

# Sudden cardiac death

## Identifying young people at risk

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*Although epidemiological risk factors for sudden cardiac death (SCD) such as age, prior myocardial infarction and low ejection fraction are well established, the syndrome also has a strong genetic component. Identifying high-risk candidates and subsequent referral can significantly reduce the incidence of SCD among first-degree relatives.*

In Australia and New Zealand, up to 80,000 people die suddenly each year from various causes.<sup>1</sup> Sudden cardiac death (SCD) is defined as an unexpected natural death due to a cardiac cause, heralded by sudden loss of consciousness within one hour of symptom onset in a person without a previously known cardiovascular abnormality.<sup>2</sup> The incidence of sudden death in young people (i.e. aged less than 35 years) is estimated to be 1.5 to 5.5 per 100,000 persons per year; however, this estimation includes noncardiac causes.<sup>3</sup> SCD can have a significant emotional and psychological impact on immediate family members.

In this article, we discuss common causes of SCD and the role of GPs in identifying high-risk patients including those who are relatives of people who have died from SCD, by taking a thorough



history, performing a focused cardiovascular examination and ECG, and referring as appropriate.

### Risk of sudden cardiac death (SCD)

The incidence and aetiology of SCD varies significantly depending on the population studied and the definition used. Studies have demonstrated a marked increase in the risk of SCD in first-degree relatives of people who have died from this cause. In the Paris prospective study, a parental history of SCD increased the risk of fatal arrhythmia in patients by 80%, and in people with both parents affected, the risk of SCD increased ninefold.<sup>4</sup>

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## Causes of SCD

In children and young adults, the aetiology of SCD can be broadly classified into structural, electrical and acquired causes. SCD in the young (aged under 35 years) has a structural basis in up to 60% of cases. The most common structural pathologies are cardiomyopathies such as hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and congenital coronary artery anomalies. Ion channelopathies constitute the electrical causes, such as Wolff–Parkinson–White syndrome, long QT syndrome and Brugada syndrome. In adults who are older than 35 years of age, coronary artery disease is the primary cause of death.

## Key points

- Sudden cardiac death (SCD) is an unexpected natural death, with loss of consciousness within an hour of symptom onset, due to a previously unknown cardiac cause.
- Taking a thorough history, performing a cardiovascular examination and ECG, and appropriate referral may reduce the incidence of SCD among first-degree relatives of people who experience SCD.
- The aetiology of SCD can be broadly classified into structural, electrical and acquired causes.
- Structural cardiac diseases, such as hypertrophic cardiomyopathy, are the most common cause of SCD in young people (aged less than 35 years).

## SCD in athletes

SCD is more common in athletes compared with their nonathletic counterparts due to the increased risk associated with strenuous exercise in the context of a quiescent cardiac abnormality. Data from Italy have shown a 2.8-fold greater risk of SCD among competitive athletes compared with their nonathletic counterparts.<sup>5</sup> There is a significant male predominance of SCD among athletes. Data from the National Center for Catastrophic Sport Injury Research in the USA on high school and college athletes reported a fivefold higher incidence of SCD in male compared with female athletes.<sup>6</sup>

In young competitive athletes, SCD most often occurs from hypertrophic cardiomyopathy (up to 48%), and in older athletes, from coronary heart disease.<sup>7,8</sup>

## Structural cardiac abnormalities

### Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy is an inherited heart muscle disorder with a known predisposition to SCD in the young. It has a diverse clinical and functional expression ranging from benign to clinically significant, such as left ventricular outflow tract obstruction, myocardial ischaemia and life-threatening arrhythmias with SCD.<sup>9</sup>

Hypertrophic cardiomyopathy affects about one in 500 of the population and has been shown to account for 4 to 48% of SCD in patients aged less than 35 years, depending on the population studied – it is the leading cause of SCD in young adult athletes in the USA.<sup>8,10</sup> In patients with hypertrophic cardiomyopathy, SCD has an annual estimated frequency of 0.5 to 1.0%, and is most common in asymptomatic young adults.<sup>11</sup> SCD is probably a result of multiple interacting pathologies. Morphologically, myocyte disarray and asymmetric left ventricular hypertrophy increase the potential for myocardial ischaemia, with replacement scarring leading to ventricular arrhythmia and SCD.<sup>12</sup> Because SCD usually occurs in asymptomatic individuals, an important role in primary care is the diagnosis and identification of those at risk of SCD.

### Case study. A first-degree relative of a person with sudden cardiac death

Nick, a 32-year-old man, presents for 'a full check up'. He is very concerned because, 10 days ago, his 25-year-old brother died suddenly while playing soccer. Generally, Nick is fit and healthy; he works as a builder. He smokes five to 10 cigarettes a day and drinks alcohol 'in moderation' (20 to 40g, three times a week). He is not on any medication.

Examination reveals a double apical pulse and grade 3/6 systolic ejection murmur, loudest in the aortic area, that intensifies during the Valsalva manoeuvre or with Valsalva strain. Nick was referred to a cardiologist for echocardiography and was subsequently diagnosed with hypertrophic cardiomyopathy. An ECG is shown below (Figure).

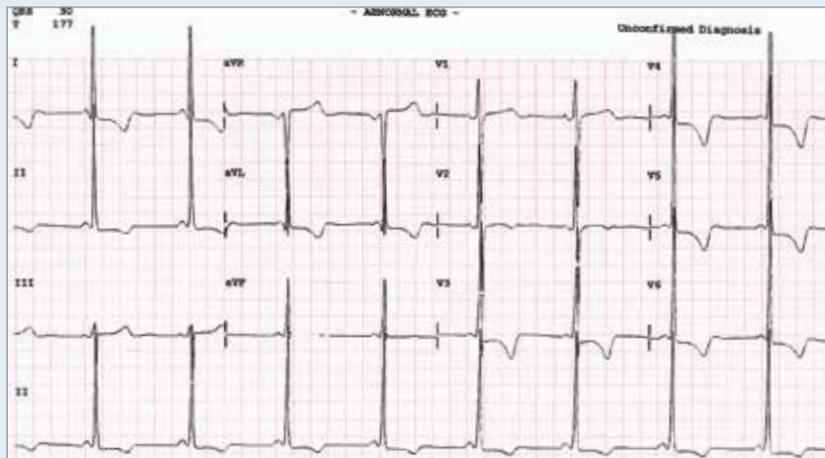


Figure. ECG showing features of left ventricular hypertrophy including high QRS voltage, with S wave in V1 and R wave height >35 mm in V5 or V6 (Sokolov-Lyon criteria) and diffuse ST depression and T wave inversion (most prominent in L1 and V3 to V6).

### Identifying patients

About 10 to 20% of patients with hypertrophic cardiomyopathy will have a family history of hypertrophic cardiomyopathy-related SCD, but fewer than 5% will have a malignant family history (i.e. multiple premature deaths).<sup>13</sup> Clinically, patients may experience unexplained syncope, and recurrent episodes on exertion or during childhood or adolescence are ominous. Patients may also report chest pain, exercise limitation and dyspnoea; however, current evidence suggests that these symptoms do not predict SCD.<sup>14</sup> Cardiac arrest from ventricular tachycardia or fibrillation may be the first clinical manifestation of the disease, with subsequent annual SCD mortality in survivors being 0.5 to 1.0%.<sup>15</sup>

A typical patient (Box) may have a jerky pulse, double apical impulse and a loud systolic ejection murmur that increases on Valsalva manoeuvre (a result of increased outflow tract obstruction due to decreased left ventricular end diastolic volume with

increased intrathoracic pressure).

The diagnosis is made using ECG and echocardiography. More than 90% of affected individuals have an abnormal resting ECG. ECG abnormalities may include voltage criteria for left ventricular enlargement, left atrial enlargement, left axis deviation, ST segment depression, T wave inversion and pathological Q waves (Figure).<sup>16</sup> Echocardiography may reveal septal hypertrophy; a septal thickness greater than 30 mm conveys an increased risk of SCD.<sup>17</sup>

### Arrhythmogenic right ventricular cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy is characterised by regional and global fibro-fatty replacement of the right, and less commonly left, ventricular myocardium. Resulting electrical instability is associated with paroxysmal ventricular tachycardia or fibrillation and SCD. It is an inherited (usually, but not always, autosomal dominantly)

condition with an estimated prevalence of one in 1000 to one in 10,000 and has been attributed as underlying about 25% of SCD in young athletes.<sup>18</sup>

It is postulated that increased afterload stretches the diseased myocardium and catecholamine interaction with the 'supersensitive' myocardium contributes to causing ventricular arrhythmias.<sup>19</sup> Patients with sustained monomorphic ventricular tachycardia are thought to have a more favourable prognosis when treated medically, with sotalol showing the higher efficacy.<sup>20</sup> In patients with aborted SCD or ventricular tachycardia refractory to medical therapy, placement of an implantable cardioverter-defibrillator is appropriate.

### Identifying patients

Generally, examination findings are unremarkable but careful ECG interpretation may show inverted T waves and a prolonged QRS complex with epsilon waves (a small positive deflection buried in the end of the QRS complex) in the right precordial leads. Strenuous exercise and acute mental stress are the major triggering mechanisms for SCD.

### Congenital coronary artery anomaly

Congenital coronary artery anomalies are rare with an estimated prevalence of 0.3% to 1.2% in patients referred for coronary angioplasty. Anomalies most responsible for SCD occur in left coronary arteries from the non-coronary aortic sinus of Valsalva or from the right, especially when the artery travels between the aortic and pulmonary roots.<sup>21</sup> Myocardial ischaemia is precipitated by impaired coronary blood flow from compression between the great arteries, coronary spasm from endothelial dysfunction or the abnormal slit-like ostium of the anomalous coronary artery compromising flow reserve.<sup>22</sup> Surgical intervention should be sought in patients at high risk of SCD.

### Identifying patients

SCD may be the first manifestation of these conditions. Clinicians should have a high index of suspicion in young patients who present with either exertional chest pain or syncope with unexplained QRS, ST or T wave

changes post syncope or after successful resuscitation.

### **Other structural heart abnormalities**

Other structural cardiac abnormalities associated with SCD in young individuals include aortic dissection, typically in the context of Marfan syndrome, mitral valve prolapse and bicuspid aortic valve with aortic stenosis.

### **Electrical cardiac abnormalities**

#### **Wolff–Parkinson–White syndrome**

Wolff–Parkinson–White syndrome induces paroxysmal arrhythmias due to an accessory pathway with anterograde conduction causing ventricle pre-excitation. SCD is characteristically a result of atrial fibrillation being conducted via the accessory pathway with a short anterograde refractory period leading to degeneration to ventricular fibrillation. Population-based studies suggest an incidence of SCD in patients with this condition of 0.15% per year.<sup>23</sup>

#### **Identifying patients**

Patients are usually asymptomatic, with symptoms occurring with tachyarrhythmias. The ECG characteristically shows a delta wave corresponding to the pre-excitation pathway. Risk factors associated with the development of SCD include: male gender, very rapid ventricular rate during atrial fibrillation (AF) due to short refractory periods of the accessory pathway, a past history of AF and presence of multiple accessory pathways.<sup>24</sup> Electrophysiology studies are important in determining the electrical properties of the accessory pathway for risk stratification and referral for catheter ablation.

#### **Long QT syndrome**

Long QT syndrome usually arises from mutations in ion channels involved in the maintenance of the cardiac action plateau and repolarisation, increasing the likelihood of dispersing refractoriness. It is defined as a corrected QT interval of at least 440 ms in men or 460 ms in women.<sup>25</sup>

Both Romano–Ward syndrome, a familial autosomal dominant condition, and Jervell and Lange–Nielsen syndrome, a familial autosomal recessive condition with

congenital deafness, are recognised as causes of long QT syndrome and have a worse prognosis than other causes.

All patients with long QT syndrome, whether asymptomatic or symptomatic, should reduce physical stress and avoid any drugs that prolong repolarisation. Only retrospective data are available to support the role of  $\beta$ -blocker treatment to improve clinical outcomes. A retrospective study of 233 patients showed a 15% mortality following the first syncope in patients treated with  $\beta$ -blockers and/or left cardiac sympathetic denervation compared with 60% mortality in patients not treated or on miscellaneous therapy.<sup>26</sup> An automatic implantable cardioverter–defibrillator is recommended for secondary prevention.

#### **Identifying patients**

Syncope is the most common symptom and characteristically the first clinical manifestation of long QT syndrome, occurring during childhood or adolescence. The earlier the age when the first syncope occurs, the higher the likelihood of SCD. Syncope before the age of 5 years indicates a severe form of the disease and if it occurs in the first year of life it carries a poor prognosis (i.e. high likelihood of SCD).<sup>13</sup>

The degree of QT prolongation is also associated with increased risk of SCD. A QT interval longer than 500 ms predisposes to torsades de points and ventricular fibrillation.<sup>27</sup>

#### **Brugada syndrome**

Brugada syndrome is an arrhythmogenic disorder of a structurally normal heart presenting with syncope due to polymorphic ventricular tachycardia or SCD from ventricular fibrillation. At three years' follow up of both symptomatic and asymptomatic patients with the condition, SCD occurred in about 30% of patients, usually aged in their 30s or 40s, and most often at rest or during sleep.<sup>28</sup> Survivors of cardiac arrest are recommended to have an implantable cardioverter–defibrillator.

#### **Identifying patients**

Brugada syndrome is more common in men, is usually diagnosed around 40 years of age

and symptoms are usually due to life-threatening arrhythmias. The ECG characteristically reveals a transient right bundle branch block and ST elevation in leads V1 to V3.

### **Acquired cardiac abnormalities**

Myocarditis, most often caused by viral infections, accounts for up to 7% of SCD in athletes.<sup>29</sup> The diagnosis of myocarditis should be considered in any healthy young individual with recent viral illness. They may have new abnormal ECG changes and regional wall motion abnormalities on echocardiography.

Blunt trauma to the chest wall can trigger ventricular fibrillation and SCD without causing direct injury to the thoracic cage or heart.<sup>30</sup> The use of performance-enhancing drugs including anabolic-androgenic steroids are known to cause SCD and their use may be underestimated. SCD in young adults can also result from premature atherosclerotic coronary artery disease. It is most commonly a manifestation of familial hypercholesterolaemia.

### **Conclusion**

Patients at risk of SCD can be identified in general practice and referred appropriately. Assessing a patient with a family history of sudden cardiac death should include a detailed history of syncope and presyncope, chest pain, palpitations and dyspnoea, as well as a history among first-degree relatives of unexplained epilepsy or drowning. Perform a careful examination for signs of structural heart disease, peripheral stigmata of familial hypercholesterolaemia and marfanoid habitus. A 12-lead ECG can be diagnostic in Wolff–Parkinson–White syndrome, long QT syndrome and Brugada syndrome. Most patients with hypertrophic cardiomyopathy will have ECG abnormalities. Echocardiography is important in excluding structural heart disease. In selected cases, cardiologists may also employ cardiac MRI, electrophysiological studies and/or genetic testing to reach a diagnosis. **CT**

### **References**

A list of references is included in the online version of this article ([www.cardiologytoday.com.au](http://www.cardiologytoday.com.au)).

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### References

1. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, et al. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project: registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation* 1994; 90: 583-612.
2. Myerburg RJ, Castellanos A. Cardiac arrest and sudden cardiac death. In: Braunwald E, ed. *Heart disease: a text-book of cardiovascular medicine*. New York: WB Saunders Publishing Co; 1997: 742-779.
3. Sen-Chowdhry S, McKenna WJ. Sudden cardiac death in the young: strategy for prevention by targeted evaluation. *Cardiology* 2006; 105: 196-206.
4. Jouven X, Desnos M, Guerot C, Ducimetiere P. Predicting sudden death in the population: the Paris Prospective Study I. *Circulation* 1999; 99: 1978-1983.
5. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol* 2003; 42: 1959-1963.
6. Van Camp SP, Bloor C, Mueller FO, Cantu R, Olson H. Nontraumatic sports death in high school and college athletes. *Med Sci Sports Exerc* 1995; 27: 641-647.
7. Maron BJ, Shirani J, Poliac LC, et al. Sudden death in young competitive athletes: clinical, demographic, and pathological profiles. *JAMA* 1996; 276: 199-204.
8. Zipes DP, Wellens HJ. Sudden cardiac death. *Circulation* 1998; 98: 2334-2351.
9. Maron BJ. Hypertrophic cardiomyopathy. *Lancet* 1997; 350: 127-133.
10. Bagnall RD, Weintraub RG, Ingles I, et al. A prospective study of sudden cardiac death among children and young adults. *N Engl J Med* 2016; 374: 2441-2452.
11. McKenna W, Deanfield J, Faruqui A, et al. Prognosis in hypertrophic cardiomyopathy: role of age and clinical, electrocardiographic and haemodynamic features. *Am J Cardiol* 1981; 47: 532-538.
12. Spirito P, Seidman CE, McKenna WJ, Maron BJ. The management of hypertrophic cardiomyopathy. *N Engl J Med* 1997; 336: 775-785.
13. Priori SG, Aliot E, Blomstrom-Lundqvist C, et al. Update of the guidelines on sudden cardiac death of the European society of cardiology. *Eur Heart J* 2003; 24: 13-15.
14. Sharma S, Elliott P, Whyte G, et al. Utility of cardio-pulmonary exercise in the assessment of clinical determinants of functional capacity in hypertrophic cardiomyopathy. *Am J Cardiol* 2000; 86: 162-168.
15. Elliott PM, Sharma S, Varnava A, et al. Survival after cardiac arrest or sustained ventricular tachycardia in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1999; 33: 1596-1601.
16. Spirito P, Seidman CE, McKenna WJ, Maron BJ. The management of hypertrophic cardiomyopathy. *N Engl J Med* 1997; 336: 775-785.
17. Spirito P, Bellone P, Harris KM, et al. Magnitude of left ventricular hypertrophy and risk of sudden death in hypertrophic cardiomyopathy. *N Engl J Med* 2000; 342: 1778-1785.
18. Goodin JC, Farb A, Smialek JE, Field F, Virmani R. Right ventricular dysplasia associated with sudden death in young adults. *Mod Pathol* 1991; 4: 702-706.
19. Marcus F, Nava A, Thienne G. Arrhythmogenic right ventricular cardiomyopathy/dysplasia: recent advances. Milano: Springer, 2007.
20. Wichter T, Borggrefe M, Haverkamp W, Chen X, Breithardt G. Efficacy of antiarrhythmic drugs in patients with arrhythmogenic right ventricular disease. Results in patients with inducible and noninducible ventricular tachycardia. *Circulation* 1992; 86: 29-37.
21. Kimbiris D, Iskandrian AS, Segal BL, Bemis CE. Anomalous aortic origin of coronary arteries. *Circulation* 1978; 58: 606-615.
22. Angelina P. Coronary artery anomalies. An entity in search of an identity. *Circulation* 2007; 115: 1296-1305.
23. Goudevenos JA, Katsouras CS, Graekas G, et al. Ventricular pre-excitation in the general population: a study on the mode of presentation and clinical course. *Heart* 2000; 83: 29-34.
24. Wellens HJ. When to perform catheter ablation in asymptomatic patients with a Wolff-Parkinson-White electrocardiogram. *Circulation* 2005; 112: 2201-2216.
25. Moss AG. Prolonged QT-interval syndrome. *JAMA* 1986; 256: 2985-2987.
26. Schwartz PJ. Idiopathic long QT syndrome: progress and questions. *Am Heart J* 1985; 109: 399-411.
27. Moss AJ, Schwartz PJ, Crampton RS, et al. The long QT syndrome. Prospective longitudinal study of 328 families. *Circulation* 1991; 84: 1136-1144.
28. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report. *J Am Coll Cardiol* 1992; 20: 1391-1396.
29. Eckart RE, Scoville SL, Campbell CL, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med* 2004; 141: 829-834.
30. Maron BJ, Gohman TE, Kyle SB, Estes NAM, Link MS. Clinical profile and spectrum of commotio cordis. *JAMA* 2002; 287: 1142-1146.