Review Article

Risk of Sudden Cardiac Death and Preventive Measures in Athletes

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Abstract

Arrhythmias, which are fatal in some patients, can be triggered by sports in vulnerable people. It is estimated that 1:40,000–1:250,000 athletes will suffer a sudden cardiac death (SCD). However, female athletes appear to have some level of cardiac protection, since suffering from SCD considerably less than male athletes during sports. Athletes with underlying coronary, valvular or myocardial disease, as well as channelopathies, may be particularly prone to SCD from exercise- and sports-related physical activity. There are three main causes of SCD in young athletes: Sudden Arrhythmic Death Syndrome (56%), congenital anomalous coronary arteries (7%–14%), and hypertrophic cardiomyopathy (36%–48%). In the context of exercise, acute ischemia, myocardial infarction, and stroke risk are increased by catecholamine surge and exercise-induced stress. In middle-aged athletes, excessive cardiovascular activity is associated with a higher risk of mortality related to cardiovascular disease. It is possible to detect at-risk athletes by conducting cardiac screening, which involves a family history, physical examination, and a resting electrocardiogram. Consequently, efforts have been made to better understand the causes of SCD in athletes and to develop appropriate prevention methods.

Keywords: Athlete's heart, cardiac screening, cardiovascular abnormalities, sports, sudden cardiac death

Introduction

The sudden cardiac death (SCD) rate among athletes is considerably lower than that of the general population. The public's response to SCD occurring during a sports event raises questions about cardiovascular risks related to sports. In this paper, we examine the pathophysiology and etiology of SCD among athletes engaged in sports and exercise. Numerous studies have found that regular exercise lowers cardiovascular mortality, including SCD significantly compared with sedentary lifestyles.[1,2] In contrast, exercise- and sports-related physical activity have been linked to SCD, particularly in athletes with underlying coronary, valvular, myocardial disease, and channelopathies. It appears that exercise may exacerbate predisposed individuals' tendency to develop malignant arrhythmias. There has been extensive research conducted by sports cardiologists worldwide to quantify the incidence of SCD in athletes, identify risk factors, develop preparticipation screening tools, and formulate plans for on-field SCD management.[3] The aim of this review is to inform the community about the current state of knowledge regarding athletes who are at risk of SCD.

Epidemiology of Sudden Cardiac Death in Athletes

Across studies, the incidence of SCD in athletes ranges from 1:40,000 to 1:250,000, with this variance being driven by different methodologies, demographics, and sports disciplines.[4] A 5-year prospective study found that 4.6 people/1 million had sports-related SCD, compared with 50–100 people per million in the general population.[5] Sudden

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death is influenced by several factors, including an athlete's age, race, gender, ethnicity, training level, and type of sport. Over 80% of sports-related SCD deaths occurred in adults aged 35 and older due to atherosclerotic coronary artery disease (CAD).[6] While preparing for any sporting event, the risk of sudden cardiac arrest (SCA) or SCD is approximately five-fold higher.[7] A higher rate of adverse events is observed in occasional runners (1/7500–18000) than in marathon runners (1/50,000–200,000).[8] Sports competition has been associated with SCD in vulnerable individuals who experience lethal arrhythmias. Unlike male athletes, female athletes appear to have some level of cardiovascular protection, since they typically do not die suddenly during sports. According to the data from the United States, black athletes are at a higher risk of SCD than white athletes.[4,9] Corrado *et al*.,[10] published one of the first large-scale studies of SCD in athletes in the Veneto area of Italy, which prospectively examined SCD events in a youth population (between 12 and 35 years of age), demonstrating an incidence rate equal to 1.0 in 100,000 people per year, including 2.3/100,000 among competitive athletes. The findings of Alattar *et al*.[11] indicate that five (2.17%) Arab athletes had an SCD-related anomaly. Two of the athletes had Wolff-Parkinson-White (WPW) syndrome, one had Atrial Fibrillation, one had Long QT syndrome (LQTS), and one had arrhythmogenic right ventricular cardiomyopathy (ARVC). According to Riding *et al*.,[12] 10 athletes (0.47%) have pathological substrate related to SCD. The hypertrophic cardiomyopathy (HCM) syndrome was detected in five black athletes and two Arab athletes, while the WPW syndrome was detected in three Arab athletes. Among younger athletes, more than half of all deaths result from nonmedical or traumatic causes. It is estimated that 0.2%–0.7% of young athletes develop cardiovascular disorders predisposing to SCD during sports. Sudden arrhythmic death syndrome-SADS (56%), HCM (36%–48%), and congenital anomalous coronary arteries originating from opposing sinuses (14%–17%) are the most common causes of SCD in athletes, while ARVC (4%–11%), myocarditis (6%–7%), and ion channelopathies (4%), are the least common. SADS is an unexplained or unexpected sudden death especially in young, despite a comprehensive autopsy and toxicological analysis. SADS may be caused by underlying primary electric disease.[13]Atherosclerotic CAD is the cause of only 2%–3% of SCD in younger athletes[7] [Figure 1].

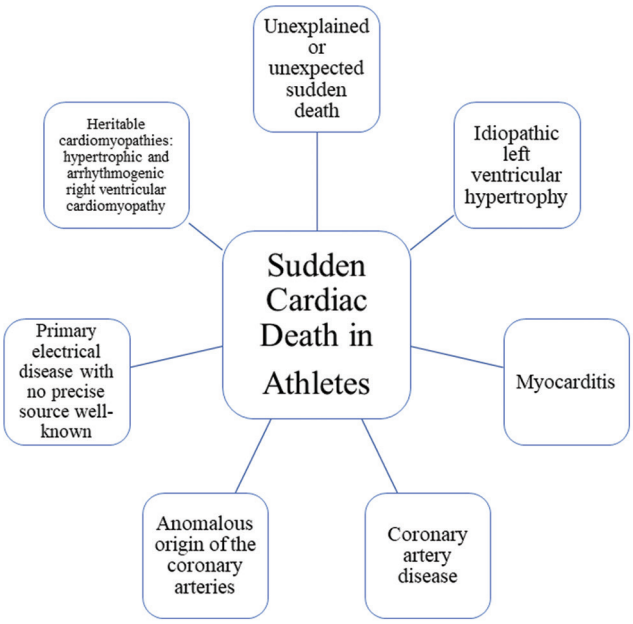

Figure 1: Sudden cardiac death in athletes

Etiology

A physical exertion-induced SCD can be deadly despite its rarity. A significant percentage of these deaths, even among young, seemingly healthy individuals, is caused by undiagnosed cardiovascular disease. Recent studies found that around 65% of sudden deaths in student-athletes did not involve cardiovascular causes, but rather a suicide, trauma, or substance abuse. A substantial number of sudden deaths were caused by drowning and heat strokes.[11] Tables 1 and 2 illustrate the pathological assessment and underlying conditions of SCD patients.[7,14] More than three-quarters of nontraumatic sudden deaths in sports are caused by cardiovascular diseases. The cause of SCD in young athletes (<35 years old) can range from hereditary, congenital, or acquired structural and electrical problems. In the United States, SCD is most commonly caused by HCM, whereas in Italy, ARVC is commonly reported. Further causes of SCD include myocarditis, coronary artery abnormalities, valvular heart diseases, aortic dissection, commotio cordis, and inherited channelopathies such as WPW syndrome, LQTS, and Brugada syndrome. Children without obvious structural heart disease are also at risk of SCD, which occurs in as many as 12% of cases.[12,15] It appears that these cases are associated with inherited arrhythmic substrates, and genetic testing of survivors of SCD might provide relevant results that explain the incident and may be valuable for family screening. Exercise-related SCD is also caused by drug use. For instance, cocaine and amphetamines can lead to myocardial infarction (MI), arrhythmias, myocarditis, and premature CAD. Chronic use of drugs can cause dilated cardiomyopathy, and performance-enhancing medications can have immediate negative effects on the cardiovascular system.[16] Athletes who use anabolic drugs may be predisposed to hypertension, dyslipidemia, ventricular hypertrophy and fibrosis, and arrhythmias because of their ability to push themselves beyond their natural limits. Previously reported higher target hemoglobin levels with erythropoietin therapy are associated with an increased risk of MI or stroke[17] [Table 3]. More than 85% of deaths among athletes over the age of 35 years are caused by atherosclerotic CAD[18] [Figure 2]. In young athletes, congenital coronary artery abnormalities are a significant cause of death, particularly when they occur in the left coronary artery, which arises from the right sinus of the Valsalva and travels between the aorta and the pulmonary artery. It is possible for athletes to develop SCD due to mitral

Table 1: Pathological assessment of sudden cardiac death

Types	Subtype	Pathology
Structural disorders	Cardiomyopathy	HCM
		Idiopathic LVH
		ARVC
		IDC
	Marfan	Aortic root dilatation/ rupture/dissection
		MVP
	Valvular disease	Bicuspid aortic AS
		Pulmonic stenosis
		Severe MR/AR
Disorders of coronary circulation	Congenital	ALCA from right sinus
		ARCA from left sinus
	Acquired	Atherosclerosis
Electrical disorders	Ion channelopathies	Long QT syndrome
		WPW syndrome
		Brugada syndrome
		Short QT syndrome
	VT	CPVT
	Ventricular fibrillation	SADS
Acquired/ environmental	Sports injury	Commotio cordis
		Physical trauma
	Heat stroke	Ventricular fibrillation
	Infection	Subacute myocarditis
	Performance-enhancing drugs	Myocardial infarction, ventricular arrhythmias
	Hypothermia	Ventricular arrhythmias

HCM: Hypertrophic cardiomyopathy, LVH: Ventricular hypertrophy, ARVC: Arrhythmogenic right ventricular cardiomyopathy, IDC: Implantable cardioverter defibrillator, MVP: Mitral valve prolapses, ALCA: Anomalous left coronary artery, ARCA: Anomalous right coronary artery, VT: Ventricular tachycardia, CPVT: Catecholaminergic polymorphic VT, SADS: Sudden Arrhythmic Death Syndrome, AR: Aortic regurgitation, MR: Mitral regurgitation, AS: Aortic stenosis, WPW: Wolff-Parkinson-White syndrome, QT: QT interval

Table 2: Cardiovascular conditions associated with sudden cardiac death

Structurally abnormal heart	Structurally normal Heart
Congenital/genetic	
HCM	Congenital long QT syndrome
ARVC	CPVT
Dilated cardiomyopathy	WPW or another accessory pathway
Another cardiomyopathy (i.e., left ventricular noncompaction)	Brugada syndrome
Congenital anomalies of coronary origin and course	Other ion channelopathies
Aortopathy (i.e., Marfan syndrome and ascending aortic aneurysm/dissection)	
Valvular heart disease (i.e., congenital aortic stenosis, mitral valve prolapse)	
Acquired	
Atherosclerotic CAD	Commotio cordis
Kawasaki's disease	Acquired long QT (i.e., drug-induced)
Myocarditis	Other substance ingestion or environmental factors (i.e., hypo- or hyperthermia)

CAD: Coronary artery disease, ARVC: Arrhythmogenic right ventricular cardiomyopathy, HCM: Hypertrophic cardiomyopathy, VT: Ventricular tachycardia, CPVT: Catecholaminergic polymorphic VT, WPW: Wolff-Parkinson-White syndrome, QT: QT interval

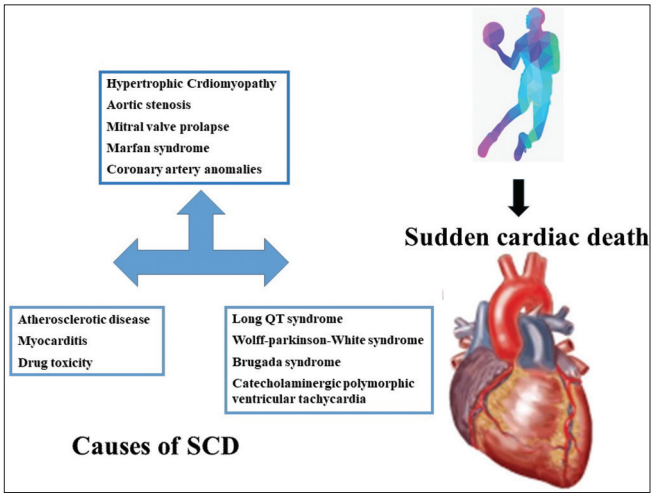

Figure 2: Sudden cardiac death causes

valve prolapse, bicuspid aortic valves, and aortopathies. There is a 0.5%–4% frequency of myocarditis in the general population; however, it may contribute to up to 22% of SCD in those under 35 years old.[19] Myocarditis produces myocardial necrosis and fibrosis, which increases the risk of SCD by predisposing to life-threatening ventricular arrhythmias, and physical activity increases this risk. It is possible that persistent scarring after the acute phase of myocarditis increases the risk of developing arrhythmias and SCD. There is evidence that more than 40% of SCD patients may have a healthy heart, according to a large autopsy investigation at an expert cardiac pathology center in the UK.[5] There is a small possibility that some patients have inherited channelopathies, such as WPW syndrome. There is growing evidence that structurally normal hearts are more prevalent than cardiomyopathy, which has led to a significant paradigm shift regarding SCD's etiology.[20] Several studies have shown that senior male athletes who have exercised vigorously for most of their lives may develop cardiovascular problems such as coronary artery calcification, atrial fibrillation, and myocardial fibrosis.[21-23] It is believed that these anomalies are probable consequences of exercise, and they were found in just a small proportion of female athletes. In spite of the fact that veteran male athletes had a higher frequency of coronary artery calcium than their sedentary counterparts, no differences were found between female athletes and controls. There has also been a report of myocardial fibrosis in experienced male athletes, but not in women. A recent study found that 17% of male triathletes exhibited late gadolinium enhancement in cardiac magnetic resonance but none of the female triathletes did.[24] The RACE Paris registry showed that SCDs caused by CAD have an

acute thrombotic occlusion, while the RACER registry of 10 million runners showed that SCDs are caused by fixed coronary stenosis without thrombosis. Therefore, there are two plausible causes for the occurrence of ventricular tachyarrhythmias and cardiac arrests during sports activities. In this condition, coronary flow cannot be increased during exercise due to tachycardia reducing diastolic duration and exhausting the coronary vasodilatory reserve beyond stenosis. A sudden discontinuance of activity can aggravate ischemia, as it reduces venous return and lowers blood pressure in a vasodilated state, eventually leading to coronary hypoperfusion. Acute ischemia is exacerbated by electrolyte imbalance, heat stroke, and an excess of catecholamines in the blood. Eventually, this leads to malignant ventricular arrhythmias, which can occur during or soon after endurance exercise.[25] The second explanation is acute plaque rupture during exercise, increased wall shear strain on the fragile plaque, along with catecholamine-induced coronary spasm and endothelial dysfunction, induces erosion of the thin fibrous cap, as well as intra-plaque hemorrhage and thrombosis.[26]

Relation between Exercise, Cardiac Disease, and Sudden Cardiac Arrest

In people with HCM, the balance between risk and benefit is unclear, with risks at extremely high levels of exercise.[27,28] Researchers recently concluded that moderate-intensity exercise is safe and beneficial for people with HCM who are asymptomatic.[29] With chronic diseases such as hypertension, a coronary disease with MI, and diabetes, regular exercise minimizes unfavorable cardiac remodeling. Heart failure, hypertension, and previous MI patients have been found to benefit from high-intensity interval training.[30] Even high-intensity exercise poses virtually no risk to an athlete without predisposing factors or underlying cardiovascular disease. Sports and exercise offer a number of health benefits, including reduced mortality and morbidity risks as well as psychological benefits for the individual [Figure 3].[31,32] In the absence of cardiac disease, long-term endurance athletes who run 15–30 h per week have an increased risk of developing lone paroxysmal atrial fibrillation. In a recent meta-analysis, athletes had a higher chance of developing lone paroxysmal atrial fibrillation than sedentary individuals. In contrast, athletes with atrial fibrillation were less likely to suffer a stroke than their age-matched peers.[33,34] The higher risk can be attributed to increased myocardial oxygen demand and adrenergic output, which can lead to an arrhythmogenic condition or ischemia.[35] The prevalence of cardiac anomalies requiring further testing in sports has been found to be between 2% and 4%, with clinically significant abnormalities occurring in about 0.3% of athletes. According to experts, many disorders that could cause SCA in athletes, such as inherited channelopathies, an abnormal origin of the coronary arteries, and premature CAD, would not be detected on a normal electrocardiogram (ECG). ECG of children and adolescents with cardiomyopathies shows that it is less sensitive than previously thought to identify

Table 3: Drugs and cardiovascular side effects

Drugs	Cardiovascular side effects
Anabolic agents	Dyslipidaemia
	Hypertension
	Pathological cardiac hypertrophy/cardiac fibrosis
	Arrhythmias
β2-adrenergic receptor antagonists (Clenbuterol)	Arrhythmias in animals
Selective estrogen receptor modulators (Tamoxifen)	Venous thrombosis
	Pulmonary embolism
Oxygen dissociation curve modulators	Cardiomyopathy
Hormone/metabolic modulators	Hypertension, hyper-or hypoglycaemia, dyslipidaemia
Oxygen-carrying modulators	Thromboembolic events
	Myocardial infarction
	Stroke
	Hypertension

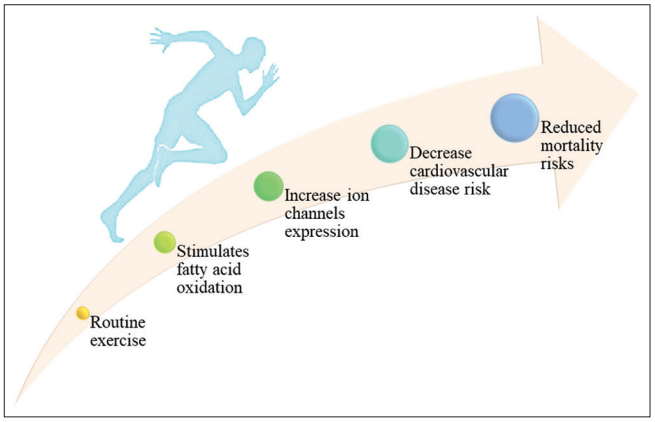

Figure 3: Cardiovascular benefits of regular exercise

cardiomyopathies.[36] Typical abnormalities are found only in 25%–75% of adolescents with ARVC and in 50%–75% of asymptomatic young patients with HCM. A recent longitudinal study of top soccer players discovered that 6 of every 8 SCDs (6/100,000/year) occurred in athletes with a negative history, physical examination, and ECG.[37]

Hearts of Athletes

The cardiovascular systems of athletes and the general population differ in terms of their functional and structural characteristics because of the type of exercise they engage in. Swimming and long-distance running belong to the endurance training category, while wrestling, weightlifting, and sports belong to the strength training category. Cardiovascular fitness affects the heart in a unique way for each athlete. As a result of exercise, around half of all athletes will show cardiac remodeling. Among the changes are increased cavity sizes on the ventricles and left atrium.[38] In endurance athletes, the left ventricular (LV) chamber may expand significantly, resulting in a moderate increase in absolute LV wall thickness. Athletes with high levels of training are also more likely to develop

left atrial remodeling. During the acute phase of endurance exercise, oxygen consumption, cardiac output, stroke volume, and systolic blood pressure increase, while peripheral vascular resistance decreases. As a result of volume overload, endurance exercise leads to the dilation of the left ventricle, whereas resistance training leads to hypertrophy of the left ventricle. The risk of acute ischemia, MI, and SCD is higher during and up to 1 h after exercise when compared with sedentary hours. Compared to resting hours, exercise increases the risk of SCD by 8–16 times and MI by 6–10 times.[39] As a result of regular and habitual physical activity, the greater relative risk associated with SCD, and acute MI is reduced.

Screening Requirement

In seemingly fit athletes, SCD usually occurs without warning symptoms or a history of heart disease. Sport-related sudden mortality can be reduced through preparticipation screening for silent cardiac conditions. The European Society of Cardiology (ESC), the American Heart Association (AHA), the International Olympic Committee (IOC), and the Federation Internationale de Football Association have endorsed preparticipation screening (PPS) cardiovascular for young athletes. It involves systematically evaluating athletes before competition to detect existing cardiac diseases that may put an athlete at risk for SCA, as well as other critical health issues. A screening program aims to detect athletes who are at high risk for sudden death and to restrict their participation in competitive or high-intensity activities to significantly reduce their risk. An examination and history of 14 points are part of the guidelines developed by the AHA for the PPS of competitive athletes.[40] During a 25-year Italian preparticipation screening program, 0.2% of athletes had a disease that led to SCD based on their medical history, physical examination, 12-lead ECG, and restricted exercise testing. As a result of the screening process, the SCD rate dropped by 90% from 3.6/100,000 person-years to 0.4/100,000 person-years, with a false-positive rate of 7%.[4]

Preventive Measures and the Best Approach to Screen Athletes in a Primary Care Setting

The assessment is primarily intended to improve athletes' health and safety. While preparticipation evaluations cannot prevent morbidity and death in sports, they can aid in the discovery of serious issues and the development of injury prevention strategies.[20,41] All ages can benefit from sports and athletics, as it improves fitness, self-esteem, and coordination, and give athletes the opportunity for creative cooperation and competition. Any sport or level of competition will be open to athletes if their clearance status has been determined following appropriate tests, treatment, or rehabilitation. According to most guidelines, clinical history, physical examination, and ECG are the least expensive methods of preparticipation screening. In 2014, the AHA developed a 14-item cardiovascular screening checklist for congenital and hereditary heart disease in young athletes.[40] A pre-participation evaluation (PPE) aims to ensure the athlete's health and safety during training and competition. Physicians will use this information to make decisions about an athlete's physical activity. Any positive reaction on any of the 14 items may be deemed sufficient by the examiner to begin a detailed cardiovascular investigation that may include an ECG, echocardiography, or stress test. The Canadian Cardiovascular Society and Canadian Heart Rhythm Society recently published a joint position statement on cardiovascular screening of competitive athletes recommending measuring and comparing blood pressure in both arms, auscultating for heart murmurs, and examining for features of Marfan syndrome.[42] Even though first affirmative responses on the PPE form are intended to be examined by a physician before an additional examination, Fudge *et al*.[43] discovered that 46% of the first affirmative responses still needed further investigation after having been reviewed by the physician. ECG screening improves sensitivity by identifying athletes with hereditary ion channel disease including accessory pathways, as well as raising suspicions of athletes with cardiomyopathy. An ECG is considered to be more sensitive than a history and physical exam in detecting underlying cardiovascular abnormalities that may place athletes at risk for SCD.[44] In a prospective study, resting ECGs have not been added to screening protocols. As of yet, there is no mandate regarding ECG screening for collegiate athletes in the US, although the ESC and IOC recommends its use, whereas the AHA recommends only a history and physical examination, primarily due to the cost and infrastructure concerns.[3] Cardiopulmonary resuscitation (CPR) and rapid defibrillation double the survival rate of sports-related SCD.[7,8,45] The first responders should be trained in recognizing symptoms, activating the emergency medical system, performing CPR, and using an automated external defibrillator (AED). Before 1995, one SCD per 55,000 finishers occurred in US Marathons, but after 1995, it decreased to one per 220,000 finishers due to emergency medical response services.[46] An athlete experiencing cardiac arrest can be efficiently revived by performing rapid CPR and using an AED in time. In a study by Weisfeldt *et al*.,[47] rapid use of an AED is associated with a higher chance of survival (odds ratio: 1.75; 95% confidence interval: 1.23–2.50; $P = 0.002$), with rates of survival to hospital discharge highest in recreational areas (49%). AED availability during a sporting event, education of trainers and bystanders, and systematic emergency response methods all contribute to high survival rates in settings with systematic emergency response methods and timely deployment of AEDs[7,48-50] [Tables 4 and 5].

Conclusion

Sudden cardiac mortality among sportsmen is relatively rare. Globally, cardiomyopathy, hypertrophic, and ARVC are the most common causes. SCD in sports might be avoided and reduced if we understand the origins and processes of such incidents. The PPS of athletes should include a history, physical examination, and ECG to identify those at high risk for SCD.

Table 4: Preparticipation screening in competitive athletes

Screening	Details
History	Unexplained or exertional syncope, exertional chest pain, dyspnoea, palpitation
Family history	Family history of MI, SCD, and coronary risk factors
	Known h/o hypertrophic or dilated cardiomyopathy, long QT syndrome, CPVT, ARVC, Brugada, Marfan Syndrome
Examination	Blood pressure
	Heart murmur/cardiomegaly
	Marfanoid features
	Xanthelasma
ECG	Ischemia/infarction
	Chamber enlargement
	Long QT/WPW/ARVC/Brugada

ARVC: Arrhythmogenic right ventricular cardiomyopathy, VT: Ventricular tachycardia, CPVT: Catecholaminergic polymorphic VT, SCD: Sudden cardiac death, WPW: Wolff-Parkinson-White, ECG: Electrocardiogram, MI: Myocardial infarction, QT: QT interval

Table 5: Advantages and disadvantages of preparticipation sudden cardiac death screening

Advantages	Disadvantages
At-risk people can be identified and reduced risk of death	Costs
Ensure that the risk is extremely low if pathological report is normal	False-negative findings
Understand sudden cardiac death risk and sports-related cardiac structures and functions	Despite the lack of evidence supporting ECG's use in screening, it remains controversial

ECG: Electrocardiogram

As well as the role of paramedics/relevant stakeholders in aiding this process, appropriate PPS is essential to prevent SCD. There is a need for more research to develop solutions that can reduce the burden of SCD on this population.

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Conflicts of interest

There are no conflicts of interest.

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