Preparticipation screening for cardiovascular abnormalities in young competitive athletes

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The cardiovascular benefits of regular physical exercise are well established.[1] However, a small proportion of young (≤35 years) athletes with unsuspected heart disease are at increased risk of exercise related sudden cardiac death.[2] The majority of such deaths are attributable to cardiac anomalies,[2-4] most of which can be identified during life. A range of therapeutic strategies can be implemented to prevent fatalities, raising support for screening young athletes in medical and sporting communities.[5-9] The efficacy, cost effectiveness, and impact of false positive tests of preparticipation screening strategies are, however, controversial. This article provides a factual overview of preparticipation screening, as more general practitioners are likely to be confronted with the questions relating to cardiovascular screening in athletes in countries where systematic screening programmes are currently not available.

Epidemiology and demographics of sudden cardiac death in young athletes

Sudden cardiac death in young athletes is uncommon. In the United States a retrospective review of 650 000 competitive high school athletes aged 15-17 reported an incidence of 0.5 per 100 000 per year.[10] In Italy, a prospective population based observational study reported the higher incidence of 2.1 per 100 000 per year in athletes aged 14-35.[2] The absence of systematic registries precludes data relating to the incidence of sudden cardiac death in young athletes in most other European countries.

Over 90% of sudden cardiac deaths in young athletes occur during or shortly after exercise.[2] A sex and sport related predilection exists, with a predominance in males (male to female ratio 9:1) and the largest number of deaths reported in soccer and basketball. Higher participation rates provide the most plausible explanation. The mean age of sudden cardiac death in young athletes ranges from 17.1 to 23.[2 3]

A broad spectrum of congenital, inherited, and acquired cardiovascular diseases causes sudden cardiac death (fig 1). Inherited cardiomyopathies are the commonest cause, with hypertrophic cardiomyopathy accounting for over one third of cases of sudden cardiac deaths in athletes in the United States[5] and arrhythmogenic right ventricular cardiomyopathy predominating in Italy.[4] Congenital coronary artery anomalies and premature atherosclerosis account for almost 20% of cases of sudden cardiac death.[4]

What is the objective of preparticipation screening?

The potential for preventing sudden cardiac death in young athletes by abstinence from exercise of moderate to high intensity, pharmacotherapy, or implantation of a cardiovertor defibrillator has prompted the medical and sporting community to recommend preparticipation cardiovascular screening to permit identification of potentially fatal disorders. Both the American Heart Association and the European Society of Cardiology agree that the justifications for providing preparticipation screening to protect athletes are compelling.[5 6] Given the low prevalence of the disorders implicated in sudden cardiac death during sport, several thousand athletes would need to be screened to identify a small number at risk, therefore the emphasis is on providing the most cost effective method for minimising sudden cardiac death.[11]

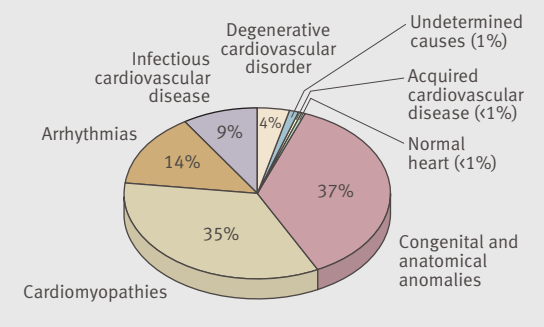

Fig 1 | Causes of sudden cardiac death in young athletes (adapted from Maron et al[5])

Sources and selection criteria

We searched PubMed and Medline from 1980 onwards using the search terms "preparticipation screening", "sudden death", "electrocardiogram", "athletes", "black athletes", and "cost-effectiveness". Although we scrutinised and selected the highest quality articles, comprising original papers, reviews, recommendations, and consensus reports, the studies are all population based, prospective or retrospective observational reports. To our knowledge the efficacy of preparticipation screening programmes in young athletes has not been subjected to controlled trials, as they would be challenging to do both ethically and technically.

What are the current practices?

Most countries do not offer systematic programmes for preparticipation screening. In the United States the American Heart Association recommends such screening using a health questionnaire and physical examination (box 1).[5] This strategy seems cheap and easy to carry out but has limited value as 80% of athletes who die as a result of sudden cardiac death are asymptomatic and physical examination identifies few implicated disorders. The lack of sensitivity of the American model was highlighted in a series of 115 reported cases of sudden cardiac deaths in young athletes who had been screened. A correct diagnosis was identified in only one athlete (0.9%), who was allowed to compete. The limited sensitivity of this strategy has been further highlighted by prospective observational studies in the United Kingdom and Italy.[12 13]

Box 1 American Heart Association guidelines for preparticipation cardiovascular screening of young, competitive athletes

Medical history*

Chest pain or discomfort on exertion

Unexplained syncope or near syncope†

Excessive exertional dyspnoea or fatigue

Prior recognition of a heart murmur

Raised systemic blood pressure

Family history

Premature death (‹50 years) from heart disease, in one or more relatives

Disability from heart disease in a close relative aged less than 50

Specific knowledge of certain cardiac conditions in family members: hypertrophic and dilated cardiomyopathy, long QT syndrome or other ion channelopathies, Marfan's syndrome, or clinically important arrhythmias

Physical examination

Heart murmur‡

Femoral pulses to exclude aortic coarctation

Physical stigmata of Marfan's syndrome

Brachial artery blood pressure (sitting position, taken in both arms)

*Parental verification is recommended for high school and middle school athletes
†Judged not to be vasovagal; of particular concern when related to exertion
‡Auscultation should be done both while supine and while standing or with Valsalva manoeuvre, specifically to identify murmurs of dynamic left ventricular outflow tract obstruction

In Italy a unique state sponsored, national preparticipation screening programme has been in operation for over 25 years. The programme, which evaluates several million athletes annually, comprises a history, examination, and electrocardiography. Athletes with abnormalities on initial evaluation are investigated further and those with potentially serious abnormalities are disqualified (fig 2).[13 14] The additional electrocardiography increases the sensitivity of the programme, enabling the diagnosis of a large proportion of cardiomyopathies and disorders of accessory pathways and ion channels. Although the definitive diagnosis of cardiomyopathies depends on cardiac imaging, electrocardiographic abnormalities are exhibited by 95% of people with hypertrophic cardiomyopathy and 80% of those with arrhythmogenic right ventricular cardiomyopathy.[15 16]

Is the Italian model effective in identifying cardiovascular disorders in young athletes?

The efficacy of the Italian screening programme in the identification of cardiomyopathies is established. Evidence suggests, however, that the strategy is not effective in detecting athletes with congenital coronary anomalies or premature coronary atherosclerosis.[17]

In a large population based study of screening outcomes in 33 735 young athletes in the Veneto region of Italy, 621 (1.8%) were disqualified because of an identified cardiovascular disorder. Of these, 22 (0.07%) were considered to have hypertrophic cardiomyopathy, predominantly (73%) on the basis of an abnormal electrocardiogram.[13] This frequency is similar to that observed in a population based study in the United States, which used echocardiography, suggesting that the Italian model performs as well as echocardiography in detecting hypertrophic cardio myopathy.[18] The specificity of the Italian programme in excluding the diagnosis of hypertrophic cardiomyopathy was also assessed in a study of 4450 elite athletes who were initially judged eligible for

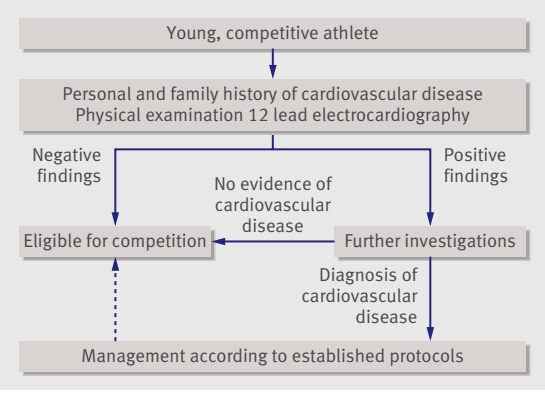

Fig 2 | Italian preparticipation screening protocol endorsed by International Olympic Committee, Fédération Internationale de Football Association, European Football Associations, and European Society of Cardiology. Reproduced from Corrado et al[6] with permission of the European Society of Cardiology

Arguments for and against preparticipation screening

Arguments in favour

Highly visible events affecting young, fit people

Association between exercise and sudden death

Identifiable conditions with acceptable interventions that can prevent sudden cardiac death

Life years lost

Acceptable screening test

The Italian experience

Arguments against

Sudden cardiac death in athletes is rare; 0.5-2.1 per 100 000 per year

Low risk even in affected athletes

Screening for several rare disorders, with diverse pathology

Cost prohibitive

Limitations of electrocardiography as a screening test

Population based observational studies

competition after preparticipation screening using 12 lead electrocardiography. The athletes underwent echocardiography to assess previously undetected hypertrophic cardiomyopathy.[19] After an average follow-up of eight years hypertrophic cardiomyopathy was diagnosed in only one (0.02%) athlete indicating that a normal electrocardiogram has a high negative predictive value (99.98%), excluding hypertrophic cardiomyopathy in most athletes. More recent experience from the Italian programme suggests that screening using 12 lead electrocardiography is also effective in detecting athletes with arrhythmogenic right ventricular cardiomyopathy.[17]

Box 2 Criteria for positive 12 lead electrocardiography according to European Society of Cardiology consensus statement[13]

P wave

Left atrial enlargement: negative portion of P wave in lead V1 of 0.1 mV or less depth and duration of 0.04 or more seconds

Right atrial enlargement: peaked P wave in leads II and III or V1 of 0.25 mV or more amplitude

QRS complex

QRS axis deviation: right 120° or more or left −30° to −90°

Increased voltage: amplitude of R wave or S wave in a standard lead of 2 mV or more, S wave in lead V1 or V2 of 3 mV or more, or R wave in lead V5 or V6 of 3 mV or more

Pathological Q waves: duration 0.04 seconds or more, or 25% or more of the height of the ensuing R wave, or QS pattern in two or more leads

Right or left bundle branch block with QRS duration of 0.12 seconds or more

R or R' wave in lead V1 0.5 mV or more in amplitude and R/S ratio of 1 or more

ST segment, T waves, and QT interval

ST segment depression, T wave flattening, or inversion in two or more leads

Prolongation of heart rate corrected QT interval of more than 0.44 seconds in males and more than 0.46 seconds in females

Rhythm and conduction abnormalities

Premature ventricular beats or more severe ventricular arrhythmias

Supraventricular tachycardias, atrial flutter, or atrial fibrillation

Short PR interval (‹0.12 seconds) with or without "delta" wave

Sinus bradycardia with resting heart rate 40 beats/min or less*

First (PR ≥0.21 seconds†), second or third degree atrioventricular block

*Increasing less than 100 beats/min during limited exercise test
†Not shortening with hyperventilation or limited exercise test

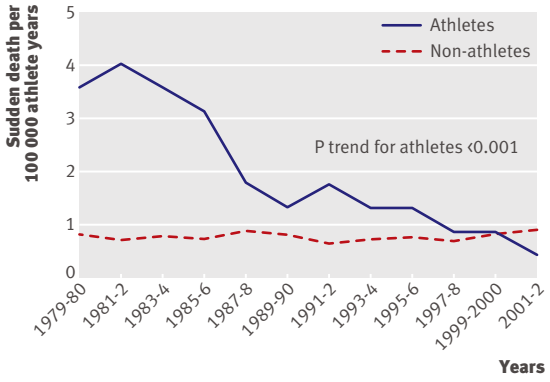

Fig 3 | Annual incidence of sudden cardiovascular death in screened competitive athletes compared with non-athletes in Veneto region, Italy, 1979-2004. Reproduced from Corrado et al[17] with permission of *JAMA*

Does the Italian model reduce the number of sudden cardiac deaths in young athletes?

Although hypertrophic cardiomyopathy is the commonest cause of exercise related sudden cardiac death in the United States, in Italy it is responsible for a much smaller proportion of deaths. Although antagonists of preparticipation screening argue that this might reflect a lower genetic cluster of people with hypertrophic cardiomyopathy in the Mediterranean region, these figures probably reflect the efficacy of the Italian programme in identifying athletes with hypertrophic cardiomyopathy and minimising deaths through disqualification from sport; none of the 22 athletes identified with hypertrophic cardiomyopathy in the Veneto region between 1979 and 1996 died during a mean follow-up of 8.2 years. Of the 49 deaths recorded among young athletes during the same period, only one had hypertrophic cardiomyopathy (2%)—lower than the incidence of 7.3% recorded in 220 sudden deaths among non-athletes.[13]

The most compelling evidence for the Italian preparticipation screening model reducing the incidence of sudden cardiac death in sport is derived from a subsequent prospective study by the same group. The group compared the incidence of sudden cardiac death between the prescreening era and a 25 year period of screening and showed a reduction in incidence of sudden cardiac death from 3.6 per 100 000 person years before screening to 0.4 per 100 000 person years in 2003-4 (fig 3).[17] These figures represent a 90% reduction in mortality since preparticipation screening was implemented and predominantly result from fewer cases of sudden cardiac death from cardiomyopathies, particularly arrhythmogenic right ventricular

cardiomyopathy—a relatively novel entity in the early screening era which cardiologists have become more effective at diagnosing. Of concern, however, was the unchanged incidence of sudden cardiac death from coronary disorders.

What are the limitations of 12 lead electrocardiography as a screening tool?

Electrocardiography is unable to identify premature coronary artery disease and congenital coronary anomalies, which account for a major proportion of sudden cardiac death in young athletes.[4 17] Testing might also fail to detect people with long QT syndrome and arrhythmogenic right ventricular cardiomyopathy with incomplete phenotypic expression.

Electrocardiographic changes associated with physical conditioning often overlap with those observed in cardiomyopathy, resulting in unnecessary investigations or false disqualification of athletes. Therefore preparticipation screening should be done by cardiologists with knowledge of cardiovascular adaptation to exercise as well as the broad phenotypic manifestations of the cardiomyopathies. Even in the most experienced hands, the false positive rate may be unacceptably high. An observational study of 1005 selected Italian athletes reported an incidence for mildly or distinctly abnormal electrocardiogram findings of 40%, only 5% of which were eventually diagnosed as a cardiovascular abnormality. The investigators reported an electrocardiographic sensitivity of 51%, specificity of 61%, positive predictive value of 7%, and negative predictive value of 96%, raising concerns about the value of such testing in preparticipation screening.[20] A large Italian study of 42 386 young athletes screened over 22 years and using more conventional electrocardiographic criteria (box 2) found a false positive rate of 7%, with only 2% of athletes being disqualified because of cardiovascular disease.[4]

The impact of ethnicity on cardiovascular adaptation in athletes has not been studied in detail; however, evidence is emerging that noticeable repolarisation changes, similar to those observed in people with cardiomyopathies, are more commonly exhibited by Afro-Caribbean athletes. Further data relating to the spectrum of physiological electrocardiographic changes in this cohort are required.[21 22]

Box 3 WHO criteria for screening[28]

- The condition should be an important health problem
- There should be an accepted treatment or useful intervention
- The natural history of the disease should be adequately understood
- There should be a latent or early symptomatic stage
- There should be a suitable and acceptable screening test
- Facilities for diagnosis and treatment should be available
- There should be an agreed policy on who to treat as patients
- Earlier treatment should be beneficial
- Case finding should be a continuing process and not a once and for all project
- The cost should be economically balanced in relation to possible expenditure on medical care as a whole

Additional educational resources

Review articles on preparticipation screening

Corrado D, Thiene G. Protagonist: routine screening of all athletes prior to participation in competitive sports should be mandatory to prevent sudden cardiac death. *Heart Rhythm* 2007;4:520-4

Viskin S. Antagonist: routine screening of all athletes prior to participation in competitive sports should be mandatory to prevent sudden cardiac death. *Heart Rhythm* 2007;4:525-8

Chaitman BR. An electrocardiogram should not be included in routine preparticipation screening of young athletes. *Circulation* 2007;116:2610-5

Myerburg RJ, Vetter VL. An electrocardiogram should be included in routine preparticipation screening of young athletes. *Circulation* 2007;116:2616-26

Crawford MH. Screening athletes for heart disease. *Heart* 2007;93:875-9

Maron BJ, Pelliccia A. The heart of trained athletes. Cardiac remodelling and the risks of sport, including sudden death. *Circulation* 2006;114:1633-44

Information for patients

Cardiac Risk in the Young (www.c-r-y.org.uk/)—subsidises cardiovascular screening in the United Kingdom, provides information and support to families of victims of sudden death, and funds research and educational events

The Cardiomyopathy Association (www.cardiomyopathy.org/index.html)—provides information and support to families with cardiomyopathy and funds research and educational events

Sudden adult death (www.patient.co.uk/showdoc/580/) and When a young person dies suddenly (www.sads.org.uk/)—information on, for example, causes of sudden death and support groups

What is the psychological impact of preparticipation screening?

No data have been published on the psychological impact of preparticipation screening in young athletes. On the basis of studies on established screening programmes[23 24] it is reasonable to assume that athletes with a false positive test result will be anxious until further investigations can provide reassurance. The psychological burden is even greater in young athletes with a diagnosis of a potentially life threatening condition and who are excluded from competing. This highlights the need for prompt evaluation of athletes who fail the initial screening, as well as the need for expert psychological support if preparticipation screening in athletes is to be adopted.

Tips for non-specialists

Symptoms, clinical signs, and electrocardiographic abnormalities of significant importance that should raise concern about young athletes and initiate a referral to a specialist are:

- Chest pain or discomfort on exertion
- Unexplained syncope or near syncope during exertion
- Dyspnoea that is disproportional to the amount of exercise being performed
- Palpitations associated with any of the above
- A family history of hereditary cardiac disorder or sudden cardiac death in a first degree relative when young (≤40 years)
- Marfanoid phenotype
- Left parasternal, systolic heart murmur that increases in intensity when standing or with Valsalva manoeuvre
- Electrocardiographic abnormalities (see box 2)

Athletes with clinical symptoms and signs of an infection—for example, flu-like symptoms, should be advised against intense exercise until they have made a complete recovery owing to the risk of myocarditis

Is preparticipation screening of young athletes cost effective?

Few data exist on the cost effectiveness of preparticipation screening in young athletes, and these are not easily comparable. The American model is cheap but relatively ineffective. A cost effectiveness analysis of a prospective observational study of 5615 high school athletes in the United States, which compared history with electrocardiographic examination (assuming that 10% of the athletes identified as being at risk would live an additional 40 years and 90% an additional 20 years), showed that electrocardiography was more cost effective than history and electrocardiographic examination combined, costing $44 000 (£24 897; €30 921) per year of life saved compared with $84 000 per year of life saved.[25 26]

An Italian cost effectiveness analysis of 33 735 athletes compared the screening cost of the Italian model with that of the American model. Using a more conservative approach (10% of affected athletes would live an additional 20 years) the study estimated the cost per year of life saved at €14 220 for the Italian model and €37 750 for the American model.[27] These estimates were in the context of a well organised, national setting where preparticipation cardiovascular screening was part of a wider screening programme. In countries such as the United Kingdom, however, where the health service is already burdened by limited finances and resources, the implementation of a national screening programme to identify silent cardiac diseases in athletes cannot be regarded as cost effective.

Ongoing research and unanswered questions

Ongoing research

Electrocardiographic and echocardiographic characteristics of athletes of Afro-Caribbean origin to identify the spectrum of electrocardiographic changes and the upper limits of physiological left ventricular hypertrophy in this cohort to facilitate the differentiation between athlete's heart and cardiomyopathy

Charity funded prospective evaluation of a large cohort of British athletes to identify the prevalence of disorders capable of causing sudden cardiac death in athletes to support arguments for or against preparticipation screening in the United Kingdom

Molecular genetics of cardiomyopathies and ion channel diseases to facilitate early diagnosis of these disorders in the future

Unanswered questions

What is the precise significance of noticeable repolarisation changes, specifically deep T wave inversions in the presence of a structurally normal heart?

What is the precise false negative rate of electrocardiographic screening in different ethnic groups and can the same criteria of electrocardiographic abnormality that warrants further investigation be used for all athletes?

Does preparticipation screening comply with the World Health Organization screening criteria?

Critics highlight that preparticipation screening does not fulfil most of the WHO criteria (box 3). Although sudden cardiac deaths of athletes may be regarded as an important health problem by some, it is uncommon and is caused by rare disorders, the clinical course of which are not always fully understood. Deaths are the result of diverse diseases and therefore no single investigation can identify all disorders capable of causing sudden cardiac death. Moreover, most countries have limited facilities for the diagnosis and treatment of athletes. Finally, even the most optimistic estimates, as reported by the Italian group, suggest that the cost of preparticipation cardiovascular screening exceeds that of established screening programmes for breast and cervical cancer.[29]

Conversely, evidence suggests that electrocardiography is a suitable and acceptable screening test (simple, safe, precise, and validated) for the identification of the cardiomyopathies and cardiac conduction tissue diseases. A long latent stage is also recognised as well as effective intervention for improved outcomes.

Conclusion

Preparticipation cardiovascular screening of young competitive athletes is recommended by both the American Heart Association and the European Society of Cardiology.[5 6] The European recommendations have been endorsed by the International Olympic Committee and the football governing bodies, with the Union of European Football Associations advocating mandatory screening of all players participating in European championships.[7 9] These recommendations are based on Italy's experience of preparticipation screening for 25 years, which has shown that screening is effective in reducing sudden cardiac death from cardiomyopathies at the expense of some false positive test results. Implementation of preparticipation screening is hampered in most countries by lack of expertise,

SUMMARY POINTS

Regular exercise is beneficial and only a small number of athletes with silent cardiovascular disease are at increased risk of sudden cardiac death during exercise

Preparticipation screening using health questionnaires and physical examination only has poor sensitivity whereas elaborate screening programmes are cost prohibitive

Screening with 12 lead electrocardiography prevents sudden cardiac death from channelopathies and cardiomyopathies but not from coronary artery disease

Electrocardiography may vary depending on athletic activity, age, race, and sex, and skilled doctors are required to avoid a large number of false positive test results

Implementation of preparticipation screening is currently hampered by the lack of resources and infrastructure and cannot be regarded as cost effective in most countries

resources, and infrastructure. Concerns are also justified that further research is required on the efficacy and cost effectiveness of preparticipation screening. The studies from Italy, however, provide the best available evidence to date, supporting the implementation of systematic preparticipation screening for the prevention of sudden cardiac death in young athletes. Although such programmes are effective at minimising deaths from cardiomyopathies and cardiac conduction tissue disorders, they have no impact on deaths from coronary anomalies or premature coronary atherosclerosis.

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Competing interests: MP is funded by a research grant from the charitable organisation Cardiac Risk in the Young, which support preparticipation screening in young athletes. CRY has provided facilities, including necessary staffing and electrocardiography and echocardiography machines for screening many national sporting squads, including rugby, tennis, boxing, swimming, athletics, and football. The data from the screening programme have resulted in several publications in major peer reviewed journals; GW is a CRY trustee. SS is consultant cardiologist to CRY and a CRY trustee.
Provenance and peer review: Not commissioned; externally peer reviewed.

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