
CME Cardiology

Sudden cardiac death: detecting the warning signs

A Merghani, cardiology research fellow; R Narain, cardiology research fellow; S Sharma, professor of cardiology

Department of Cardiovascular Sciences, St George’s University of London, London, UK

Introduction

Sudden cardiac death (SCD) is defined as a non-traumatic, non-violent and unexpected fatality resulting from sudden cardiac arrest within 6 h of previously witnessed normal health.1 The majority of victims are elderly patients with a history of coronary artery disease or heart failure. However SCD may also occur in young individuals in the context of an underlying inherited or congenital abnormality that specifically affects the myocardium or electrical system. The premature and sudden termination of young lives is particularly tragic and has a devastating impact on the community as a whole. A significant proportion of deaths may be preventable if the clinical symptoms, family history and electrocardiogram are interpreted appropriately. Furthermore, the accessibility of automated external defibrillators and more rapid paramedic response times has improved survival from <6% to >30% in some cases.2 This article will outline the epidemiology and aetiology of SCD, indicating the warning symptoms, signs and findings, as well as describing appropriate strategies for prevention.

Epidemiology and demographics

Sudden cardiac death accounts for approximately 100,000 deaths per year in the UK.3 The vast majority are due to coronary artery disease (CAD) and occur in middle-aged and elderly patients. The incidence increases from 1/100,000 for those aged <35 years to 1/1000 in individuals aged ≥35 years old.4 There is a substantial male bias of approximately 4:1 that may be partially explained by the protection from CAD seen in premenopausal women. Risk also varies according to ethnicity, with African-Caribbean individuals being more susceptible to SCD.5

Aetiology

The causes of SCD are multiple (Fig 1). The prevalence of the different aetiologies is age dependent. CAD is the most common cause in patients aged ≥35 years. In younger patients, the underlying aetiology is often an inherited cardiomyopathy such as hypertrophic cardiomyopathy (HCM) or arrhythmogenic right ventricular cardiomyopathy (ARVC). In some instances, an obvious cause is not identified despite a comprehensive post-mortem evaluation and toxicology screen. Such deaths are classified as sudden arrhythmic death syndrome (SADS) and are most commonly due to an ion channel disease such as Brugada syndrome, long QT syndrome (LQTS), short QT syndrome or catecholaminergic polymorphic ventricular tachycardia (CPVT), or congenital accessory pathways such as Wolff–Parkinson–White (WPW) syndrome. Acquired causes other than CAD include aortic dissection, aortic stenosis, severe electrolyte disturbance, myocarditis and recreational drug use.

Coronary artery disease

Over half of all coronary artery deaths are sudden in nature and often occur in the context of an acute myocardial infarction.5 SCD most frequently occurs between 6 to 18 months after a myocardial event, usually in patients with anginal symptoms or exertional breathlessness.5 Risk factors for SCD include smoking, diabetes, hypertension and obesity. Primary prevention with implantation of an implantable cardiac defibrillator (ICD) is recommended in patients with myocardial infarction complicated by left ventricular impairment (ejection fraction <30%) or evidence of documented sustained ventricular tachycardia.6

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) has a prevalence of 1/500.7 Mutations in sarcomeric contractile proteins are associated with left ventricular hypertrophy, histological evidence of myocardial disarray and fibrosis, and a predilection for potentially fatal arrhythmias. Although symptoms of chest pain, dyspnoea, syncope and palpitations are recognised, a significant proportion of patients may be asymptomatic. SCD may be...
the first presentation, especially in young adults and adolescents, particularly those who engage in vigorous physical activity. However, the overall prognosis is relatively good and the annual mortality risk is only 0.5–3%.8 Definite risk factors for SCD that warrant an ICD implant include aborted SCD and sustained ventricular tachycardia. A prophylactic ICD should be offered to patients exhibiting two of more of the following: a family history of premature sudden death (aged <40 years) from HCM, severe (>30 mm) left ventricular hypertrophy, non-sustained ventricular tachycardia and a flat blood pressure (BP) response to exercise (systolic BP rising by <25 mmHg during exertion).9 Sudden cardiac death may also be prevented by simple lifestyle advice, such as cessation of intense athletic activity.

**Arrhythmogenic right ventricular cardiomyopathy**

Arrhythmogenic right ventricular cardiomyopathy (ARVC) has a prevalence of between 1/1,000 and 1/5,000. Mutations within genes encoding the cardiac desmosomal proteins are thought to lead to myocyte detachment and an abnormal repair process, resulting in fibro-fatty replacement of the myocardium. The right ventricle is most frequently affected. The diagnosis is difficult in the early or concealed stage of the disease. Overt cases frequently exhibit abnormalities on the electrocardiogram (ECG) and cardiac imaging studies that require careful interpretation in the context of symptoms, family history and history of athletic training. Patients may present with palpitations, syncope, heart failure, thromboembolic events or, indeed, SCD. Young age, extensive right ventricular dysfunction, left ventricular involvement, polymorphic ventricular tachycardia, late potentials, epsilon waves and a family history of SCD are high-risk features and may indicate therapy with an ICD.10

**Coronary artery anomalies**

Coronary artery anomalies (CAA) describe variants of coronary artery anatomy. They are a relatively common finding, occurring in just under 1% of the general population. The vast majority of cases are benign and cause no symptoms. However, individuals with anomalous coronary origins may be at risk of SCD. The most common presentation is with exertional chest pain with syncope. Exercise testing rarely reveals myocardial ischaemia and the diagnosis is best established with CT coronary angiography. Treatment usually involves surgical correction in high-risk variants.

**Ion channel disorders**

**Brugada syndrome**

Brugada syndrome is an autosomal dominant inherited disorder of the sodium ion channels of cardiac myocytes. Mutations in the SCN5A gene are the most frequently recognised, but many others have been described. Victims are often asymptomatic and typically die during rest or sleep. The typical ECG pattern exhibits ‘coved’ ST elevation in leads V1–V2 (Fig 2). The only established treatment is offered by ICDs and these are reserved for individuals with high-risk features, such as aborted SCD, documented sustained ventricular arrhythmias, unheralded syncope and nocturnal agonal respiration, in addition to the typical ECG pattern. Lifestyle advice should include abstaining from heavy meals prior to sleep and avoidance of particular drugs (www.brugadadrugs.org).

**Long QT syndrome**

Congenital long QT syndrome (LQTS) is an inherited group of potassium or sodium ion channel disorders within cardiac myocytes that commonly manifest as a prolonged corrected QT (QTc) interval on the 12-lead ECG (see Fig 2). A number of culprit genes have been discovered with multiple modes of inheritance. The commonest subtypes of LQTS are LQTS-1, LQTS-2, and LQTS-3, which account for 95% of all cases. Adrenergic surges by well-identified triggers cause the characteristic polymorphic ventricular tachycardia that can then degenerate to ventricular fibrillation. Different triggers for SCD have been attributed to each subtype: exercise (particularly swimming) in LQTS-1, auditory stimuli in LQTS-2 and rest/sleep in LQTS-3. Patients are advised to avoid medications that prolong the QT interval (www.qtdrugs.org) and are initiated on β-adrenerceptor blocking drugs. ICD

<table>
<thead>
<tr>
<th>Table 1. Key points for taking history in SCD.</th>
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<tbody>
<tr>
<td><strong>Personal</strong></td>
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<tr>
<td>• Exertional chest pain</td>
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<tr>
<td>• Exertional dizziness</td>
</tr>
<tr>
<td>• Unhanded syncope</td>
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<tr>
<td>• Excessive breathlessness</td>
</tr>
<tr>
<td>• Palpitations</td>
</tr>
<tr>
<td>• Epilepsy</td>
</tr>
<tr>
<td>• Prior cardiac disease</td>
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<td>• Drug history</td>
</tr>
<tr>
<td><strong>Family</strong></td>
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<tr>
<td>• Known heritable disorder</td>
</tr>
<tr>
<td>• Premature CAD (&lt;50 years)</td>
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<tr>
<td>• SCD</td>
</tr>
<tr>
<td>• Epilepsy</td>
</tr>
<tr>
<td>• Unexplained drowning</td>
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<td>• Road traffic accidents</td>
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CAD = coronary artery disease; SCD = sudden cardiac death.

Fig 2. ECG examples of common ion channel disorders. (a) 12-lead ECG showing typical appearance of the Brugada pattern with partial right bundle branch block and coved ST-segment elevation in leads V1–V2. (b) 12-lead ECG with long QT syndrome. ECG = electrocardiogram.
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insertion is reserved for high-risk cases (including those with QTc >500 ms), syncope (despite β-adrenoceptor blockers) or aborted sudden death.11

Preventative strategies

Strategies to reduce the incidence of SCD involve both the identification and treatment of high-risk individuals through screening programmes and also the institution of effective, immediate resuscitative procedures for the victims of SCD.

Screening

All first-degree blood relatives of patients with inherited cardiac diseases or victims of SADS should be investigated in an expert cardiac setting. Particular emphasis should be placed on the personal and family history (see Table 1) in conjunction with a potentially comprehensive array of investigations (outlined in Fig 3). In cases where no cardiac pathology is identified at initial screening, an ajmaline or flecainide provocation test is advised to unmask concealed forms of Brugada syndrome.

Most SCDs in young individuals occur in the absence of prodromal warning symptoms, particularly in the athletic community. Data from Italy, where sports screening is mandatory, have led to a 90% fall in the rate of SCD in competitive athletes.12 Indeed, screening competitive athletes is now widely accepted and endorsed by many sporting governing bodies. Whether screening should be offered to all young persons of senior school age is highly controversial when consideration is given to the low diagnostic yield, cost and the feasibility of running a national screening programme.

Automated external defibrillators

Early defibrillation is a crucial part in the chain of survival. For every 1-min delay in defibrillation, the survival rate of a cardiac arrest victim decreases by 7–10%. After >12 min of ventricular fibrillation, the survival rate is <5%.13 These remarkable statistics have galvanised the argument for easily accessible automated external defibrillators (AEDs), which have improved survival rates in, for example, schools, airports and casinos to between 60–74%.14

Conclusion

To conclude, sudden cardiac death is caused by a diverse group of acquired and inherited heart conditions. All physicians will encounter a case of SCD or manage relatives of SCD victims. A significant proportion of sudden cardiac deaths may be preventable if the clinical symptoms, family history and electrocardiogram are interpreted appropriately. Strategies such as cardiac screening, particularly in high-risk groups, and the accessible use of defibrillators have a role in the prevention of sudden cardiac death.

References


Address for correspondence: Prof S Sharma, Department of Cardiology, St George’s University of London, Cranmer Terrace, London SW17 0RE. Email: ssharma21@hotmail.com

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