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Sudden death in athletes

Vimal Patel and Perry Elliott

ABSTRACT – Sudden cardiac death in an athlete is a rare and heartrending event, often occurring in the absence of warning symptoms. The causes of sudden cardiac death in athletes are age dependent and demonstrate a degree of geographical variation. Pre-participation screening is recommended by both the European Society of Cardiology and the American Heart Association although there is no consensus regarding the utilisation of an electrocardiogram. This article will review the aetiology of sudden cardiac death and will present the evidence for pre-participation screening.

KEY WORDS: sudden cardiac death, hypertrophic cardiomyopathy, arrythmogenic cardiomyopathy, channelopathies, coronary artery anomalies, pre-participation screening

Introduction

Sudden death in a previously healthy young person is always tragic, but the emotional and psychological impact is heightened when the victim is a competitive athlete. Such events are fortunately very rare, but whenever they occur, medical, political and media interests naturally focus on the prevention of similar tragedies. In this short article, we review the common causes of sudden cardiac death in athletes and discuss the evidence for systematic pre-participation screening in this population.

Epidemiology

Most studies of deaths in athletes are retrospective and subject to reporting bias. The incidence of sudden cardiac death in young competitive athletes varies between 0.5 and 1.21 per 100,000 person-years,[1–4] but the best prospective data come from the Veneto region of Italy, where the annual incidence of sudden death in athletes was 2.3 per 100,000 person-years from all causes and 2.1 per 100,000 person-years from cardiovascular diseases.[5] Most series have a male predominance[2,5–8] and most events occur during or shortly after exercise.[2,5,7]

Aetiology of sudden death in athletes

Vimal Patel, clinical research fellow in inherited cardiovascular disease; **Perry Elliott,** reader in inherited cardiovascular disease

The Heart Hospital, University College London

The aetiology of sudden cardiac death in athletes is age dependent. Coronary atherosclerosis is the most common cause of sudden death in individuals older than 35 years, whereas inherited and structural heart disease predominate in younger athletes (Table 1).[6,9] As with the incidence of sudden death, there are geographic differences in reported aetiology. For example, arrhythmogenic right ventricular cardiomyopathy (ARVC) is the most common cause of death in the Veneto region of Italy (Fig 1),[5] whereas hypertrophic cardiomyopathy is the major cause in many series from the USA.[2,7] This difference has been suggested to result from regional variations in the prevalence of these diseases, but it is possible that a particular focus on detailed postmortem examination of the right ventricle explains the higher incidence of ARVC in Italy.

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM), defined as left ventricular hypertrophy in the absence of abnormal loading conditions (valve disease, hypertension and congenital heart defects),[10–12] occurs in about one in every 500 adults.[13] Pathologically, the disease is characterised by myocardial hypertrophy, myocyte disarray and myocardial fibrosis, and it is usually inherited as an autosomal dominant trait caused by mutations in genes that encode contractile proteins of the cardiac macromere.[11] Individuals with HCM are often asymptomatic but can present throughout life with chest pain, symptoms of heart failure, syncope and sudden ventricular arrhythmias. Although HCM is reported in 10–51% of all sudden or aborted cardiac deaths in young athletes,[2,7,8,14–16] it is rarely found during pre-participation screening.[17] Moreover, the incidence of sudden death in non-athletic individuals with the disease is also very low (<1% per annum).[11] Explanations for these apparent contradictions include an inability of most individuals with HCM to attain athletic status and a particularly high risk of fatal ventricular arrhythmia in the very small number of individuals who can overcome the physiological limitations imposed by the disease. Little evidence supports either hypothesis, but the high incidence of HCM-related deaths in athletes remains the major justification for the exclusion of individuals with HCM from sporting activities.

Idiopathic left ventricular hypertrophy

Idiopathic left ventricular hypertrophy (LVH) is defined histologically by the presence of myocyte hypertrophy, sometimes in association with myocardial fibrosis but in the absence of myocyte disarray. In an autopsy study based in the UK, idiopathic LVH was the most frequently reported cardiac anomaly in young

Table 1. Causes of sudden cardiac death in athletes.

Heritability	Structurally abnormal heart	Structurally normal heart
Inherited	• Cardiomyopathies – Hypertrophic cardiomyopathy – Arrythmogenic cardiomyopathy – Dilated cardiomyopathy • Coronary artery anomalies • Valvular heart disease • Aortic disease	• Channelopathies – Brugada syndrome – Long QT syndrome – Catechol-aminergic polymorphic ventricular tachycardia
Acquired	• Ischaemic heart disease • Myocarditis	• Commotio cordis • Substance misuse • Electrolyte imbalance

athletes experiencing sudden cardiac death.[15] This phenomenon is poorly understood but may represent physiological adaptation in response to intense training. Other possible explanations include the use of anabolic steroids and hypertension.

Arrhythmogenic right ventricular cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy is an inherited heart muscle disease characterised by loss of myocytes, with fatty or fibro-fatty replacement of the right ventricle, ventricular arrhythmias, congestive heart failure and sudden cardiac death. The estimated prevalence of the disease is 1:1000–1:5000.[6,18,19] The disease frequently is inherited, with most cases caused by mutations in genes encoding desmosomal proteins.[18,20] In the early 'concealed' stage of the disease, patients are usually asymptomatic but can be at risk of life-threatening ventricular arrhythmias.[21] The prevalence of ARVC in young athletes experiencing sudden or aborted cardiac death in the US and France is about 3–4%.[2,7,14] In the UK, ARVC is reported as the primary cause of death in 10% of athletes younger than 35 years and 24% of those older than 35 years.[15] In Italy, ARVC accounts for nearly one quarter of all sudden cardiovascular deaths in young athletes.[5] The relation between exercise and disease progression in ARVC is controversial. Evidence from animal models suggests that endurance training accelerates expression of the clinical phenotype.[22]

Coronary artery abnormalities

Coronary artery anomalies are present in 1.3–5.6% of the general population,[23,24] but may be as common as 24% in young athletes who experienced sudden cardiac death.[16] Most sudden cardiac deaths related to coronary abnormalities in athletes are caused by an anomalous origin of the left coronary system from the right coronary sinus.[7,16,25] The trigger for sudden death is thought to be myocardial ischaemia caused by compression of the anomalous coronary artery as it passes between the aorta and pulmonary artery, the slit-like opening at the ostium and the acute angle at its origin. Other coronary abnormalities identified in athletes who experienced sudden death include coronary hypoplasia, coronary aneurysm, acute angulation at the coronary insertion and intussusception.[7]

Ion channel disease

Despite extensive pathological and toxicological assessment, a large proportion of sudden cardiac deaths in athletes remain unexplained.[2,15] This entity of sudden arrhythmic death syndrome (SADS) is often caused by diseases of the cardiomyocyte membrane ion channels (channelopathies) – a heterogenous group of disorders that include long QT syndrome (LQTS), Brugada syndrome and catecholaminergic polymorphic ventricular tachycardia (CPVT). The first presentation of such disorders may be life-threatening cardiac arrhythmia occurring at rest or during exercise. Characteristic electrocardiographic changes in many disorders may be evident only after pharmacological or exercise provocation, and the diagnosis requires a high degree of clinical suspicion, often precipitated by a tragic event in the family (see Ref 26 for a more detailed review of this topic).

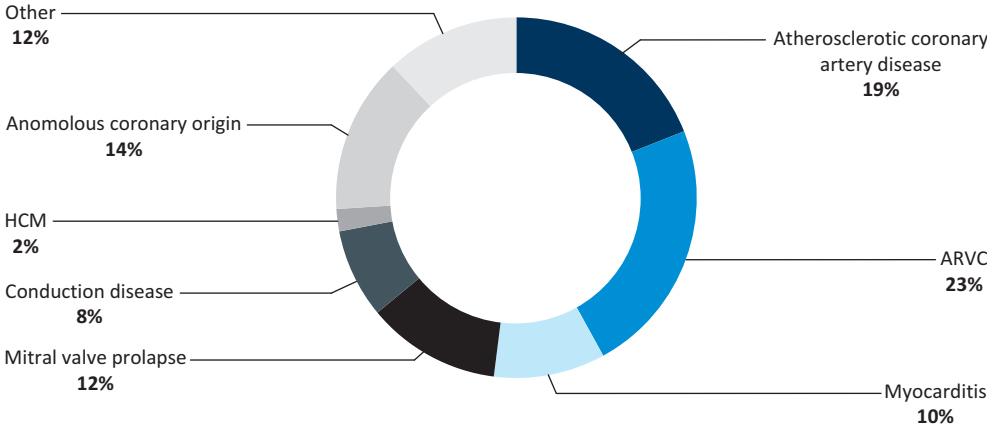

Fig 1. Causes of sudden cardiovascular deaths in athletes (aged <35 years) in the Veneto region of Italy from 1979 to 1999. Modified from Corrado *et al*, 2003.[5]

Prevention of sudden death in athletes

In an attempt to reduce sudden deaths in young athletes, both the European Society of Cardiology (ESC) and American Heart Association (AHA) recommend screening of all individuals who participate in high-level sports. The AHA advises that all athletes should undergo screening solely with a detailed clinical history and physical examination.[27] In contrast, the ESC recommends that an electrocardiogram (ECG) should be routinely used in screening – a stance endorsed by the International Olympic Committee.[28] Justification for the inclusion of an ECG in the screening strategy is a prospective study from Italy, where pre-participation screening involving history taking, examination and ECG has been mandatory for 26 years. Data from the Veneto region of Italy show that the incidence of sudden death in young athletes fell from 3.6 per 100,000 person-years to 0.4 per 100,000 person-years during this period. A comparable reduction in the rate of sudden death among unscreened non-athletes was not seen, which led to the conclusion that screening was responsible for the decline in events.[6] However, these data need to be interpreted cautiously, as the incidence of sudden death in Veneto, prior to implementation of pre-participation screening, was unusually high compared to that in the USA and other European countries (3.6 per 100,000 person-years vs 0.46–1.21 per 100,000 person-years).[1–4]

The sensitivity and specificity of an ECG-based screening programme is dependent on the criteria used to differentiate physiological adaptation from disease. In a study of 1,005 consecutive athletes, a mildly or distinctly abnormal ECG was 51% sensitive and 61% specific for identifying cardiovascular abnormalities, with a positive predictive accuracy of only 7% and a false-positive rate of 39%.[29] In 2005, the ESC published criteria for detecting ECG abnormalities in athletes,[28] which increased the sensitivity for detecting structural cardiovascular disease from 45% with history and examination alone, to almost 91%.[30] However, there was an associated reduction in specificity (from 94.4% to 82.7%) and an increase in the rate of false-positive results (from 5.5% to 16.9%). In 2010, new guidelines that reclassified some electrocardiographic features (previously described as pathological) as normal variants were proposed (Table 2).[31] When compared with the original criteria, the 2010 criteria resulted in a reduction in the rate of false-positive results to 10%, without altering sensitivity.[32] Although the latest guidance has improved the performance of ECGs for screening in adults, the applicability of ECGs in younger age groups and different ethnic groups is unknown.[33] This screening strategy will also miss conditions in which ECG changes can be transient (for example, Brugada syndrome and CPVT) or absent (as in anomalous coronary arteries).

Table 2. Classification of an athlete's electrocardiogram. Adapted from the 2010 European Society for Cardiology criteria.[31]

Common findings	Pathological findings
• Sinus bradycardia	• T-wave inversion
• First-degree atrioventricular block	• ST-segment depression
• Incomplete right bundle branch block	• Pathological Q waves
• Early repolarisation	• Left atrial enlargement
• Isolated QRS voltage for left ventricular hypertrophy	• Left-axis deviation/left anterior hemiblock
	• Right-axis deviation/left posterior hemiblock
	• Right ventricular hypertrophy
	• Ventricular pre-excitation
	• Complete right or left bundle branch block
	• Long or short QT interval
	• Brugada-like early repolarisation

Cost effectiveness

As the incidence of sudden death among athletes is low, the costs of implementing a screening programme are substantial. Estimates suggest that the inclusion of an ECG would increase the cost of pre-participation screening in the US by $500 million to an annual total of $2 billion, with a cost of $3.4 million per theoretical life saved.[27] Other studies have shown that screening with ECG costs about $44,000–76,100 per year of life saved and is more cost effective than screening history and examination alone.[34,35]

Irrespective of the financial arguments about screening, the fact that a substantial proportion of sudden deaths in young individuals are attributable to genetic cardiovascular diseases means that their surviving relatives are also at risk. The first-degree relatives of young victims of sudden death therefore should be counselled on their risk of a similar event and offered systematic cardiac evaluation in expert centres. This systematic approach has a high yield in terms of identifying other affected family members and may prevent further catastrophic events in the same family.

Conclusions

Sudden cardiac death in athletes is a tragic and potentially preventable event. The aetiology of sudden death is age dependent and frequently relates to inherited cardiovascular disease in the young. Pre-participation screening may help to reduce the incidence of sudden death, although equal focus should be given to evaluation of the families of victims of sudden death.

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Address for correspondence: Dr Perry Elliott, The Heart Hospital, 16–18 Westmoreland Street, London W1G 8PH.
Email: perry.elliott@ucl.ac.uk