CURRENT CONCEPTS

SUDDEN DEATH FROM CARDIAC CAUSES IN CHILDREN AND YOUNG ADULTS

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ALTHOUGH sudden death in a young person is rare, it can have a great impact on both the lay and the medical communities. Such unanticipated deaths sometimes occur in dramatic circumstances and often have medical and legal ramifications. Some of these deaths are not predictable or preventable by current practical means; however, in many cases there are premonitory symptoms, a family history of sudden death at a young age, clinical or electrocardiographic abnormalities, or high-risk behavior.

Among older adults, sudden deaths are often due to atherosclerotic coronary artery disease and terminal ventricular fibrillation. Each year there are 300,000 such deaths in this country. In contrast, sudden deaths from cardiac causes in young people are few but have numerous causes. This review focuses on persons between 1 and 30 years of age who die unexpectedly, including persons thought to be free of cardiac abnormalities, as well as those with known heart disease, some of whom have had heart surgery.

Despite numerous reports, there is a paucity of demographic data on sudden death from cardiac causes in the young. The rate of sudden death in these populations ranged from 1.3 to 8.5 per 100,000 patient-years, with males consistently outnumbering females. In two thirds of the cases, a specific cardiac cause was identified. Extrapolation of these data suggests that each year several thousand Americans under the age of 20 years die suddenly from cardiac disorders.

Among children under one year of age, sudden death is usually due to ductus-dependent, complex, cyanotic congenital cardiac lesions. In a coroner's review of 126 sudden deaths before the age of two years, 10 percent were associated with congenital cardiac lesions, and 6 percent with myocarditis. It is postulated that 10 percent of the 7000 annual crib deaths are the result of unrecognized cardiac causes — notably, occult cardiac arrhythmias, including those related to a prolonged QT interval. Potentially fatal cardiac arrhythmias occur in 3 percent of babies considered to be at high risk for crib death, but the QT intervals in such infants are not correlated with sudden death.

After the first year and through the third decade of life, the most common cardiac causes of sudden death include myocarditis, hypertrophic cardiomyopathy, coronary artery disease, congenital coronary-artery anomalies, conduction-system abnormalities, mitral-valve prolapse, and aortic dissection (Table 1). Although underrepresented in community-based reviews, sudden deaths also occur among persons with underlying congenital heart disease, including some who have had prior heart surgery.

Table 2 shows data from two large hospital-based reviews involving a total of 327 sudden deaths in young people known to have had heart disease during a period that spanned the early and modern era of cardiac surgery. Ten conditions were responsible for most of these deaths, and aortic stenosis, tetralogy of Fallot and its variant forms, and pulmonary vascular obstruction accounted for half of them. Among the patients who had not undergone surgery, aortic stenosis and pulmonary vascular obstruction were common, and among those who had undergone surgery, tetralogy of Fallot and transposition of the great arteries were common.

The clinical profile in Table 2 shows that three quarters of the patients who died were in New York Heart Association class III or IV, 87 percent had radiographic evidence of cardiomegaly, 46 percent had poor hemodynamic values at the time of postoperative catheterization, 43 percent had pulmonary hypertension, and 57 percent had arrhythmia (premature ventricular beats, heart block, or atrial flutter) during the year before death. Thus, patients with these characteristics require further surgical, medical, or electrophysiologic intervention. In recent decades there has been a decline in the incidence of sudden death in patients with congenital heart disease, coinciding with the evolution of therapeutic interventions.

The incidence of reported prodromal symptoms among persons who die suddenly varies according to the study methods but is generally around 50 percent. The most common symptoms are chest pain and actual or near syncope, both of which are common in the young and may be caused by many cardiac and noncardiac disorders. Prompt cardiac evaluation is indicated for children or young adults with exertional chest pain not affected by movement, inspiration, or palpation and without an apparent noncardiac cause, particularly if the patient has a high-risk cardiac disorder, a family history of sudden death, or exertion-related, unexplained syncope that is unheralded or preceded by palpitation.

A family history of sudden death may be associated with the diagnosis of hypertrophic or dilated cardiomyopathy, right ventricular cardiomyopathy, coronary artery disease, mitral-valve prolapse, Marfan's syndrome, or the long-QT syndrome (Table 3). Hence, a family history of sudden death should be sought on routine and sports-related physical examinations and when evaluating symptoms of chest pain or syncope. One review noted that 16 percent of young persons who had died suddenly had a family history of sudden death.

Electrocardiographic abnormalities occur in many young persons at risk for sudden death and should be
sought in the evaluation of chest pain, syncope, known or suspected lesions associated with a high risk of sudden death, and a family history of sudden death (Table 3). Flat or inverted T waves in leads V6, V5, I, and aVL often accompany cardiomyopathy and coronary-artery abnormalities. Diagnostic electrocardiographic findings include a prolonged QT interval, ventricular preexcitation, sinus-node dysfunction, ventricular tachycardia, and heart block.

The large majority of sudden deaths in young persons are caused by a small subgroup of disorders — abnormalities of the myocardium or coronary vessels, specific congenital heart lesions, or arrhythmia and conduction disorders — or by high-risk behavior. Table 3 lists these conditions and the clinical characteristics often associated with them.

**Myocardial Abnormalities**

Sudden deaths are reported annually in up to 4 percent of patients with hypertrophic cardiomyopathy, although this figure is probably an overestimate because of patient selection. Sixty percent of patients have affected first-degree relatives. Since diagnostic findings may not be evident until adolescence or later, in involved families interval reevaluation is appropriate. Syncope, a very young age at presentation, extreme degrees of ventricular hypertrophy, a strong family history of sudden death from cardiac causes, and unsustained ventricular tachycardia are associated with the highest risk. The electrocardiogram usually reveals lateral ST-T wave flattening or inversion. Ultrasonography is diagnostic. Beta-blockers or calcium-channel blockers are indicated, although they may not prevent sudden death. Amiodarone and implantable defibrillators are appropriate in some patients. Strenuous physical exertion, including participation in competitive sports, should be restricted. In some cases, however, the first manifestation of the disorder is sudden death.

**Myocarditis** accounts for 20 to 40 percent of sudden deaths from cardiac causes and is most often due to involvement of first-degree relatives. Sixty percent of patients have affected first-degree relatives. Sixty percent of patients have affected first-degree relatives. Sixty percent of patients have affected first-degree relatives. Sixty percent of patients have affected first-degree relatives.
fection with group B coxsackievirus. Cardiac involvement is unpredictable and may involve the conduction system, causing heart block, or the myocardium, causing ventricular tachyarrhythmia. A recent influenza-like illness is common, although the symptoms may be mild and clinical signs of heart failure may be subtle or absent. The electrocardiogram shows diffuse low voltage, ST-T changes, and often heart block or ventricular arrhythmia. The results of echocardiography and myocardial biopsy are confirmatory. Management is supportive, must be individualized, and may include ventricular pacing and antiarrhythmic agents. Rest and avoidance of exertion are important during the acute and healing phases and until the results of ultrasonographic studies, ambulatory electrocardiographic monitoring, and stress testing are normal.

Dilated cardiomyopathy is familial in 11 percent of cases \(^{23}\) and may represent late-stage myocarditis. Ten percent of affected children die suddenly — notably, those who have persistently abnormal ventricular function. \(^{23}\) The risk may be higher with first- or second-degree heart block. \(^{24}\) Exertion should be avoided. Electrophysiologically guided therapy, implantable defibrillators, or beta-blockers \(^{25}\) may have a role in the treatment of selected high-risk patients with malignant ventricular tachyarrhythmia.

Right ventricular cardiomyopathy (arrhythmogenic right ventricular dysplasia) involves the replacement of myocardial cells with fibrous or fatty tissue, mostly in the right ventricular free wall, resulting in right ventricular tachyarrhythmia and sudden death. The cause of this condition is unclear. It is particularly common in northern Italy. \(^{13,14}\) Death often occurs with exertion \(^{13}\) and may be the initial manifestation of the disease. The symptoms are few. The electrocardiogram shows a pattern of right bundle-branch block in sinus rhythm and left bundle-branch block with ventricular tachycardia. Ultrasonography or magnetic resonance imaging (MRI) may be diagnostic. Cases of familial occurrence have been reported. \(^{13}\) Electrophysiologically guided antiarrhythmic therapy or ablation is indicated. Occasionally, the disease resolves spontaneously.

### Coronary-Artery Abnormalities

In a recent study of sudden death from cardiac causes in patients between the ages of 18 and 35 years, 23 percent of the deaths were due to coronary artery disease. \(^{14}\) Nearly all the patients were men, and none had prior angina pectoris or myocardial infarction. Nearly all the patients had single-vessel disease (in each case involving the proximal left anterior descending artery), and only one quarter had acute thrombosis. These findings suggest that even in the second and third decades, aggressive management of coronary risk factors is warranted.

Kawasaki’s disease occurs throughout the world but is most common in Asians. The coronary-artery aneurysms are usually proximal and visible on ultrasonographic evaluation. The aneurysms are often multiple and usually affect the left coronary artery. Coronary dilatation occurs acutely in nearly half the patients, and in most cases, death occurs during the third or fourth week of the acute illness. However, coronary abnormalities persist in 23 percent of patients after three months and in 8 percent after two years. \(^{16}\) A large angiographic
A review of patients studied two years after the acute illness revealed coronary-artery lesions in 25 percent, consisting of aneurysms, stenosis, or occlusion. Since there have been late sudden deaths, continued vigilance is warranted, but most patients now receive immune globulin during the acute illness, and the incidence of coronary-artery aneurysms is decreasing.

The most frequent congenital coronary-artery anomalies causing sudden death in the young involve an ectopic origin of either the right or left coronary artery in the left or the right aortic sinus of Valsalva, respectively. The aberrant artery arises at an acute angle, often from a slit-like hypoplastic ostium, traverses the aortic wall obliquely, emerges between the aorta and the right ventricular outflow tract, and then proceeds to its usual area of distribution. With exertion, proximal angulation or compression obstructs the blood flow in the aberrant artery, leading to distal ischemia, ventricular tachycardia, and fibrillation. The patients at highest risk for sudden death are those with a dominant aberrant artery that perfuses a large region of myocardium, and the risk is greatest during the first three decades of life. Nearly one third of the patients who die suddenly from this disorder have had prior exertional syncope or angina.

The anomaly can be demonstrated by ultrasonography, but physiologic assessment requires catheterization and angiography. Some patients have abnormal thallium perfusion during exercise. Patients with documented ischemia, life-threatening arrhythmia, or syncope should undergo surgical revascularization. One review reported 49 deaths due to an aberrant left coronary artery from the right sinus of Valsalva, of which 25 percent were sudden and half were related to exertion.

A left coronary artery originating in the pulmonary trunk is rare, and most patients with this anomaly die in infancy. However, 5 to 10 percent survive an early myocardial infarction, with the subsequent development of right-to-left coronary collateral vessels. These survivors may present as children or adults with angina, ventricular tachycardia, or fibrillation. Typically, they have mitral insufficiency and collateral-flow murmurs, apical aneurysms, and Q-wave electrocardiographic infarction. Echocardiography is diagnostic. One review reported 37 deaths, of which 38 percent were sudden and 14 percent were related to exertion. Surgical revascularization is indicated in patients with this disorder.

**Congenital Heart Lesions**

Sudden death occurs in 60 percent of patients with secondary pulmonary vascular obstruction and in 43 percent of those with primary plexogenic pulmonary arteriopathy. Death is often precipitated by general anesthesia, dehydration, exertion, or pregnancy. Avoidance of these risks and education of patients and their families are important.

Patients with tetralogy of Fallot who have undergone reparative surgery have a 6 percent risk of sudden death between 3 months and 20 years of age; sudden death occurs most often in patients with residual defects, right ventricular hypertrophy, and ventricular arrhythmia. Ambulatory electrocardiographic monitoring at regular intervals is advisable. Repair of existing residual defects and electrophysiologic study may be indicated. Betablockers, antiarrhythmic agents, phenytoin, and implantable defibrillators all have a role.

Transposition of the great arteries after an atrial-switch operation is associated with a 2 to 8 percent rate of late sudden death, which is usually due to sinus-node dysfunction but in some cases is due to ventricular tachyarrhythmia. Patients should undergo ambulatory electrocardiographic monitoring for signs of both disorders, and suppression of atrial and ventricular tachycardia, as well as placement of a ventricular pacemaker, may be indicated.

Mitrval-valve prolapse is common, but rarely results in sudden death. It may occur with exertion and may be due to ventricular tachyarrhythmia. One review cites a total of 60 reported sudden deaths among patients with mitral-valve prolapse, and only 4 of the patients were younger than 20 years. Nevertheless, between 5 and 24 percent of sudden deaths from cardiac causes are attributed to mitral-valve prolapse.
highest risk are patients with a family history of sudden death, previous syncope, electrocardiographic abnormalities at rest, a prolonged QT interval, and complex ventricular tachyarrhythmia. Although beta-blockers are often used, it is not clear whether antiarrhythmic therapy can prevent sudden death, and electrophysiological studies are rarely helpful. Most clinicians adopt a permissive attitude toward participation in sports.\textsuperscript{26,38}

For patients at highest risk and those in whom stress testing or ambulatory monitoring reveals a worsening of arrhythmia or symptoms with exercise, a more cautious approach is advised.

Aortic dissection is the cause of sudden death in patients with Marfan’s syndrome. This disorder may be present in children but occurs most often during the fourth decade. In a review of 257 patients with Marfan’s syndrome between 1939 and 1972, there were 72 deaths at a mean age of 32 years.\textsuperscript{38} Serial ultrasonography and MRI can identify persons at risk who have progressive dilatation of the aortic root, which may require surgical intervention. Prompt attention to chest pain and frequent assessment of peripheral pulses and aortic size with serial ultrasonography or MRI are advised. Long-term administration of beta-blocking agents is also indicated. Although Marfan’s syndrome is not always familial, family screening is warranted. Monitoring and early intervention, of course, depend on the recognition of the syndrome.

**ARRHYTHMIA AND CONDUCTION ABNORMALITIES**

The congenital long-QT syndrome occurs with or without neurosensory deafness and is familial in 60 percent of cases.\textsuperscript{10,41} Ventricular tachycardia, which may be related to exertion or stress, occurs in 80 percent of untreated patients.\textsuperscript{10,41} Beta-blockers and phenytoin are recommended, but in some patients, left cardiac sympathetic denervation\textsuperscript{10} or implantation of a defibrillator is indicated. Patients with corrected QT intervals of more than 500 msec are at greatest risk for sudden death. Family screening is warranted.

In patients with the Wolff–Parkinson–White syndrome, there is a small risk of sudden death associated with short antegrade refractory periods and atrial fibrillation (although the latter is rare in children).\textsuperscript{5} Since the risk is predominantly associated with digitalis or calcium-channel blockers, which enhance preferential conduction over the bypass tract, these agents should be avoided. Beta-blockade, electrophysiologically guided therapy, and ablation can reduce or eliminate the risk. Ventricular preexcitation may resolve spontaneously. Ablation is advisable before participation in sports.

Incessant ventricular tachycardia may be due to Purkinje-cell or other cardiac tumors,\textsuperscript{34} which are amenable to surgical excision. Hence, aggressive diagnostic evaluation is indicated for children with this disorder.

**HIGH-RISK BEHAVIOR**

Between 10 and 25 percent of sudden deaths in the general population are related to physical exertion (Table 1).\textsuperscript{5,12,13,50} Data from five reports of 74 exertion-related sudden deaths in young people, nearly all of whom had structural heart disease, are summarized in Table 4, along with the common causative lesions.\textsuperscript{5,12,43}

Symptoms of palpitation, syncope, dyspnea, and chest pain and a history of cardiac abnormalities were common (Table 4).\textsuperscript{42,43}

Sudden deaths in athletes have focused public and medical attention on the importance of high-risk cardiac disorders, a family history of sudden death in a young person, and prodromal symptoms. For athletes at potential risk, advice about participation in sports must rest on a thorough evaluation and be presented with care. Advice that is poorly understood can be paralytic to the patient, and advice that is improperly followed can be lethal. A recent symposium\textsuperscript{25} and several reviews\textsuperscript{46-48} provide clinical and screening guidelines for young persons with known cardiac disease. One must keep in mind just how rare these events are. Between 10 and 25 sports-related sudden deaths from cardiac causes occur annually in the United States,\textsuperscript{49} and 5 young athletes in 100,000 have a predisposing condition.\textsuperscript{48} The annual rate of sudden death is 1 per 75 million among Air Force recruits who have been pre-screened by general physical examination\textsuperscript{11} and 1 per 250,000 among unscreened young runners.\textsuperscript{43}

In a review of 41 survivors of prehospital ventricular fibrillation who were 18 to 35 years old, one third had ingested alcohol or drugs (cocaine, heroin, or tricyclic agents).\textsuperscript{30} Cocaine causes coronary vasoconstriction, myocardial ischemia, and ventricular tachyarrhythmia and simultaneously increases the heart rate and blood pressure. Sudden death can occur irrespective of the amount ingested, prior use, or route of administration and regardless of whether there is an underlying cardiac abnormality.\textsuperscript{55} Since tricyclic agents may cause heart block and sudden death, electrocardiographically guided adjustment of the dose is advised. There is a risk of sudden death in persons with anorexia nervosa or extreme bulimia because of an imbalance in electrolytes, extreme bradycardia, and a prolonged QT interval,\textsuperscript{52} all of which are remediable with treatment.

To conclude, sudden cardiac death is rare in children

\*Based on data from Phillips et al.,\textsuperscript{15} Maron et al.,\textsuperscript{42} Ragosta et al.,\textsuperscript{43} Tsung et al.,\textsuperscript{44} and Corrado et al.\textsuperscript{45}

\textsuperscript{†}Chest pain, syncope, or palpitation.

### Table 4. Characteristics of Sudden Deaths Associated with Strenuous Physical Exertion or Sports in Young Persons.\textsuperscript{42,43}

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age range (yr)</td>
<td>11–35</td>
</tr>
<tr>
<td>Prior symptoms (% of patients)\textsuperscript{†}</td>
<td>26</td>
</tr>
<tr>
<td>Prior question of cardiac abnormality (% of patients)</td>
<td>26</td>
</tr>
<tr>
<td>Structural heart lesion (% of patients)</td>
<td>95</td>
</tr>
<tr>
<td>Cause (% of patients)</td>
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</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
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</tr>
<tr>
<td>Congenital coronary anomaly</td>
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<tr>
<td>Coronary artery disease</td>
<td>12</td>
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<tr>
<td>Myocarditis</td>
<td>9</td>
</tr>
<tr>
<td>Right ventricular cardiomyopathy</td>
<td>8</td>
</tr>
<tr>
<td>Idiopathic left ventricular hypertrophy</td>
<td>7</td>
</tr>
<tr>
<td>Mitral-valve prolapse</td>
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<tr>
<td>Conduction system disease</td>
<td>4</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>4</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
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</table>
and young adults and is usually related to one of a small group of disorders. Many of these disorders can be identified beforehand on the basis of associated lesions, prodromal symptoms, a family history of sudden death at a young age, or high-risk behavior. A risk that cannot be eliminated calls for a frank, compassionate discussion with the patient and his or her family about the patient’s uncertain future.

REFERENCES


