Athlete Screening and Sudden Cardiac Death

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EDUCATION GAP

Primary care providers play an instrumental role in preventing sudden cardiac deaths in young athletes. Therefore, primary care providers should be familiar with warning signs and risk factors of cardiac conditions that can cause sudden death, preparticipation screening guidelines, and secondary prevention measures.

OBJECTIVES *After completing this article, readers should be able to:*

1. Identify the causes of sudden cardiac death in young athletes.
2. Describe screening guidelines and be aware of controversies in screening.
3. Recognize and promote secondary prevention measures.

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ABBREVIATIONS

AAOCA	anomalous aortic origin of a coronary artery
AAP	American Academy of Pediatrics
AC	arrhythmogenic cardiomyopathy
AED	automated external defibrillator
AHA	American Heart Association
ALCA	anomalous left coronary artery
ARCA	anomalous right coronary artery
CERP	Cardiac Emergency Response Plan
CMR	cardiac magnetic resonance
CPR	cardiopulmonary resuscitation
CPVT	catecholaminergic polymorphic ventricular tachycardia
ECG	electrocardiogram
HCM	hypertrophic cardiomyopathy
ICD	Implantable cardioverter-defibrillator
LQTS	long QT syndrome
LV	left ventricular
PPE	preparticipation physical evaluation
SCA	sudden cardiac arrest
SCD	sudden cardiac death

INTRODUCTION

Sudden cardiac death (SCD) is defined as unexpected and abrupt death caused by a cardiovascular condition, symptoms of which have begun within the past hour. Although SCD is rare, each death has a significant and long-lasting effect on the victim's family and community. Athletes with preexisting cardiac conditions are at increased risk for SCD during training and competition. (1) Conducting preparticipation physical evaluations (PPEs) of athletes is an important step in preventing SCD in susceptible individuals, partly because many of the predisposing conditions would otherwise not be noticeable. To ensure proper screening, primary care providers should be familiar with cardiac conditions associated with SCD.

Because no screening program can eliminate the risk of SCD, secondary preventive measures, such as increasing access to training in cardiopulmonary resuscitation (CPR) and automated external defibrillators (AEDs), as well as establishing emergency response plans at schools, are essential. This review provides an overview of the epidemiology and causes of SCD in young athletes as well as preparticipation screening and secondary prevention.

EPIDEMIOLOGY

SCD has an estimated incidence ranging from 1:917,000 to 1:3,000 athletes younger than 40 years in the United States per year. (2) Most cases occur at the

high school or college level, often during practice or competition. (3) The overall risk is higher in male compared with female athletes, with a 9:1 ratio, and more than 3 times higher in black versus white athletes. (3)

Although some data suggest that SCD is more common in nonathletes than in athletes, it is clear that intense physical activity increases the risk of SCD in individuals with predisposing cardiovascular disease. (4)(5)(6) Certain sports are more strongly associated with SCD, such as football, basketball, and baseball in male athletes. In contrast, female athletes are at greater risk while participating in basketball, cross-country/track, and soccer. (3) Although speculation attributes the increased risk of SCD in these sports to each sport's popularity, intensity of training, and genetic predispositions of athletes, further studies are needed to confirm this possibility.

CAUSES OF SUDDEN DEATH

Based on data from the US National Registry of Sudden Death in Athletes from 1980 to 2011, 40% of sudden deaths in young athletes occur in the absence of a preexisting cardiac condition. Approximately half of these deaths are due to blunt trauma (51%), with commotio cordis composing a much smaller percentage (7%). (3)

In large autopsy-based studies of athletes in the United States, hypertrophic cardiomyopathy (HCM) has consistently been the most common confirmed cardiovascular cause of sudden death, followed by coronary artery anomalies. Table 1 lists the most common cardiac conditions associated with SCD. In this section, we highlight the most prominent causes of SCD. An overview of these conditions and some others is provided in Table 2.

Table 1. Cardiovascular Causes of Sudden Cardiac Death (SCD) in Young Athletes

CONDITION	SCD, %[a]
Hypertrophic cardiomyopathy	36
Anomalous coronary artery	19
Myocarditis	7
Arrhythmogenic cardiomyopathy	5
Coronary artery disease	4
Mitral valve prolapse	4
Aortic rupture	3
Aortic stenosis	2
Dilated cardiomyopathy	2
Other[b]	18

[a]Percentages are based on 842 young athletes in the United States from 1980 to 2011 with confirmed cardiac causes of sudden death. (3)
[b]Other conditions include (in decreasing order of frequency) left ventricular hypertrophy of unresolved etiology, bridged left anterior descending artery, long QT syndrome, congenital heart defect, Wolff-Parkinson-White syndrome, myocardial infarction, sarcoidosis, stroke, conduction system abnormality, cardiac rupture, cardiac tumor, tetralogy of Fallot, electrolyte abnormality, ruptured cerebral arteriovenous aneurysm.

Hypertrophic Cardiomyopathy

HCM is a genetic disorder affecting sarcomere proteins, the basic contractile unit in cardiomyocytes. As previously noted, it is the most frequently identified cause of SCD in young athletes in the United States, with an estimated prevalence of 1:500. (7)(8) However, as of 2019, only 1:1,250 individuals are clinically diagnosed, suggesting that 60% of affected individuals remain undiagnosed. (9)

More than 900 mutations have been identified in patients with HCM, most commonly located in the genes encoding β-myosin heavy chain (*MYH7*), cardiac myosin binding protein C (*MYPBC3*), and cardiac troponin (*TNNT2*). The clinical course of the disease varies considerably, with some patients presenting in childhood and others remaining asymptomatic through adulthood. Chest pain and dyspnea on exertion are commonly reported symptoms. In addition, the physical examination may reveal a systolic murmur that becomes louder with reduced preload (eg, Valsalva maneuver or standing) and quieter with increased preload (eg, squatting) or afterload (eg, handgrip). A family history of sudden unexplained death is another important clue because HCM is usually inherited as an autosomal dominant trait. (10)

The 12-lead electrocardiogram (ECG) is abnormal in most patients with HCM, with findings suggestive of left ventricular (LV) hypertrophy and repolarization abnormalities (eg, T-wave inversion). (10) Ambulatory ECG monitoring also provides valuable information for risk stratification, as nonsustained ventricular tachycardia is a risk factor for SCD. Other risk factors for SCD in patients with HCM include history of syncope or cardiac arrest, family history of SCD, severe LV hypertrophy (in adults, LV maximal wall thickness ≥30 mm), and abnormal blood pressure response to exercise. (11) However, these risk factors are extrapolated from adult data, and pediatric-specific risk factors and calculators are currently under investigation.

Echocardiography is the principal diagnostic imaging modality for HCM (Fig 1). Although diastolic LV wall thickness of 15 mm or greater without a known underlying cause is diagnostic in adults, a body surface–adjusted *z* score of 2 or greater suggests HCM in children. (10)(12) Regardless of age, asymmetrical septal hypertrophy is a common and distinctive feature of HCM. Cardiac magnetic resonance (CMR), which offers enhanced spatial resolution and image quality, can be helpful in patients with diagnostic uncertainty or poor echocardiographic imaging windows. Late gadolinium enhancement,

a marker of replacement fibrosis found in approximately half of patients, is a risk marker for adverse outcomes in HCM. (13)

Screening is recommended for first-degree relatives of patients with HCM, who can manifest at any age and thus warrant surveillance imaging every 1 to 3 years. In addition, genetic testing with counseling is offered to individuals with HCM. If genetic testing reveals a pathogenic variant, cascade genetic testing should be offered to first-degree relatives, with clinical surveillance for those who carry the pathogenic variant. If a pathogenic mutation is not identified in the proband, cascade genetic testing is not recommended for first-degree relatives. (10)

Guidelines, which have historically recommended against participation in most competitive sports for patients with HCM, are complicated and have recently evolved. Although HCM is the most common cause of SCD in young athletes, growing evidence shows that recreational exercise of mild to moderate intensity is safe and beneficial in these patients. (10)(14) As of 2020, class I recommendations permit mild to moderate exercise in most patients with HCM. (10) Athletes with HCM are encouraged to undergo a comprehensive evaluation and shared discussion of the potential risks and benefits of sports participation with an expert. (10)(15) Although participation in low-intensity competitive sports is reasonable in most cases, if certain conditions are met, participation in moderate- to high-intensity sports can also be considered through shared decision-making. (10)

Coronary Artery Anomalies

Coronary artery anomalies are a diverse group of congenital conditions with a wide range of clinical manifestations. Anatomic variations in coronary anatomy are common and range from benign and not causing myocardial ischemia or SCD to life-threatening. (16)(17) In fact, anomalous aortic origin of a coronary artery (AAOCA) is the second most common cause of SCD in young athletes. (3)

Blood flow to the myocardium is derived from 2 main coronary arteries, each arising from a different location of the aorta. In most individuals, the right coronary artery arises from the right aortic sinus and supplies blood to the right side of the heart, whereas the left main coronary artery arises from the left aortic sinus and bifurcates into the left anterior descending and circumflex arteries, together supplying blood to the left side of the heart.

In patients with AAOCA, 1 of the coronary arteries arises from an abnormal location on the aorta, creating an abnormal coronary artery opening (ostium), take-off angle, and course. If the coronary artery becomes stretched, kinked, or compressed, blood flow to the myocardium can be disrupted and result in myocardial ischemia, ventricular arrhythmias, and SCD. Due to the silent nature of coronary anomalies, the true prevalence of AAOCA and absolute risk of SCD are unknown. (18) However, studies suggest that although anomalous left coronary artery (ALCA) is at least 6 times less common than anomalous right coronary artery (ARCA), it has a much higher risk of SCD. (19)

Although half of SCD cases occur in previously asymptomatic individuals, patients may present with chest pain, exertional syncope, or diminished exercise tolerance. (18) Results of physical examination, ECG, and stress testing are often normal. Coronary anomalies are typically diagnosed by transthoracic echocardiography and advanced imaging modalities, which should also be directed at identifying high-risk anatomic features that increase the risk of SCD. These high-risk anatomic features include slitlike ostium, acute take-off angle, intramural course (within the wall of the aorta), and interarterial course (between the aorta and the pulmonary trunk).

Restriction from competitive sports is recommended for patients who have ARCA with high-risk features, symptoms, arrhythmias, or evidence of ischemia. Athletes can generally resume competitive sports 3 months after reparative surgery if they are asymptomatic and if testing reveals no evidence of ischemia. For patients with ARCA without symptoms or concerns for arrhythmias or ischemia, participation in competitive sports is acceptable with adequate counseling and a discussion about the potential risk of cardiac events. In athletes with ALCA, restriction from competitive sports is generally recommended. As with ARCA, athletes with ALCA may be cleared for competitive sports 3 months after surgery if they are asymptomatic and have no evidence of ischemia. (20)

Myocarditis

Myocarditis, the third most common cause of SCD in young athletes, is an inflammatory disease of the myocardium due to infections, systemic diseases, drugs, and toxins. (3) Viral infections, particularly due to enteroviruses (eg, coxsackieviruses) and adenoviruses, are the most common causes of myocarditis in the Unites States. Clinical manifestations vary widely, ranging from asymptomatic cases to heart failure and potentially fatal arrhythmias. Common symptoms associated with myocarditis are fatigue, shortness of breath, nausea (and/or abdominal pain), and chest pain. (21)(22) The diagnosis is usually suspected due to the presence of cardiac symptoms, elevated plasma troponin level, nonspecific ECG abnormalities (ST/T-wave changes), and echocardiographic findings, such as cardiac chamber enlargement and/or

Table 2. Cardiovascular Conditions Associated with Sudden Cardiac Death

CONDITION	CAUSE	PHYSICAL EXAMINATION	ECG/HOLTER	ECHOCARDIOGRAM	SPORTS GUIDELINES (USA)[a]	MANAGEMENT	NOTES
HCM	Sarcomere mutations (mostly AD)	Systolic murmur	LV hypertrophy and/or RV hypertrophy, large R or S waves; left axis deviation; ventricular arrhythmias	LV wall thickness ≥15 mm or 2 SD for weight; small LV cavity size; abnormal mitral valve +/− mitral regurgitation; LV outflow tract obstruction	Restrict from high-intensity sports, encourage mild-intensity activity; shared decision-making[b]	Consider ICD if high risk β-Blockers may improve symptoms but do not reduce mortality	High risk: previous cardiac arrest or sustained VT; family history of SCD; syncope; nonsustained VT; abnormal blood pressure response to exercise; severe LV hypertrophy
AAOCA	Abnormal coronary embryogenesis	Normal	Usually normal; ischemic changes; arrhythmias	Abnormal coronary artery	*Anomalous left coronary artery* Restrict from competitive sports *Anomalous right coronary artery* Restrict from competitive sports if symptoms, arrhythmias, or evidence of ischemia	Surgical repair Surgical repair if high-risk features, symptoms, arrhythmias, or evidence of ischemia	Coronary angiography is recommended Stress tests may yield false-negatives Consider sports participation 3 mo after reparative surgery if asymptomatic and no evidence of ischemia
Myocarditis	Acquired; usually viral infection	Evidence of cardiogenic shock, sinus tachycardia or tachyarrhythmias, gallop or hepatomegaly	Nonspecific ST-segment and T-wave abnormalities; ectopy/arrhythmias	Wall motion abnormalities; ventricular dysfunction; mitral regurgitation; pericardial effusion	Restrict from sports for at least 3–6 mo	Supportive	Clearance depends on normalization of serum markers of cardiac injury, normalization of systolic function, and resolution of any arrhythmias on exercise ECG
AC	Mutations in desmosomal proteins, eg, *PKP2* (mostly AD) Fatty fibrous tissue replaces heart muscle	Normal	Epsilon wave; localized QRS widening; prolonged S-wave upstroke; T-wave inversion in leads V_1 through V_3; LBBB, PVCs, or VT	Enlarged RV, LV, or both; ventricular dysfunction	Restrict to low-intensity sports[c]	ICD if high risk	Cardiac MRI is recommended High risk: aborted SCD, sustained VT, severe ventricular dysfunction
Channelopathies							
LQTS	*Congenital:* mutations in potassium or sodium channels (mostly AD) *Acquired:* medications, electrolyte abnormalities, etc	Normal	QTc prolongation Abnormal T-wave morphology	Normal	Restrict to low-intensity sports if symptomatic or prolonged QTc[c] LQTS type 1 genotype should avoid competitive swimming	β-blockers ICD if high risk	Often incidental detection on ECG; consider in patients with syncope or atypical seizures Risk of SCD is related to QTc duration, genotype, history of symptoms, sex of individual

Continued

Table 2. Cardiovascular Conditions Associated with Sudden Cardiac Death (Continued)

CONDITION	CAUSE	PHYSICAL EXAMINATION	ECG/HOLTER	ECHOCARDIOGRAM	SPORTS GUIDELINES (USA)[a]	MANAGEMENT	NOTES
Brugada syndrome	Mutations in sodium channels, eg, *SCN5A* (mostly AD)	Normal	Coved ST-segment elevation in leads V_1 and V_2; abnormal T-wave morphology	Normal	Restrict to low-intensity sports[bc] If asymptomatic, participation can be considered with precautionary measures	Quinidine Ablation ICD if high risk	Highest risk of SCD with type 1 Brugada pattern on ECG Fevers increase risk; treat with antipyretics
CPVT	Calcium dysregulation Mutation in ryanodine receptor 2 (*RyR2*) (mostly AD)	Normal	Normal	Normal	Restrict to low-intensity sports[c]	Antiarrhythmic medications (eg, nadolol, flecainide) Left cardiac sympathetic denervation ICD if high risk	Exercise stress test may reveal ectopy, polymorphic VT
WPW syndrome	Accessory pathway; unknown cause	Normal	Slurred QRS upstroke ("delta wave"), short PR interval	Normal	Asymptomatic: No restriction Symptomatic: EPS recommended	β-Blockers or ablation useful to prevent SVT	Return to competitive sports 4 wk after radiofrequency ablation

AAOCA=anomalous aortic origin of a coronary artery, AC=arrhythmogenic cardiomyopathy, AD=autosomal dominant, CPVT=catecholaminergic polymorphic ventricular tachycardia, ECG=electrocardiogram, EPS=electrophysiology study, HCM=hypertrophic cardiomyopathy, ICD=implantable cardioverter-defibrillator; LBBB=left bundle branch block, LQTS=long QT syndrome, LV=left ventricle, MRI=magnetic resonance imaging, PVC=premature ventricular contraction, RV, right ventricle, SCD=sudden cardiac death, SVT=supraventricular tachycardia, VT=ventricular tachycardia, WPW=Wolff-Parkinson-White.

[a]Sports restriction guidelines are from Maron BJ, Zipes DP, Kovacs RJ; on behalf of the American Heart Association Electrocardiography and Arrhythmias Committee of the Council on Clinical Cardiology, Council on Cardiovascular Disease in the Young, Council on Cardiovascular and Stroke Nursing, Council on Functional Genomics and Translational Biology, and the American College of Cardiology. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: preamble, principles, and general considerations: a scientific statement from the American Heart Association and American College of Cardiology. *Circulation*. 2015;132:e256–e261.

[b]Individuals who are genotype positive but phenotype negative can continue to participate in all competitive sports.

[c]Low-intensity class 1A sports have low static (<20% of maximum voluntary contraction) and low dynamic (<40% of maximum oxygen uptake) components. These sports include billiards, bowling, cricket, curling, golf, and riflery.

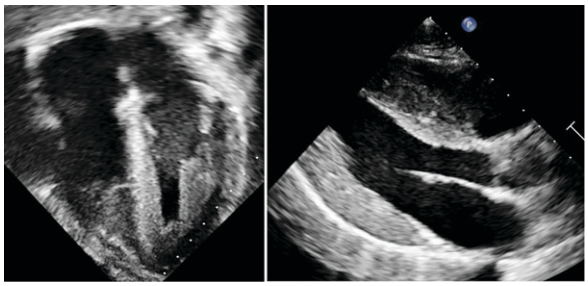

Figure 1. Echocardiograms showing left ventricular hypertrophy in a teenager with hypertrophic cardiomyopathy.

impaired LV systolic or diastolic function. Although endomyocardial biopsy remains the gold standard, CMR has emerged as a more sensitive and less invasive test to confirm the diagnosis.

To promote the resolution of inflammation, athletes diagnosed as having myocarditis should be restricted from exercise for 3 to 6 months, depending on the extent of cardiac injury and inflammation on CMR. (15) Because SCD in myocarditis is most likely due to development of ventricular tachyarrhythmias resulting from myocardial scarring, ambulatory ECG monitoring and/or exercise stress testing are used in addition to CMR to evaluate for arrhythmias before clearing patients for return to competitive sports. (23)

Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy (AC), previously known as arrhythmogenic right ventricular cardiomyopathy, is an inherited cardiomyopathy characterized by progressive replacement of myocardium with fibrofatty tissue and a predisposition for ventricular arrhythmias and SCD. Although structural abnormalities of the right ventricle predominate, LV involvement is also possible. (24)

AC is usually inherited in an autosomal dominant manner with incomplete penetrance and variable expressivity. Most cases involve mutations in genes encoding proteins in desmosomes, the membrane structures that regulate intercellular adhesion and maintain structural integrity of tissues during mechanical stress. Mutations in the plakophilin-2 (*PKP2*) gene are the most frequent cause. (25) AC predominantly affects men, whereas women with an associated gene mutation have a lower chance of expressing the disease and are more likely to be asymptomatic carriers. (25)

The prevalence of AC is challenging to estimate because it is often discovered postmortem. Its association with the Mediterranean region explains why it is the most common cause of SCD in young athletes in Italy while accounting for less than 5% in the United States. (24)(26)(27)

Clinical signs or symptoms of AC such as dizziness, syncope, or palpitations are rarely recognized before puberty, with onset typically ranging from the late 20s to early 30s. (27) As a result, the condition is not likely to be detected based on history and physical examination findings unless there is a family history notable for SCD or relatives diagnosed as having AC. Although ECG has low sensitivity for this condition, it may show important abnormalities, including a widened QRS, epsilon wave (Fig 2A), and inverted T waves in the right precordial leads (V_1 through V_3), the latter of which is abnormal after 14 years of age. (25)(28) Although echocardiography is generally normal, especially in the early stages of the disease course, a normal study does not exclude the diagnosis. If clinical suspicion is high, CMR should be performed to evaluate for myocardial changes consistent with the disease.

There is no cure for AC. When the diagnosis is made, the individual should be restricted from competitive sports with the possible exception of low-intensity class 1A sports, which include billiards, bowling, cricket, curling, golf, and riflery. (15) Patients who meet specific high-risk criteria usually undergo insertion of an implantable cardioverter-defibrillator (ICD). (29)

Ion Channelopathies

Ion channelopathies are a group of hereditary defects in the membrane channel proteins that can cause lethal arrhythmias and SCD in individuals with structurally normal hearts. These disorders are suspected to account for a significant proportion of cases in which the autopsy reveals a structurally normal heart with no identifiable cause of SCD. (30) Long QT syndrome (LQTS), Brugada syndrome, and

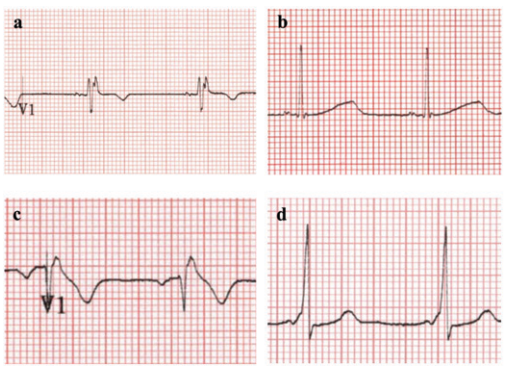

Figure 2. Electrocardiographic findings associated with cardiac diseases. A. Epsilon wave in arrhythmogenic right ventricular cardiomyopathy. B. Prolonged QT interval in long QT syndrome. C. Coved-type ST-segment elevation in Brugada syndrome. D. Delta wave in Wolff-Parkinson-White syndrome.

catecholaminergic polymorphic ventricular tachycardia (CPVT) are the most common channelopathies associated with SCD. Patients with these disorders may report palpitations and syncope (particularly exertional or with auditory stimulation) and a family history notable for early and/or unexplained death. Although findings from physical examination and echocardiography are generally normal, each channelopathy has a unique ECG fingerprint.

LQTS, which can be inherited or acquired (eg, QT-prolonging drugs), is characterized by prolonged ventricular repolarization leading to ventricular arrhythmias, classically *torsade de Pointes* ("twisting of peaks" in French). The risk of arrhythmias and SCD is directly related to the duration of the QTc interval; each 10-millisecond increase in QTc has been shown to increase the risk of malignant arrhythmias. (31) QTc intervals are considered prolonged when they are greater than 460 milliseconds in males or greater than 470 milliseconds in females and highly abnormal regardless of sex when greater than or equal to 500 milliseconds (Fig 2B). Although QTc prolongation is a hallmark of LQTS, 40% of patients with genetically confirmed LQTS have a normal QTc duration on baseline ECG, with only subtle T-wave abnormalities. (32)(33) In such cases of concealed LQTS, exercise stress testing can unmask ECG abnormalities. On the opposite end of the spectrum, LQTS is also frequently overdiagnosed, especially in patients with prolonged QTc secondary to vasovagal syncope. (34)

At least 17 different genes are associated with LQTS, of which 90% are accounted for by 1 of 3 major genes: *KCNQ1* (LQTS1), *KCNH2* (LQTS2), and *SCN5A* (LQTS3). (35) SCD associated with mutations in each have signature triggers: exercise, especially swimming, for LQTS1; arousal, especially a sudden loud noise (along with one-third of SCDs during exercise) for LQTS2; and during sleep (and <5% of SCDs during exercise) with LQTS3. (35)

Current guidelines recommend restriction of individuals with LQTS to class 1A sports if they have symptoms, ICDs, or significant QTc prolongation (males: >470 milliseconds; females: >480 milliseconds), although participation may be considered after initiation of treatment and appropriate precautionary measures. (36) Genetically positive individuals who have normal QT intervals can compete in sports without restriction, except for individuals with symptomatic LQTS1, who should be restricted from competitive swimming. β-Blockers, particularly nadolol and propranolol, are the first-line therapy for patients with LQTS and are most effective in LQTS1. Other therapeutic options reserved for high-risk patients include ICD placement and left cardiac sympathetic denervation to reduce adrenergic stimulation of the heart. (37)

Brugada syndrome commonly involves autosomal dominant mutations in the cardiac sodium channel *SCN5A* gene, although pathogenic variants in other genes have been identified. (38) Patients with this condition may report a history of palpitations or syncope triggered by fever and a family history of Brugada syndrome or sudden death. The cardiac examination is usually normal; however, the diagnosis is based on ECG abnormalities that may occur spontaneously or be unmasked by a sodium channel blocker (ie, provocative drug testing). ECG may demonstrate pathognomonic abnormalities, including a "coved-type" ST-segment elevation (Fig 2C) or "saddleback" ST-segment elevation in the right precordial leads, V_1 through V_3, whereas Holter monitoring is useful to evaluate for asymptomatic arrhythmias. Lethal arrhythmias may be triggered by increased vagal tone (eg, during exercise recovery or sleep) as opposed to during exercise. (39) Despite the absence of a clear association between exercise and SCD in Brugada syndrome, previous US guidelines recommended restriction from competitive sports with the potential exception of class 1A sports. (39)(40) Current guidelines specify that participation in competitive sports may be considered once appropriate precautionary measures and treatments are in place provided that the athlete has been asymptomatic for at least 3 months. (36) Treatment has historically been limited to drugs and ICDs for high-risk patients, although catheter ablation—a minimally invasive procedure used to destroy abnormal tissue—has also been suggested as a therapeutic option. (38)

CPVT results from genetic mutations—most commonly autosomal dominant in the *RyR2* gene encoding a ryanodine receptor in the sarcoplasmic reticulum—that cause abnormal calcium release in cardiomyocytes. The disease is characterized by adrenergic-induced ventricular tachyarrhythmias, including bidirectional ventricular tachycardia, a rare tachyarrhythmia in which dual QRS morphologies alternate on a beat-to-beat basis. In this condition, syncope or sudden death is usually triggered by acute emotional stress or exercise. History and physical examination findings are often normal, with a positive family history of exercise/emotion syncope in approximately one-third of cases. (41) Although resting ECG is usually normal, ventricular ectopy and arrhythmias can be provoked by exercise (ie, exercise stress testing) or epinephrine. With mortality in this condition high if untreated (30%–50% by age 40 years), those diagnosed as having CPVT are generally restricted from competitive sports and treated with antiarrhythmic medications,

including β-blockers (ie, nadolol) and sodium channel blockers (ie, flecainide), left cardiac sympathetic denervation, and occasionally ICD implantation. (36)(41)(42)

Commotio Cordis

Commotio cordis (Latin etymology, "agitation of the heart") refers to a disruption of the normal heart rhythm due to a direct blow to the chest and is particularly distressing because commotio cordis usually occurs in an otherwise healthy athlete with no identifiable heart problem. Each year in the United States, there are approximately 10 to 20 cases of this condition, which is primarily an electrical phenomenon that does not result from structural damage to the myocardium. (43) For ventricular fibrillation to be induced, the blunt impact must involve a minimum pressure of 250 mm Hg and must occur during a narrow window of vulnerability during the cardiac cycle (ie, during the T-wave upslope). (43)

Approximately 95% of cases occur in males, with a mean age of 15 years. (43) Baseball has the highest incidence of commotio cordis. Although commercial protective equipment may be helpful in preventing commotio cordis, it can still occur when the victim is wearing a chest guard. (44)(45)

During the past 2 decades, survival rates of patients with commotio cordis have increased from 15% to 60%, largely due to improved recognition of sudden cardiac arrest (SCA), bystander-initiated CPR, and the widespread availability of AEDs at sporting events. (46) In fact, the survival rate drops to 3% when resuscitation is delayed beyond 3 minutes. (44) If no underlying cardiac abnormality is identified, survivors of commotio cordis are allowed to resume training and competition on full recovery. (46)

Other Causes

Several other conditions are associated with SCD, including severe obstructive lesions such as aortic stenosis or pulmonary stenosis, aortopathies such as Marfan syndrome (ie, due to aortic rupture or dissection), primary pulmonary hypertension, sarcoidosis, and sickle cell trait. Patients with complex congenital heart defects, including those status post repair or palliative procedures, are at risk for arrhythmias and SCD due to surgical scarring, hemodynamic abnormalities, residual lesions, or ventricular dysfunction. (47) Wolff-Parkinson-White syndrome (Fig 2D) is considered a rare cause of SCD, which likely occurs due to the rapid conduction of atrial fibrillation to the ventricles via the accessory pathway, resulting in ventricular fibrillation. (48) Although mitral valve prolapse is typically considered a benign condition, it may pose an increased risk of SCD. (49) Finally, atherosclerotic cardiovascular disease is a major cause of SCD in older athletes but rarely causes SCD in young athletes, although the likelihood is higher if there are risk factors such as a history of Kawasaki disease. (50) Although performance-enhancing drugs can increase cardiac risk, evidence has been inconclusive about their involvement in SCD. (51)

NORMAL FINDINGS IN ATHLETES

The physiological and benign profile of an athlete's heart (so-called athlete's heart) can be difficult to differentiate from cardiovascular abnormalities. Because ECG changes are observed in approximately 40% of trained athletes, international consensus standards for normal, abnormal, and borderline ECG findings in this population have been established. (52)(53) Examples of findings that are considered normal for trained athletes include high QRS amplitude (meeting voltage criteria for LV hypertrophy), early repolarization, sinus bradycardia, sinus arrhythmia, and first-degree atrioventricular block. Such findings are attributed to intense athletic conditioning resulting in structural cardiac remodeling and increased vagal tone and do not warrant further evaluation.

Morphologic remodeling associated with intense athletic training, such as increased LV chamber dimensions and wall thickness, can mimic features of genetic and acquired heart disease such as cardiomyopathies. Certain echocardiographic features are helpful in distinguishing between benign adaptive remodeling and heart disease, and a complete description is beyond the scope of this review. However, a thorough evaluation of LV wall thickness and morphology, diastolic LV cavity size, atrial size, systolic function, and diastolic function is required. For cases in which echocardiographic findings are equivocal, repeated evaluation after a period of deconditioning (ie, avoiding exercise) can be helpful because ECG and echocardiographic changes associated with an athlete's heart should normalize during this time. (54) The distinction between physiological and pathological changes in athletes is important because an incorrect diagnosis can have significant consequences, such as exclusion from competitive sports or inappropriate reassurance and a missed opportunity for therapeutic intervention.

SCREENING GUIDELINES

The primary goal of screening is to identify conditions that predispose individuals to SCA or SCD. Personal history, family history, and physical examination findings are

the core components of screening. The American Academy of Pediatrics (AAP) recommends that all children undergo screening for the risk of SCD regardless of athletic status. (55) Screening should occur during the PPE, a minimum of every 3 years, or on entry into middle or junior high school and into high school. Four main screening questions are recommended:

1. Have you ever fainted, passed out, or had an unexplained seizure suddenly and without warning, especially during exercise or in response to sudden loud noises, such as doorbells, alarm clocks, and ringing telephones?
2. Have you ever had exercise-related chest pain or shortness of breath?
3. Has anyone in your immediate family (parents, grandparents, siblings) or other more distant relatives (aunts, uncles, cousins) died of heart problems or had an unexpected sudden death before age 50 years? This would include unexpected drownings, unexplained car accidents in which the relative was driving, or sudden infant death syndrome.
4. Are you related to anyone with HCM or hypertrophic obstructive cardiomyopathy, Marfan syndrome, AC, LQTS, short QT syndrome, Brugada syndrome or CPVT, or a condition requiring implantation of a pacemaker or ICD at younger than 50 years?

The AAP's recommended screening questions are based on expert consensus and have not been scientifically validated in a prospective study. These questions were designed to be simple and easy to incorporate into a family questionnaire. (55) The first question focuses on personal history of sudden loss of consciousness, particularly events triggered by exertion or sudden loud noises, which tend to occur in patients with channelopathies such as LQTS. The second question focuses on symptoms of chest pain or shortness of breath on exertion, which can signal myocardial ischemia, congestive heart failure, arrhythmias, and valvar disease. The other 2 questions inquire about family members with heart conditions, potentially pointing to a familial inheritance pattern. Steinberg et al (56) previously showed that cardiac abnormalities can be identified in nearly one-third of first-degree relatives of SCA survivors or SCD victims.

Meanwhile, the American Heart Association (AHA) has published guidelines for preparticipation screening of competitive athletes, which consists of a 14-element (previously 12-point) history and physical examination (Table 3). Use of this 14-element checklist for preparticipation screening is a class I recommendation based on a scientific statement jointly published by the AHA and American College of Cardiology. (57)(58) As with the AAP's screening questions, the AHA's 14-element screening tool was developed based on expert opinion and over time has become the most commonly accepted screening method for young athletes. (55)(57)(58) In addition, it has also been incorporated into other screening guidelines, such as a revised version with changes in language and wording that has been incorporated into the *PPE: Preparticipation*

Table 3. The 14-Element American Heart Association Recommendations for Preparticipation Screening of Competitive Athletes (57)

Personal history:
1. Chest pain/discomfort/tightness/pressure related to exertion
2. Unexplained syncope/near-syncope[a]
3. Excessive exertional and unexplained dyspnea/fatigue or palpitations, associated with exercise
4. Previous recognition of a heart murmur
5. Elevated systemic blood pressure
6. Previous restriction from participation in sports
7. Previous testing for the heart, ordered by a physician
Family history:
8. Premature death (sudden and unexpected, or otherwise) before age 50 y attributable to heart disease in ≥1 relative
9. Disability from heart disease in a close relative aged <50 y
10. Hypertrophic or dilated cardiomyopathy, long QT syndrome or other ion channelopathies, Marfan syndrome, or clinically significant arrhythmias; specific knowledge of certain cardiac conditions in family members
Physical examination:
11. Heart murmur[b]
12. Femoral pulses to exclude aortic coarctation
13. Physical stigmata of Marfan syndrome
14. Brachial artery blood pressure (sitting position)[c]

[a]Judged not to be of neurocardiogenic (vasovagal) origin; of particular concern when occurring during or after physical exertion.
[b]Refers to heart murmurs judged likely to be organic and unlikely to be innocent; auscultation should be performed with the patient in both the supine and standing positions (or with the Valsalva maneuver), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction.
[c]Preferably taken in both arms.

Physical Evaluation, 5th Edition, a monograph published by the AAP in collaboration with 5 other medical societies. (59)

However, despite being endorsed by medical societies, the 14-element screening tool remains heavily underused. A recent study in *Pediatrics* found that a minority (27%) of the 48 states providing PPE forms incorporate all 14 elements in their screening forms. (60) Moreover, a quality review by Miliaresis et al (61) found that only one-third of pediatricians are familiar with the AHA's recommended screening form and that, on average, only 3.5 of 14 elements are documented in visit notes. Barriers to PPE use include lack of awareness of the 14-element screening form, use of a different form, and time constraints. Of note, the authors did increase use of the PPE through standard quality improvement methods. (61)

Although the need for preparticipation screening of young athletes is widely supported, the optimal approach has long been debated. Studies have shown that the 14-element screening has sensitivity and specificity of 20% and 68%, respectively, for cardiac risk factors among high school athletes. (62) The incorporation of ECG screening would certainly increase screening sensitivity, as evidenced by a meta-analysis published in 2015, based on screening of 47,137 athletes from several regions, that revealed a 5-fold and 10-fold increase in sensitivity of ECG in detecting cardiac conditions relative to history and physical examination, respectively. (63) However, incorporating ECG screening would also involve a substantial cost that medical societies such as the AHA view as prohibitive. With nearly 10 million student athletes in the United States annually, the widespread implementation of ECG screening would cost billions of dollars. One must also consider the additional monetary, legal, and emotional cost of dealing with false-positive and false-negative test results. Therefore, ECG is usually reserved for patients at increased risk for SCD based on routine screening with the PPE.

SECONDARY PREVENTION

Preparticipation screening is useful for identifying athletes with high-risk cardiac conditions, but no screening strategy can single-handedly prevent SCD. In addition, despite improvements in survival rates after SCA, disparities in outcomes based on race and socioeconomic status continue to exist, with studies showing worse cardiac emergency preparedness and lower survival rates in low-income neighborhoods versus high-income neighborhoods. (64) To address these disparities, it is essential to target these demographics in the implementation of secondary prevention measures.

CPR and AEDs

SCD can be prevented through prompt recognition, administration of high-quality CPR, and early defibrillation. This "Chain of Survival" is highly dependent on public engagement. Administration of bystander CPR is associated with increased survival and improved neurologic outcome. (65) Although previous CPR training increases bystanders' willingness to perform CPR, only a small percentage (<3%) of the US population receives training each year. (66)(67)(68) In recent years, self-directed online courses have emerged as an acceptable alternative to in-person courses. Furthermore, statewide laws requiring CPR training in high schools have also translated to more laypersons learning this lifesaving skill, although the quality of such training is inconsistent and has striking geographic disparities. (69) Currently, the AHA recommends training students as early as middle school on how to perform high-quality CPR.

Early defibrillation is another important intervention affecting outcomes after SCA, and arguably the most important determinant of survival. Despite the fact that most cases of SCA involve a shockable rhythm (ie, ventricular fibrillation), the probability of surviving SCA caused by ventricular fibrillation diminishes rapidly over time, declining approximately 10% each minute defibrillation is delayed. (70)(71) From 2000 to 2006, exercise-related SCA in the young had an overall survival rate of 11%. (72) A more recent study analyzing events from 2014 to 2018 reported a higher overall survival rate of 68% among student athletes, with a survival rate of 85% if an on-site AED is used. (73)

Emergency Preparedness

Schools have a responsibility to prepare for cardiac emergencies that goes beyond the mere presence of an AED or bystander with CPR training. The AHA recommends that schools and/or school districts implement Cardiac Emergency Response Plans (CERPs), which are associated with a lower incidence of SCD. (74)(75) Core components of a CERP include establishing a Cardiac Emergency Response Team (a team of athletic trainers, teachers, and other staff members with CRP/AED training), creating an emergency activation system, ensuring AED equipment is easily accessible and properly maintained, offering frequent CPR/AED training, performing practice drills, and reviewing the plan on an ongoing and annual basis. (76) Documents needed to implement a CERP are available on the AHA's website. (77)

The AHA also recommends that states enact legislation that requires and funds the creation and maintenance of CERPs in schools. (76) State legislation requiring schools to have an AED has been shown to significantly increase

AED availability across high schools, with public schools being most affected by such legislation. (78) As of 2022, according to data collected by the Sudden Cardiac Arrest Foundation, only 20 states require AEDs. (79)

FUTURE DIRECTIONS

The absolute risk of SCD is low, even among athletes with high-risk conditions, and the known detriments of lack of physical activity have led to a recent focus on shared decision-making. Moreover, machine learning algorithms can potentially help clinicians diagnose the conditions that cause SCD and can already detect HCM and LQTS from standard ECGs with excellent sensitivities and specificities, and it is possible that artificial intelligence can similarly be trained to facilitate more accurate risk stratification, resulting in a lower burden of unnecessary sports disqualification. (80)(81) Finally, gene therapy is an emerging area of interest in SCD prevention, as investigators recently published the first hybrid gene therapy for LQTS1, which is now advancing to animal model studies. (82)

CONCLUSION

SCD is a rare but devastating event that is often preventable. When SCD occurs in a young athlete, it is frequently due to an underlying cardiac condition. Due to lack of demonstrated efficacy as well as prohibitive costs and feasibility of large-scale ECG and echocardiography screening, routine PPE is limited to history and physical examination. Primary care providers and pediatric cardiologists can prevent SCD by identifying red flags associated with the most common causes of SCD. Because the PPE is imperfect at identifying athletes with high-risk conditions, secondary measures are also essential to preventing SCD.

Summary

- Preparticipation screening for young athletes is important because it can potentially reduce the risk of sudden cardiac death (SCD). (Based on research evidence and consensus) (55)(58)(59)(60)(83)
- Several cardiac conditions are associated with SCD. Hypertrophic cardiomyopathy, coronary artery anomalies, and myocarditis are the 3 most common identifiable causes. Ion channelopathies may account for a significant number of autopsy-negative SCDs. (Based on research evidence and consensus) (3)(30)
- A focused history and physical examination is the recommended preparticipation screening method, although the American Heart Association's 14-element screening tool has low sensitivity. (Based on research evidence and consensus) (58)(62)
- Universal electrocardiographic screening is not recommended in the United States. This is partly due to prohibitive cost and the potential for false-positives resulting in additional unnecessary testing. (Based on research evidence and consensus) (57)(58)(84)
- Providers should follow US guidelines for determining the appropriate sports restriction for individuals with high-risk cardiac conditions. However, it is also important to recognize that these conditions have a low risk of SCD and that shared decision-making has emerged as an important framework for the contemporary sports eligibility discussion. (Based on research evidence and consensus) (10)(15)(36)
- High-quality cardiopulmonary resuscitation and prompt defibrillation are integral to preventing SCD once sudden cardiac arrest (SCA) has occurred. The probability of surviving SCA caused by ventricular fibrillation is reduced by 10% each minute defibrillation is delayed. (Based on research evidence and consensus) (71)(75)
- Schools and/or school districts should implement Cardiac Emergency Response Plans, which can help schools prepare for SCAs and prevent SCDs. (Based on some research evidence and consensus) (74)(75)(77)
- Machine learning could play an important role in SCD prevention in the future. In addition, new gene therapies may be available for individuals diagnosed as having predisposing conditions. (Based on some research evidence) (80)(81)(82)

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References and teaching slides for this article can be found at https://doi.org/10.1542/pir.2023-005975.

PIR QUIZ

1. A 16-year-old male basketball player is brought to the pediatric outpatient clinic by his parents for evaluation of chest pain and syncope with exertion. The boy's father and paternal uncle have been diagnosed as having hypertrophic cardiomyopathy (HCM). On physical examination the patient has a systolic murmur that becomes louder when he performs a Valsalva maneuver. Of the following cardiac imaging findings, which one is considered a distinctive feature of HCM diagnosis?

   A. Asymmetrical septal hypertrophy.
   B. Early gadolinium enhancement on cardiac magnetic resonance imaging.
   C. Impaired left ventricular diastolic function.
   D. Impaired left ventricular systolic function.
   E. Left ventricular wall thickness greater than 30 mm.

2. A 17-year-old female athlete is diagnosed as having HCM based on family history and echocardiography findings. She is asymptomatic. She has undergone extensive evaluation and is found not to exhibit high-risk features of HCM. The patient and her family have had a comprehensive discussion about the risks and benefits of physical activity for individuals with HCM. They also ask whether the patient requires placement of an implantable cardioverter-defibrillator (ICD). Which one of the following management and physical activity recommendations is most appropriate to discuss with this patient and her parents?

   A. Do not place an ICD, and clear her for participation in only low-intensity physical activity.
   B. Do not place an ICD, and clear her for participation in moderate- to high-intensity physical activity.
   C. Place an ICD, and subsequently clear her for low-intensity physical activity.
   D. Place an ICD, and subsequently clear her for moderate- to high-intensity physical activity.
   E. Place an ICD, and subsequently recommend that she not participate in any physical activity.

3. A 17-year-old female athlete is brought to the outpatient clinic by her parents for sports preparticipation clearance. She was diagnosed as having viral myocarditis 3 months ago after she developed chest pain and dyspnea with exercise. She recently completed follow-up testing; echocardiogram demonstrated normal ventricular function, exercise testing and 24-hour Holter monitor showed no evidence of arrhythmia, and cardiac magnetic resonance imaging did not show any cardiac injury or inflammation. The girl is hoping to return to competitive basketball. Which one of the following is the most appropriate recommendation of the timing to return to play in this patient?

   A. In 3 months after an additional round of testing.
   B. In 6 months without additional testing.
   C. In 9 months without additional testing.
   D. She can now return to training and competition.
   E. She should be restricted from high-intensity physical activity permanently.

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4. An adolescent male athlete with a family history of sudden unexplained death dies after collapsing while playing football. There is no history of trauma to the chest. The autopsy does not reveal findings of any structural heart or lung disease. Which one of the following is the most likely cause of death in this patient?

   A. Arrhythmogenic cardiomyopathy.
   B. Commotio cordis.
   C. Long QT syndrome.
   D. Myocarditis.
   E. Sarcoidosis.

5. An adolescent presents to the outpatient pediatric office for preparticipation physical evaluation before the soccer season. The patient's pediatrician discusses the 14 elements of the American Heart Association's (AHA) screener for heart disease with the medical students attending the clinic. The AHA screening criteria include which one of the following elements?

   A. Blood pressure in supine and standing positions.
   B. Echocardiogram.
   C. Electrocardiogram.
   D. Family history of ion channelopathies.
   E. Radial and pedal pulses.