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Sudden cardiac death in athletes

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Sudden cardiac death is defined as an unexpected death, occurring usually within one hour from onset of symptoms in cases where the death is witnessed and in unwitnessed cases within 24 hours of the individual last being seen alive and well.¹ Sudden cardiac death in athletes is the leading cause of medical death in this subgroup, with an estimated incidence of 1 in 50 000 to 1 in 80 000 athletes per year, although a wide range has been reported, from 1 in 3000 in some subpopulations to 1 in 1 000 000.² Males, black or African Americans, and basketball players seem to be at a higher risk than other subgroups.²

Although rare, sudden cardiac death in athletes is important because of its impact within both the sporting community and the general community. The widely held perception is that athletes represent examples of health and vitality, so the sudden cardiac death of an athlete can evoke strong emotions and disbelief. The esteem in which athletes are held, in combination with often highly emotive reporting from the media, means that these events are tragedies not only on a personal family level but also at a public level.³ This review summarises the common causes of sudden cardiac death in athletes and examines whether systematic training can confer increased risk for the condition. Also considered are the measures that can be undertaken to prevent sudden cardiac death.

What is an athlete?

A competitive athlete is defined as “one who participates in an organised team or individual sport that requires regular competition against others as a central component, places a high premium on excellence and achievement, and requires some form of systematic (and usually intense) training.”⁴ Although this generally includes students in high school, college, and university and those participating in paid

SOURCES AND SELECTION CRITERIA

We searched PubMed and the Cochrane Database of Systematic Reviews using the search terms “sudden cardiac death” and “athletes”. To ensure that we represented a diversity of opinion worldwide, particularly on preparticipation screening, we focused on review articles. Owing to the nature of the subject matter, a substantial proportion of the available literature comes from retrospective studies, which can have limited data. We also consulted comprehensive consensus guideline documents and population based studies.

professional sports, there is no reason that children and adolescents younger than 14 years who satisfy this definition should not be considered as athletes. The distinction between competitive athletes and those involved in recreational sports is in the ability and freedom of the participant to judge when it is prudent to pull back or stop physical exertion, with competitive athletes more likely to be under the direction and encouragement of someone else, such as a coach.⁴

What are the causes of sudden cardiac death in athletes?

Sudden cardiac death in athletes is most often caused by an underlying heart condition, which may or may not have been diagnosed previously. In athletes aged 35 years or older, most sudden cardiac death events are due to atherosclerotic coronary artery disease.⁵ In those under 35, genetic and other acquired cardiovascular abnormalities, particularly the cardiomyopathies, are more commonly responsible.^{3, 5-7} The box shows the common causes of sudden cardiac death in athletes, including structural, arrhythmogenic, and acquired cardiac abnormalities. For many of these conditions, the sentinel symptom might be sudden cardiac death, whereas other athletes may have experienced previous symptoms such as syncope, chest pains, and sudden ventricular arrhythmias.⁸ In cases of sudden cardiac death, non-cardiac causes have been excluded and toxicology screens are negative. Autopsy negative sudden unexplained death, where no cause of death can be determined at postmortem examination, is also important and accounts for approximately 30% of sudden deaths in athletes.⁷ Diagnosis in these athletes may be made after comprehensive cardiac evaluation of family members, with one study reporting diagnosis based on family screening in approximately 50% of the unexplained deaths in the cohort.⁹

Inherited causes

Studies in the United Kingdom¹⁰ and the United States⁶ have found definite or possible hypertrophic cardiomyopathy to be one of the most common causes of sudden cardiac death in athletes in these countries. Hypertrophic cardiomyopathy is a genetic condition, with an estimated prevalence of up to 1 in 200 and is characterised by unexplained left ventricular hypertrophy, which can lead to

THE BOTTOM LINE

- Sudden cardiac death in athletes aged less than 35 years is most commonly caused by an underlying genetic heart disorder, such as hypertrophic cardiomyopathy; however, up to half of all sudden cardiac deaths may be associated with a structurally normal heart at postmortem examination and are referred to as autopsy negative sudden unexplained deaths
- Systematic and intense physical training can lead to changes in the heart; however, these are not always detrimental
- Pathological changes to the heart caused by exercise may mimic characteristics of genetic heart diseases—for example, hypertrophy and fibrosis
- There is much debate worldwide regarding the implementation and extent of preparticipation screening for athletes, with the main issue being the balance between lives saved; athletes tested; psychological, ethical, and legal issues; and the economic cost
- Increased education and awareness about sudden cardiac death, training in cardiopulmonary resuscitation, and accessibility to automated external defibrillators can help prevent sudden cardiac death in athletes, as well as non-athletes

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Causes of sudden cardiac death in athletes. Adapted from Chandra et al 2013⁵

Inherited: structurally abnormal heart

Cardiomyopathies

- Arrhythmogenic cardiomyopathy, right ventricular cardiomyopathy, or dysplasia
 - Dilated cardiomyopathy
 - Hypertrophic cardiomyopathy
- Other*
- Coronary artery abnormalities
 - Valvular heart disease (for example, bi-leaflet mitral valve prolapse syndrome)
 - Aortopathies (for example, ascending aortic aneurysm)

Inherited: structurally normal heart

Channelopathies

- Brugada syndrome
- Catecholaminergic polymorphic ventricular tachycardia
- Idiopathic ventricular fibrillation
- Long QT syndrome

Acquired: structurally abnormal heart

- Ischaemic heart disease
- Myocarditis

Acquired: structurally normal heart

- Commotio cordis
- Substance misuse
- Other environmental factors (for example, hypothermia or hyperthermia)

ventricular tachycardia/fibrillation and sudden cardiac death.⁵⁻¹¹ Other studies undertaken in Italy and Denmark found arrhythmogenic right ventricular cardiomyopathy/dysplasia to be a more common cause of death than hypertrophic cardiomyopathy in young athletes.⁷ Arrhythmogenic right ventricular cardiomyopathy/dysplasia is another form of genetic cardiomyopathy, characterised by fibrofatty replacement in the myocardium and right ventricular dilatation. Biventricular involvement and exclusively left ventricular involvement are also possible. Arrhythmogenic right ventricular cardiomyopathy/dysplasia has a reported overall prevalence of 1 in 5000 in the general population and can be exacerbated by intense endurance training.⁵ Congenital coronary artery abnormalities also contribute to sudden cardiac death in athletes, with one study showing coronary artery abnormalities to be responsible for 17% of cardiovascular deaths in a cohort of athletes.⁶

In addition to the structural causes of sudden cardiac death, primary arrhythmogenic diseases, also known as the cardiac channelopathies, contribute to sudden cardiac death in athletes, especially those with autopsy negative sudden unexplained death. These channelopathies, such as familial long QT syndrome, can cause life threatening ventricular arrhythmias, including torsade de pointes and ventricular fibrillation, resulting in sudden cardiac death.³ Other arrhythmogenic disorders include Wolff-Parkinson-White syndrome, which can cause supraventricular tachycardia, atrial fibrillation, ventricular fibrillation, and sudden cardiac death, and catecholaminergic polymorphic ventricular tachycardia, which is characterised by exercise induced (or emotional stress induced) polymorphic ventricular tachycardia and syncope.⁵ Further evaluation is

required to determine the propensity of these conditions to cause sudden cardiac death in athletes.

Acquired causes

Acquired forms of cardiac abnormalities may be responsible for causing sudden cardiac death, such as viral infection leading to myocarditis, vascular abnormalities such as aortic dissection, or drug misuse (including performance enhancing drugs).³ Commotio cordis also falls into this category and involves the triggering of ventricular fibrillation and sudden cardiac death from blunt force trauma to the chest.¹²

Can exercise trigger sudden cardiac death?

The occurrence of sudden cardiac death in an otherwise healthy and fit athlete can lead to the question, “Can exercise trigger sudden cardiac death?” In those with a genetic heart disease or other cardiac abnormality (for example, valve malformation), exercise may predispose to an increased risk of sudden cardiac death or cardiac arrest.¹³ Studies suggest that participation in competitive sports might confer an increased risk of a sudden cardiac event owing to the nature of the underlying cardiac condition and effect of exercise on the heart.¹⁴⁻¹⁶ Commonly, the underlying condition provides a “substrate,” such as hypertrophy or fibrosis in the heart, and the exercise provides a “trigger” for generation of arrhythmias through the physiological changes induced, such as increased catecholamine levels, acidosis, and dehydration.¹⁷

Studies, including a 21 year prospective study in Italy, have shown a higher relative risk of sudden cardiac death in athletes compared with non-athletes.¹⁶⁻¹⁸ Conversely some studies have observed no difference in incidence of sports related sudden cardiac death between athletes and those involved in recreational sports.¹⁹ At this time the answer remains unclear and may well depend on cardiac lesions; however, the evidence suggests that exercise is a potential trigger for sudden cardiac death.

Can intense training lead to cardiac remodelling and sudden cardiac death?

Cardiac diseases aside, since the 19th century it has been known that the heart of an athlete differs from that of a sedentary individual.²⁰ The intense and systematic training undertaken by athletes, particularly endurance athletes, induces structural, functional, and electrical remodelling

TIPS FOR NON-SPECIALISTS

Be aware and able to recognise early clinical warning signs (for example, exercise induced syncope or seizures) that might herald the presence of a potentially life threatening heart condition

Understand the importance of a family history of premature sudden death or childhood onset cardiac disease as potential risk factors for sudden cardiac death

Early referral to a specialised cardiac clinic is often recommended given the complexities of genetic heart disease, the challenge in distinguishing between athlete’s heart and cardiomyopathies, and the multiple factors influencing clinical decision making and potential return to play considerations for athletes with heart disease predisposing to sudden cardiac death

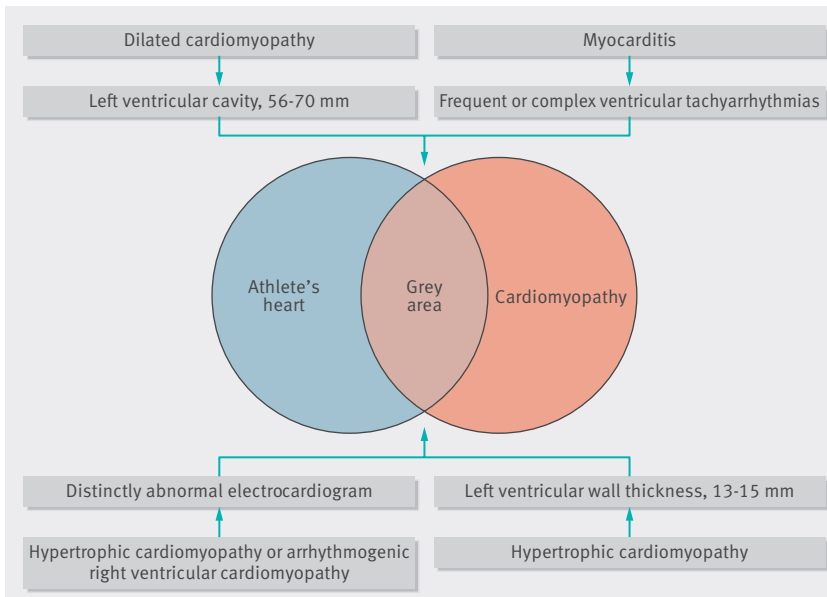


Fig 1 | Important diagnostic features compatible with both physiologically based adaptations to athletic training (athlete's heart) and cardiomyopathies. Adapted from Maron et al 2003³

of the heart, which can manifest as cardiac enlargement and abnormal patterns on electrocardiography (ECG), such as bradycardia and repolarisation abnormalities.^{3 20} This is termed “athlete’s heart.” These changes are not generally detrimental but represent physiological adaptations that aid athletes’ performance.²⁰ However, there are some cardiovascular diseases—predominately the cardiomyopathies—that may overlap with the athlete heart phenotype. It is important to distinguish the athlete with athlete’s heart from the athlete with a pathogenic cardiomyopathy. This is not always straightforward, with the presence of a “grey zone” between the pathogenic conditions and the physiological adaptations causing a major clinical challenge in the assessment of such patients (fig 1).

Structural changes suggestive of athlete’s heart depend on the form of activity performed and include eccentric hypertrophy with larger left ventricular cavity size in those involved in dynamic exercises (such as long distance running) and concentric hypertrophy with cavity dimensions closer to the normal range in athletes who engage in static exercise (such as weight lifters).²⁰ Electrical remodelling changes in the athlete’s heart include sinus bradycardia and incomplete right bundle branch block; however, the presence of widespread inferolateral T wave inversions, left bundle branch block, and pathological Q waves are not normal features of an athlete’s heart and may indicate an underlying disease substrate.²⁰

In some endurance athletes, with no history of genetic heart disease, intense and frequent physical activity may induce more dangerous alterations in cardiac function, and this has been shown in animal model studies²¹ as well as studies in humans.²² Arrhythmogenic right ventricular cardiomyopathy/dysplasia is a genetic disorder caused by mutations in desmosomal genes, characterised by myocardial atrophy and fibro-fatty replacement of mainly the right ventricular myocardium.²³ It has been hypothesised that intense physical training may lead to cumulative microscopic cardiac injury and progressive dilatation of the right

ventricle, resulting in what has been termed “exercise induced arrhythmogenic right ventricular cardiomyopathy/dysplasia” in those without a desmosomal mutation.²⁴ This evidence suggests that in some cases intense training may move beyond the provision of beneficial health outcomes and actually start to cause potentially adverse structural and electrical adaptations in the heart. Interestingly, exercise at a lower intensity and frequency has also been shown to induce ECG changes in asymptomatic people with an arrhythmogenic right ventricular cardiomyopathy genotype, showing an association between exercise and increased phenotype expression.²⁵

Should all athletes undergo preparticipation screening?

As sudden cardiac death can be the first symptom of an underlying genetic heart disease, there have been numerous proposals for the development of preparticipation screening programmes for athletes. This has led to much debate as to the utility and feasibility of such programmes, with evidence from retrospective studies available for both sides of the argument. The main argument in support of screening is clear—the potential to prevent sudden cardiac death and reduce mortality through detection of cardiovascular abnormalities, initiation of effective disease specific treatments, and possible disqualification from competitive sports if necessary.²⁶

The evidence base for preparticipation screening

Preparticipation screening aims to identify those affected by cardiovascular diseases who may be at higher risk of sudden cardiac death during sports.²⁷ Screening programmes may involve all or a combination of the following: taking a family and personal history, physical examination, and 12 lead ECG (with positive findings triggering further examinations such as an echocardiogram, stress testing, 24 hour Holter monitoring, and cardiac magnetic resonance imaging).²⁷ One programme incorporating all these aspects is in Italy where systematic screening was first introduced in 1982.²⁸ A 26 year study of the Veneto region showed an 89% decrease in the incidence of sudden cardiac death, although the analysis was performed retrospectively and the number of events was small.²⁹

Conversely, studies in other parts of the world have had a low yield of detection. A study screened 3500 athletes in the United Kingdom and only found two to have possible hypertrophic cardiomyopathy, although on further evaluation the features were considered more likely to be physiological left ventricular hypertrophy.³⁰ The study did find a further 26 athletes with some potentially relevant disease, which provided a rate of detection of 0.8%, slightly above that of other studies.^{31 32} Poor yield in screening programmes may be related to the way in which screening is done—for example, with or without ECG.

Use of ECG as a screening tool

The use of ECG as a screening strategy has been questioned, with a large number of abnormal test results observed in athletes, owing partly to the differences between the untrained and highly trained athletes’ heart.³³ To tackle the problem of low specificity using

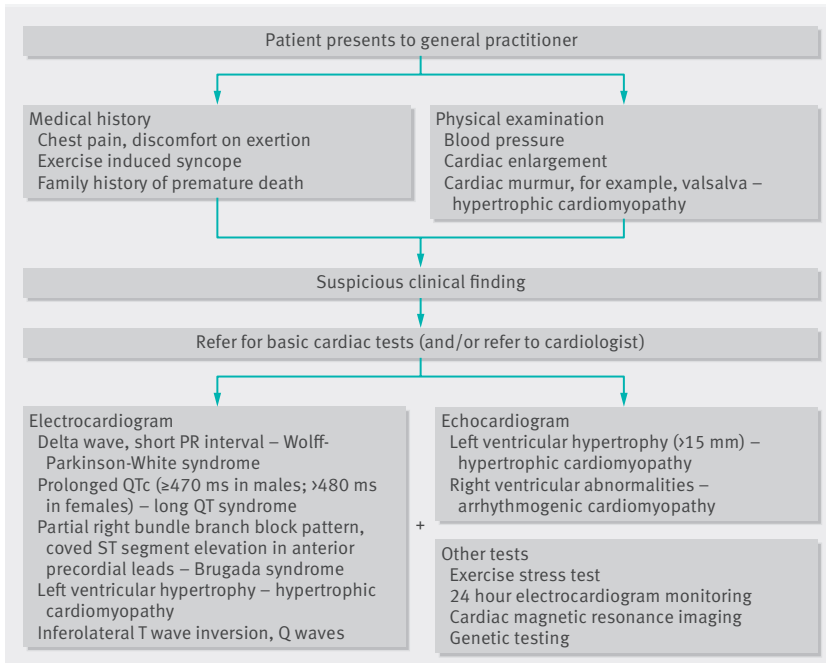


Fig 2 | Important clinical history, examination findings, and basic cardiac investigations that may indicate underlying cardiac disease in athletes^{5 37}

ECG, interpretation criteria have been developed to help doctors differentiate between potentially disease related and benign ECG alterations in athletes, including the Seattle criteria and the European Society of Cardiology criteria.^{25 34} Further recommendations have been suggested recently that enhance the specificity of ECG screening in athletes through reducing the number of false positive test results.³⁵ However, problems may be encountered with the use of the echocardiogram following abnormal ECG results, which again may give ambiguous results owing to the physiological changes observed in athlete’s heart.³³ These false positive test results are not confined to the cardiovascular evaluation solely, with other studies showing false positive rates of 31% for patient history and 9.3% for physical examinations.³⁶

Distinguishing between normal and abnormal hearts

With the difficulties in distinguishing the benign “athlete’s heart” from disease related cardiovascular abnormalities, even with extensive diagnostic testing, it follows that some athletes may be excluded unnecessarily from competitive sports. This raises the issue of not only diagnosis of an underlying heart condition, but also the complex decisions about returning to exercise and at what level. Concomitantly, in some cases athletes may be cleared erroneously of having dangerous cardiovascular abnormalities and be permitted to compete, only for sudden cardiac death to occur later in their sporting career, and opening up the potential for liability.³⁷ In addition, with some studies showing a similar risk of sports related sudden cardiac death between competitive athletes and those involved in recreational sports,¹⁹ it follows that a screening programme developed solely for competitive athletes could be seen as unethical.³⁸ However, other studies have shown a higher incidence of sudden cardiac

death in athletes, and therefore it could be argued that this justifies targeted screening.

Cost-benefit ratio

The cost-benefit ratio has also been identified as an argument against screening programmes that include ECG, with data from the Italian study showing that 33 000 athletes would need to be screened to save one life at a cost per life saved of \$1 320 000 (£861 000; €1 185 000).³³ Some argue that this money may be better spent in secondary prevention of sudden cardiac death in sports³⁹ or allocated to urgent healthcare needs that affect a higher proportion of the population, such as the increasing rates of obesity.⁴⁰

International recommendations

Based on the available information, two leading cardiac societies have produced consensus documents on preparticipation screening recommendations for athletes. The American Heart Association and the European Society of Cardiology both advocate screening of elite athletes. However, they differ in that the American Heart Association recommends taking a thorough medical and family history alongside a physical examination, whereas the European Society of Cardiology recommends the addition of 12 lead ECG in the initial screening stages.^{37 41} Some global sporting organisations such as the Fédération Internationale de Football Association (FIFA) have implemented screening programmes for all players.⁴² Interestingly, the World Health Organization has designated the Wilson and Jungner criteria for appraisal of mass screening programmes (not restricted to athletes), such as preparticipation cardiac screening of all schoolchildren. One study provides a critical evaluation of preparticipation screening in light of these criteria, and although some of the criteria are met, some are not and the researchers conclude that initiation of mass ECG based screening programmes is premature at this stage.²⁸

What else can be done to prevent sudden cardiac death in athletes?

Increasing awareness about sudden cardiac death in athletes among general practitioners and primary care providers is an important step in helping to prevent events. Recognition of clinical features and symptoms that may indicate the presence of an underlying cardiac condition and the need for early referral to a cardiologist are essential for early diagnosis and initiating appropriate action (for example, retirement from competitive sports or continuation after implementation of an effective treatment programme). Figure 2 identifies the stages of diagnosis and the common warning signs for some of the cardiac conditions that may cause sudden cardiac death, and at which point specialist opinion should be sought. The basic clinical history should include questions about previous syncope (“blackouts”), exercise related symptoms such as rapid palpitations and presyncope, and a family history of either cardiac disease or sudden cardiac death in a young person (<40 years). The physical examination should include measuring heart rate and blood pressure; looking for cardiac enlargement, indicated by a displaced apex beat in the chest; and careful auscultation listening

Increased awareness and access to automated external defibrillators along with training in cardiopulmonary resuscitation can help reduce the number of sudden cardiac deaths

for any murmurs or additional heart sounds. When to refer the patient for specialist cardiologist review depends largely on the skills of the general practitioner, the clinical findings, and patient preference. All patients should have a history, a physical examination, and if accessible in primary care, an ECG. If there are suspicious findings in the history or physical examination, or an abnormal ECG, then early referral to a cardiologist is indicated. Subsequent investigations, such as echocardiogram, exercise testing, and 24 hour ECG Holter monitoring, can then be decided. While such specialist investigation is being undertaken, patients should be advised against playing any competitive or strenuous sports.

Some athletes may be completely asymptomatic and seek assessment for a clearance to play sports. In this situation, an unremarkable clinical history, completely normal physical examination, and a normal 12 lead resting ECG would be sufficient to give the “all clear” for participation in most sports. Occasionally, echocardiography may also be required to assess cardiac structure and function in more elite athletes such as marathon runners and triathletes.

Secondary prevention strategies are available to help prevent sudden cardiac death in athletes. For those diagnosed as having a genetic heart disease, the globally accepted lifestyle modification recommendation, as published in consensus documents from both Europe and the United States, is withdrawal from competitive sports (with the exception of class I sports, which are billiards, bowling, cricket, curling, golf, and riflery).⁴³⁻⁴⁵ However, the latest data suggest that even these guidelines may be too restric-

QUESTIONS FOR FURTHER RESEARCH

- Can clinical diagnostic tools be developed to more precisely and accurately differentiate between an athlete’s heart and an underlying cardiomyopathy?
- What genetic factors may specifically increase the risk of sudden cardiac death in at risk people?
- How do environmental factors such as hot weather, electrolyte imbalances, or fever contribute to sudden cardiac death?
- What effective, widespread community programmes can be established to prevent sudden cardiac death through increased availability of automated external defibrillators or mandatory cardiopulmonary resuscitation training, or both?

tive, with a study of participants with long QT syndrome who chose to continue competing, showing a low rate of cardiac events.⁴⁶⁻⁴⁷ Following recommendations of restriction from competitive sports, the subsequent treatment of those with a genetic heart disease otherwise reflects that of non-athletes, with the potential for drug interventions such as β blockers⁴⁸ and surgical intervention in the form of an implantable cardioverter defibrillator that can shock the heart from life threatening ventricular arrhythmias to normal sinus rhythm. Nearly 400 athletes with cardioverter defibrillators have remained engaged in competitive sports, with short term follow-up revealing no sports or disease related mortality and no evidence of increased damage or malfunction of the cardioverter defibrillator hardware.⁴⁹ In addition, since a genetic heart condition may also affect other family members, as part of patient management, family members should undergo cardiac screening and be counselled about their own risk.⁸

At a community level, increased awareness and access to automated external defibrillators along with training in cardiopulmonary resuscitation can help reduce the number of sudden cardiac deaths.⁵⁰ FIFA has recognised the need to establish a standardised and consistent level of emergency medical care on the football field and has developed a medical emergency bag along with a series of 11 steps to help prevent sudden cardiac death in football players, both professional and amateur.⁴² The 11 steps include training in cardiopulmonary resuscitation and the use of the automated external defibrillator (provided in the medical emergency bag), ensuring the bag is present at the sideline of football games and that team staff are educated to recognise a possible sudden cardiac arrest and how to respond.⁴¹ Other community run initiatives are also in place to increase awareness and encourage community groups to place more defibrillators in sporting clubs and schools. Finally, promotion of cardiopulmonary resuscitation training (including use of automated external defibrillators) in the general community can help prevent sudden cardiac death through heightened awareness and improved response rates to sudden cardiac death and sudden cardiac arrest events.⁵⁰ Some countries, such as Japan and Austria, mandate that anyone applying for a driver’s licence must complete cardiopulmonary resuscitation training to increase the prevalence of trained people in the community and thereby enhance the so called chain of survival.⁵¹⁻⁵²

ADDITIONAL EDUCATIONAL RESOURCES

Resources for healthcare professionals

Pelliccia A, Fagard R, Bjørnstad HH, Anastassakis A, Arbustini E, Assanelli D, et al. Recommendations for competitive sports participation in athletes with cardiovascular disease: a consensus document from the Study Group of Sports Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur Heart J* 2005;26:1422-45—European perspective

Maron BJ, Zipes DP. Introduction: eligibility recommendations for competitive athletes with cardiovascular abnormalities—general considerations. *J Am Coll Cardiol* 2005;45:1318-21—North American perspective

FIFA player health programme: how to prevent sudden cardiac death in football (www.fifa.com/aboutfifa/footballdevelopment/medical/playershealth/risks/heart.html)—resource for players to highlight the warning signs and causes of sudden cardiac death in athletes

Resources for patients

SADS (Sudden Arrhythmia Death Syndrome) Foundation (www.sads.org)
—provides support and information for patients and families affected by SADS and aims to raise public awareness

CRY (Cardiac Risk in the Young) Foundation (www.c-r-y.org.au)
—works with cardiologists and family doctors to promote and protect the cardiac health of young people by establishing good practice and facilities to reduce the frequency of young sudden cardiac death

Australian Genetic Heart Disease Registry (www.heartregistry.org.au)
—patient resources and educational materials available for all major genetic heart diseases that can lead to sudden cardiac death, latest information about treatments and prevention strategies, and recommendations for athletes

Mayo Clinic (www.mayoclinic.org)
—patient resources and educational materials available for the major channelopathies and cardiomyopathies predisposing to sudden cardiac death