waves out to V5, fat arrows show ventricular ectopic beats with left bundle branch morphology, ie originating from the right ventricle.

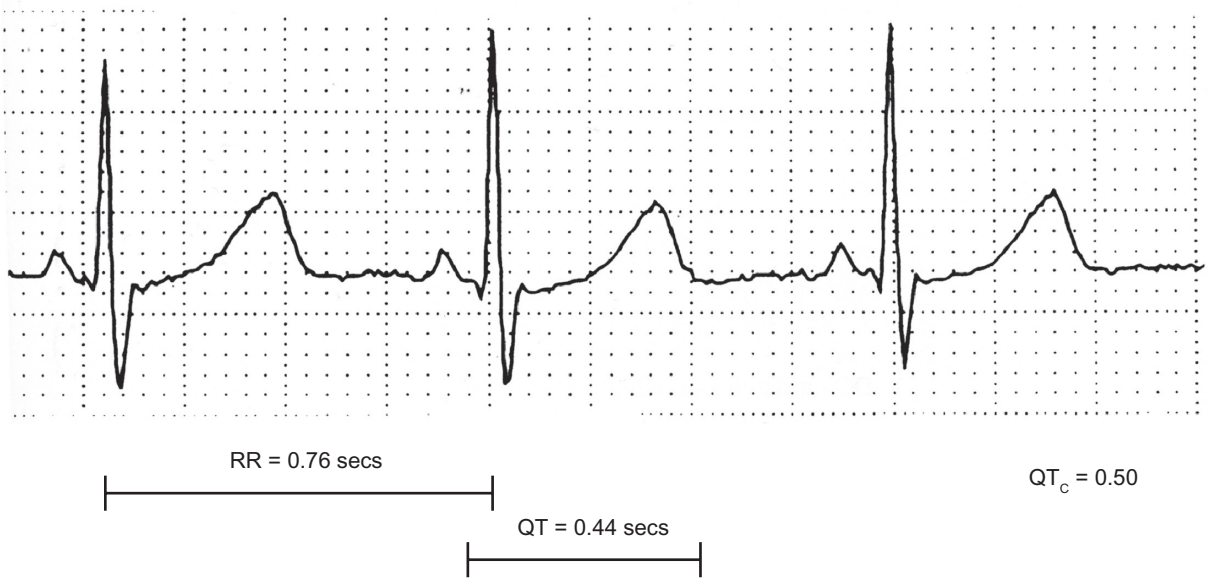

Figure 3 The ECG from a patient with Long QT-syndrome; QTc is easily calculated by Bazett's formula: QTc = QT-interval: ($\sqrt{RR}$-interval).

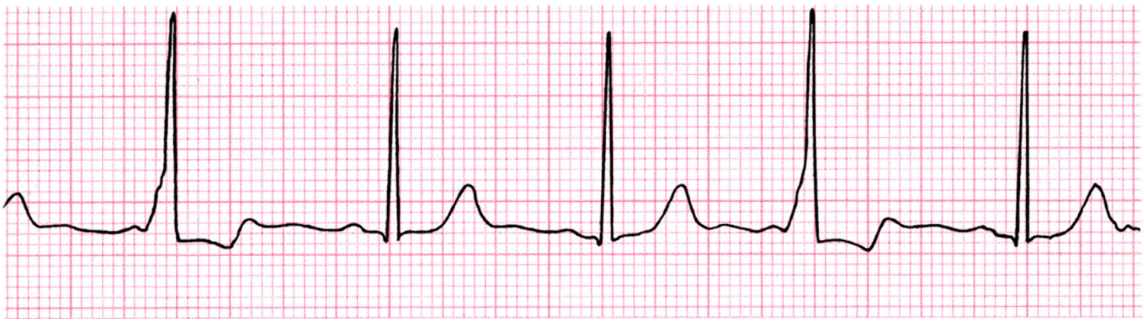

Figure 4 Wolff–Parkinson–White syndrome with every third beat conducted with pre-excitation, and a typical delta-wave.

it is mandatory that at least preparticipation screening of first degree relatives of known cases of hereditary heart disease is performed considerably earlier, ideally no later than around 6 to 7 years of age before organized sports activities are started. The Swedish experience, where even junior sport clubs since 2006 have been recommended to use preparticipation questionnaires to identify children with a family history of heart disease, or suspect symptoms, appears

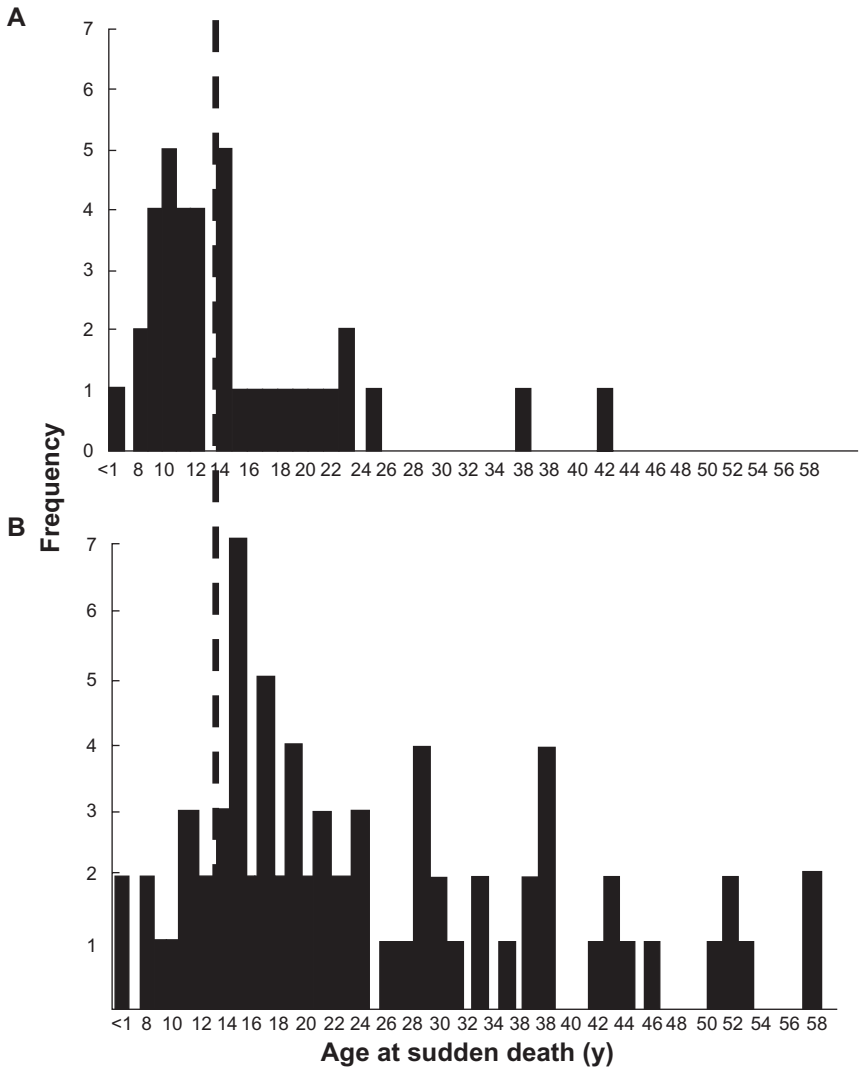

Figure 5 Figure illustrating the age-profile at sudden death of patients with hypertrophic cardiomyopathy (HCM). **A**) Patients from a geographical cohort diagnosed with HCM in childhood (data from ref 14), and in **B**) a group of HCM patients of all ages from a tertiary referral center. Copyright © 1982. Reproduced with permission from Wolters Kluwer Health. Maron BJ, Roberts WC, Epstein SE. Sudden death in hypertrophic cardiomyopathy: a profile of 78 patients. *Circulation*. 1982;65: 1388–1394.[56] The dashed line indicates 14 year of age, the age recommended for initial pre-participation screening of active athletes. As is very obvious from this figure, a considerable amount of sudden deaths due to HCM occur before the age of 14.

to be associated in time with a reduction in sudden deaths during sports activity (see above). There is the additional factor of the immense psychological trauma caused to teenagers who are suddenly banned from continuing in a sport in which they have been active since early childhood, and where they have developed their whole social network among fellow players. They might even have arranged their schooling with the ambition of becoming a professional soccer or ice-hockey player. It is very much my experience that children with familiar heart muscle disorders accept exercise restrictions much more readily, and are psychologically less affected by them, if they are told about it in the 6 to 8 year age range, where they early on can be steered into alternative suitable sports, and suitable other leisure activities such as music or art.

How do you best differentiate physiological hypertrophy in an athlete, the so-called "athlete's heart", from hypertrophic cardiomyopathy?

Regular physical training by itself is associated with cardiac remodelling and cardiac hypertrophy, which in endurance athletes consists of a proportional increase in wall thickness and cavity size, so that the wall:cavity ratio remains normal.[39–42] Additional isometric training such as weight lifting can cause more concentric hypertrophy. In one study on elite athletes (Olympic candidates) only 16 out of 947 athletes had a wall thickness of 13 mm or above, and 15/16 were rowers or canoeists.[43] The wall-to-cavity ratios have a great advantage for screening in having the same normal values for males and females,[42] and normal values from birth to young adults have been published.[42] The normal values increase marginally during the pubertal growth, and the normal values for those ages relevant for preparticipation screening (range 6–35) are given in Table 5. Normal values for junior athletes were not significantly higher, being 0.19 (±SD of 0.03) for left ventricular wall-to-cavity ratios, and 0.19 (±0.02) for septum-to-cavity ratio.[42] Older endurance athletes also had a septum-to-cavity ratio of 0.19 (±0.02). Elite rowers instead had an average septum-cavity ratio of 0.23 (±0.03), with 2/17 having a septum-to-cavity ratio >0.26, ie, they would be false-positives on screening using 99% prediction limits in normals for septum-to-cavity ratio as a cut-off.[41] However, typical for the athlete's heart is that the circumferential contractility is normal, or even low-normal, whereas circumferential contractiliy in HCM patients, particularly young ones, is often increased. This could be used to differentiate between physiological hypertrophy (athlete's heart) and HCM, because a cut-off of systolic wall-to-cavity ratio of >0.63 has a 94% detection rate for HCM, and 0% false positive rate for athletes.[41] Longitudinal function is often supernormal in athletes,[44] whereas it is often reduced in hypertrophic cardiomyopathy,[45] and this can be measured simply with systolic AV (atrioventricular)-plane excursion on M-mode, and more exactly using septal and lateral tissue Doppler velocity measurements.[46] A low early-diastolic septal tissue Doppler velocity, resulting in a high ratio to trans-mitral diastolic flow rate, is also a marker of high risk for adverse complications in hypertrophic cardiomyopathy.[47] Further approaches to risk assessment in children and adolescents with confirmed HCM have been reviewed recently by Östman-Smith.[48]

What is the position of children with congenital heart disease?

There are two main types of congenital heart disease that may necessitate restrictions on participation in organized

Table 5 Normal values of wall-to-cavity ratios

Measure	Mean	95% CI of mean	95% prediction limit	99% prediction limit
SEPCAVR				
Age 6–10 yrs	0.17	0.17–0.18	0.12–0.21	0.12–0.24
Age 11–15 yrs	0.18	0.17–0.19	0.13–0.23	0.12–0.25
Age 16–35 yrs	0.18	0.18–0.19	0.14–0.23	0.12–0.25
LVCAVR				
Age 6–10 yrs	0.17	0.16–0.17	0.13–0.20	0.13–0.21
Age 11–15 yrs	0.18	0.17–0.19	0.13–0.23	0.11–0.24
Age 16–35 yrs	0.18	0.17–0.19	0.13–0.22	0.12–0.24
SYSCAVR				
Age 6–10 yrs	0.46	0.43–0.48	0.34–0.58	0.30–0.59
Age 11–15 yrs	0.48	0.46–0.50	0.36–0.61	0.32–0.62
Age 16–35 yrs	0.47	0.46–0.49	0.34–0.61	0.30–0.65

Note: Wall and cavity measurements as measured by long-axis M-mode echocardiography.
Modified from Östman-Smith and Devlin.[42]
Abbreviations: SEPCAVR, diastolic septal thickness: diastolic left ventricular diameter; LVACVR, diastolic posterior left ventricular wall thickness: diastolic left ventricular diameter; SYSCAVR, systolic posterior left ventricular wall thickness: systolic left ventricular diameter.

sport and vigorous leisure activities, and they are firstly the presence of a significant outflow obstruction providing a pressure overload on the right or left ventricle with exercise, and secondly, the presence of myocardial scars causing increased risk of arrhythmias after reconstructive surgery including large myocardial incisions.

The influences of different types of congenital heart disease on eligibility for sports participation have been updated by a task force recently, and the reader is referred there for a detailed review.[11] As a brief summary, the recommendations are that valvar pulmonary artery stenosis with a peak instantaneous Doppler gradient of 40 to 60 mm Hg, should participate only in particularly low intensity sports, and should generally be referred for balloon valvuloplasty before participation. Patients with a gradient >60 mm Hg must not participate in sports until adequately treated.[11] Patients with valvar aortic stenosis and a mean gradient <25 mm Hg, and a peak gradient of <40 mm Hg, who have a normal ECG on exercise test, and who are also completely free of symptoms can participate in sports,[11] but the examiner must be alert to the possibility of underestimating the aortic valve gradient because of a suboptimal Doppler angle, and it is recommended that the degree of left ventricular hypertrophy is also assessed by M-mode echocardiography, as the systolic and diastolic wall-to-cavity ratios are a very good marker for severity of valvar aortic stenosis,[42,49] and thus a significant left ventricular hypertrophy (left ventricular wall-to-cavity ratio >0.24) suggests that a Doppler gradient <40 mm Hg is an under-estimate.[42] Patients with mean gradients >40 mm Hg, or peak gradients >70 mm Hg should be completely banned from sports participation.[11] Significant coarctation of the aorta should clearly not be left untreated because of the risk of sequelae from cerebral hemorrhage, but patients with an arm-to-leg blood pressure difference of ≤20 mm Hg, and a maximal exercise systolic blood pressure <230 mm Hg can participate in sports. Treated patients with a residual coarctation gradient of >20 mm Hg arm-leg difference, and an exercise maximal systolic blood pressure >230 mm Hg may only take part in low intensity exercise.[11] Patients with previous reconstructive surgery such as Mustard, Senning or arterial switch correction of transposition, surgical correction of tetralogy of Fallot, and corrections involving insertion of conduits, should be evaluated with history, examination, and ECG, ambulatory ECG, maximal exercise test and chest X-ray before being allowed to participate, and ought to be evaluated by physicians experienced in congenital heart disease.[11] Patients with a functional univentricular circulation, corrected by a Fontan-operation or a total cavo-pulmonary bypass, can only participate in low-intensity exercise and need full assessment for arrhythmia risk with 24-hour ECG and exercise tests before any participation. As the pulmonary circulation is only driven by the systemic venous pressure, extreme care must be taken to avoid dehydration and hypovolemia during prolonged exercise or exercise during high environmental temperatures.[11] Patients with a coronary artery anomaly resulting in a coronary artery passing between the great arteries should be excluded from all competitive sports.[11] Late risk for arrhythmias on exercise after different types of surgical corrections are well covered in a task force report on management of adults with congenital heart disease, and the reader is referred there for detailed management advice.[13] When counseling adolescents with significant sports restrictions, due to inherited heart muscle disease or congenital heart disease, it is important that they and their parents are given clear advice about what kind of sports and leisure activities are still allowed according to American Heart Association Guidelines, so that these adolescents can be encouraged to transfer their leisure activities to something more suitable, for example golf.

Commotio cordis

Commotio cordis, a condition where a hard precordial blow hitting the heart while it is in a vulnerable repolarization phase induces ventricular tachycardia or fibrillation even in the absence of any myocardial tissue damage, causes about the same number of deaths during sports activities as acute myocarditis.[3,50,51] The degree of force and velocity necessary to cause arrhythmia have been studied,[52] but this is obviously a chance event that you cannot diminish with screening. Some types of body protection in sports prone to ball trauma have been assessed,[53,54] but the most important preventative measure that can be adopted is to educate sports coaches and athletes in the condition, so that prompt and adequate bystander resuscitation can be initiated.[55] Availability of defibrillation equipment at sports arenas would obviously facilitate early effective treatment.

Conclusion

Athletic activity is associated with an increased risk of sudden death for individuals with some congenital or acquired heart disorders. However experience from Italy and Sweden suggests that the premature mortality of athletes can be reduced by formal, organized preparticipation screening including ECG-screening, and probably also to some extent by a targeted cascade screening of individuals

with a family history of heart muscle or ion channel disorders, and a search by preparticipation questionnaire for symptoms suggestive of a potential cardiac problem. Thus there is little doubt that some kind of preparticipation screening of children and adolescents, as well as adults, wanting to take part in organized sports activities should take place. With existing ECG screening criteria, the false positive rate is acceptable, and could be lowered by the latest suggestions (see Table 4), but there is still a need for further research to base improved ECG-screening criteria on firm data rather than on consensus opinions from experts, in order to bring the false positive rate down further without sacrificing sensitivity.

Disclosure

The author has no conflicts of interest to declare.

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