REVIEW

CURRENT OPINION

Sudden cardiac death in young athletes: what is the role of screening?

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Purpose of review
To review the recent literature and recommendations for cardiovascular screening in young athletes.

Recent findings
The primary purpose of the preparticipation examination is to detect the cardiovascular disorders known to cause sudden cardiac arrest in the athlete. Studies demonstrate that the traditional history and physical-based examination has a limited sensitivity, does not detect the majority of athletes with at-risk conditions, and may provide false reassurance for athletes with disorders that remain undetected. Electrocardiogram (ECG) screening increases the sensitivity of the examination to detect disease, and cost modeling suggests protocols inclusive of ECG are the only screening strategies to be cost-effective. Proper ECG interpretation that distinguishes physiologic cardiac adaptations in athletes from findings suggestive of underlying cardiac pathology is essential to avoid high false-positive rates.

Summary
The goal of cardiovascular screening is to maximize athlete safety. This includes the detection of underlying cardiac disease associated with sudden cardiac death and reduction of risk through both medical management and activity modification. Greater physician education and research are needed to improve the preparticipation examination in athletes.

Keywords
athlete, prevention, sport, sudden cardiac arrest

INTRODUCTION

Sports-related sudden cardiac death (SCD) is widely reported in the media and breeds intense concern regarding the accountability of screening programs. Exercise is recommended because of numerous health benefits such as primary and secondary prevention of cardiovascular disease [1]. However, the physiologic demands of vigorous activity in competitive athletes with occult cardiac conditions carry an inherent risk of SCD that is 2.8–4.5-fold greater than in age-matched sedentary individuals or recreational athletes [2,3]. Proper screening is necessary for the early detection of potentially lethal cardiovascular disease with the goal of SCD risk reduction through subsequent medical management.

CAUSES OF SUDDEN CARDIAC DEATH

SCD is the leading cause of death during exercise. A recent study in National Collegiate Athletic Association (NCAA) athletes found that nearly 75% of deaths during exertion were cardiac related [4]. A wide spectrum of structural and electrical cardiovascular abnormalities places athletes at risk for SCD (Table 1). Studies using noninvasive screening tools such as electrocardiogram (ECG) and echocardiogram consistently show that 0.2–0.7% of competitive athletes harbor an underlying cardiovascular disorder associated with SCD [5–11].

Hypertrophic cardiomyopathy (HCM, 36%) and coronary artery anomalies (17%) have been cited as the leading identifiable causes of SCD in athletes from the United States [12]. In the northeastern region of Italy, arrhythmogenic right ventricular cardiomyopathy (ARVC) is reported as the leading

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KEY POINTS

- Sudden cardiac death (SCD) is the leading cause of death in athletes during exertion and the result of intrinsic cardiac conditions largely detectable through screening.
- The goal of cardiovascular screening in athletes is early disease detection and risk reduction through medical management and activity modifications.
- Customary cardiovascular preparticipation screening involving a history and physical examination alone has a poor sensitivity to detect conditions associated with SCD.
- ECG screening greatly increases the sensitivity of cardiovascular screening in athletes, but must be performed using proper ECG interpretation criteria.
- Physician training and education aimed at improving ECG interpretation and secondary evaluations for abnormal findings should advance the cardiovascular care of athletes.

cause (22%) of SCD [13]. Recent studies suggest that primary electrical diseases may play a larger role in SCD than previously recognized. A prospective evaluation found that autopsy-negative sudden unexplained death (SUD) was responsible for 41% of sudden deaths in military personnel less than age 35 [14▪▪]. Autopsy-negative SUD may be due to inherited arrhythmia syndromes and ion channel disorders such as long QT syndrome (LQTS), short QT syndrome, Brugada syndrome, or familial catecholaminergic polymorphic ventricular tachycardia [15]. In studies performing post-mortem genetic testing (molecular autopsy) for autopsy-negative cases, over one-third of cases were found to have a pathogenic cardiac ion-channel mutation [16,17].

INCIDENCE OF SUDDEN CARDIAC DEATH

Understanding the true frequency of SCD is challenging and a source of controversy. Defining the incidence of SCD requires accurate case identification and a defined study population [11]. Without these elements, study calculations may be inaccurate. Initial studies in the USA relied heavily on media reports for case identification and likely underestimated the magnitude of the problem with estimates generally near 0.5/100 000 athlete deaths per year [12,18,19]. A recent study by Steinvil *et al.* [20] also relied solely on retrospectively searching two newspapers over a 24-year period. The passive nature of this surveillance method, coupled with the lack of a defined number for the sample athletic population, raises concerns about the reliability of the incidence calculations and overall study conclusions [20,21]. The limitations of using media reports as the chief method for case identification is highlighted by a study using an internal reporting structure for the NCAA, demonstrating that intensive search of public media reports missed nearly half of SCD cases despite the high profile nature of collegiate athletics [4].

Studies using additional methods for case identification have found a higher incidence of SCD in athletes and active populations. In a 5-year retrospective analysis of SCD in the NCAA with a defined study population, the annual incidence of SCD in all athletes was 2.28/100 000 athletes per year, with higher rates in men 3.0/100 000 and black

Table 1. Causes of sudden cardiac death in athletes

Structural/functional	Electrical	Acquired
Myocardium	Long QT syndrome (LQTS)	Myocarditis
Hypertrophic cardiomyopathy (HCM)	Short QT syndrome	Commotio cordis
Arrhythmogenic right ventricular cardiomyopathy (ARVC)	Catecholaminergic polymorphic ventricular tachycardia (CPVT)	Drugs and stimulants
Dilated cardiomyopathy (DCM)	Brugada syndrome	
Left ventricular noncompaction	Wolff–Parkinson–White (WPW) syndrome	
Coronary arteries		
Coronary artery anomalies		
Coronary artery atherosclerotic disease		
Aorta/valvular		
Aortic rupture/Marfan syndrome		
Aortic stenosis		
Bicuspid aortic valve with aortopathy		
Mitral valve prolapse (MVP)		

athletes (5.89/100 000) [4]. Eckart *et al.* [14■■] used a mandatory reporting system, with autopsy, from the Department of Defense and reported an incidence of SCD in US military personnel aged 18–35 of 4.0/100 000 persons per year. These statistics mirror studies performed in Italy citing a SCD incidence of 3.57/100 000 in competitive athletes (age 12–35) prior to the implementation of an ECG-inclusive athletic screening protocol [5].

CARDIOVASCULAR SCREENING: THERE IS NO DEBATE

Despite uncertainty over the exact risk of SCD in athletes, there is universal agreement from the American Heart Association (AHA), European Society of Cardiology (ESC), International Olympic Committee (IOC), and Federation Internationale de Futbol Association (FIFA) that cardiovascular screening in athletes should be undertaken [22–25]. The sudden death of a young athlete is a catastrophic event resulting in the loss of a substantial number of quality life-years [26]. Indeed, a working group from the National Heart, Lung, and Blood Institute (NHLBI) recently stated that SCD in young individuals was a critical public health concern and called for additional research and resources to advance SCD prevention [27].

Physical activity appears to transiently increase the likelihood of sudden death in those with underlying cardiovascular abnormalities. A 5-year prospective observational study by Marijon *et al.* [3] found that the risk of sudden death was 4.5 times higher in competitive athletes compared with non-competitive sports participants. Vigorous exercise can abruptly lead to the onset of electrical instability and cardiac arrest in individuals with occult cardiac disease [2,3,28]. In fact, approximately 80% of sudden death in athletes with a pathologic heart condition occurs during exercise, rather than at rest or during daily activity [29,30].

Preparticipation cardiac screening aims to identify athletes with occult cardiac disease at risk for SCD during exercise. According to the American College of Cardiology, the 'ultimate objective of the preparticipation screening of athletes is the detection of ''silent'' cardiovascular abnormalities that can lead to SCD' [31]. The major dilemma is not whether to screen, but, rather, what is the most practical, evidence-based protocol for screening. A fundamental necessity for an evidence-based strategy is that sufficiently robust data must guide clinical practice. For screening programs, this includes a thorough understanding of risk and benefits, cost-effectiveness, and feasibility. In addition, the screening protocol must detect disease early and when an intervention can be implemented to reduce potential morbidity or mortality.

CUSTOMARY SCREENING RECOMMENDATIONS IN THE USA

The current protocol endorsed by the AHA includes a 12-point history and physical exam. This includes five elements related to personal history, three elements of family history, and four elements for physical exam (see list below) [24]. However, studies show that a history and physical examination has limited effectiveness in detecting occult cardiac disease predisposing athletes to sudden death. In a study of 115 cases of SCD, only one case (0.9%) was identified using history and physical examination [29]. Similarly, low sensitivity can be found in other US and international studies in which a history and physical examination appropriately detected an underlying abnormality in 0–33% of cases identified (Table 2) [6,8–10,32]. Customary cardiovascular screening protocol recommended by the AHA is as follows:

(1) personal history:
   (a) exertional chest pain/discomfort;
   (b) unexplained syncope/near syncope;
   (c) excessive exertional and unexplained dyspnea/fatigue, associated with exercise;
   (d) prior recognition of a heart murmur;
   (e) elevated systemic blood pressure;
(2) family history:
   (a) premature death (sudden and unexpected) before age 50 years old because of heart disease;
   (b) disability from heart disease in a close relative less than 50 years of age;
   (c) specific knowledge or certain conditions in family members: HCM or dilated cardiomyopathy, LQTS or other ion channelopathies, Marfan's syndrome, or clinically important arrhythmia;
(3) physical examination:
   (a) heart murmur;
   (b) femoral pulses to exclude aortic coarctation;
   (c) physical stigmata of Marfan's syndrome;
   (d) brachial artery blood pressure (sitting).

The underlying limitation of screening by history and physical examination alone is that the majority of competitive athletes who have pathologic cardiac disease are asymptomatic. Reports have shown that 60–80% of victims do not have warning signs or symptoms, and cardiac arrest is the first

Table 2. Comparison of history and physical examination versus ECG in the screening of young competitive athletes

		Positive results requiring further testing			Sensitivity to detect potentially lethal cardiovascular disease		
Study	Population	History and physical	ECG	Total	No. of cases	History and physical	ECG
Wilson [8]	2720 athletes and children aged 10–17 (UK)	2.5%	1.5%	4%	9	0%	100%
Bessem [9]	428 athletes aged 12–35 (Netherlands)	8%	8%	13%	3	33%	67%
Hevia [10]	1220 amateur athletes (Spain)	1.2%	6.1%	7.4%	2	0%	100%
Baggish [6]	510 college athletes (USA)	6%	16%	20%	3	33%	67%
Vetter [33]	400 children and adolescents (USA)	23.5%	7.8%	–	10	20%	70%

manifestation of their disease [29,30,34–36]. Thus, any screening protocol rooted in history and physical examination alone will result in a high number of false-negatives and false reassurance to some athletes with potentially lethal cardiovascular disease.

Importantly, there are a small percentage of athletes with cardiovascular warning symptoms, such as syncope, unexplained seizure activity, exertional chest pain, or a family history of early (<50 years old) SCD, that should not be missed by the screening physician and are readily detected by a careful evaluation [37■].

ENHANCED DISEASE DETECTION WITH ELECTROCARDIOGRAM

ECG improves the ability to detect many of the diseases associated with SCD. The ESC, IOC, FIFA, and many professional US sporting organizations (National Football League, Major League Baseball, National Basketball Association, Major League Soccer, and National Hockey League) endorse cardiovascular screening by ECG [22–25].

The enhanced sensitivity of ECG is intuitive for ion channelopathies and primary electrical diseases, which are routinely diagnosed by an ECG. In addition, more than 95% of SCD cases caused by HCM demonstrate abnormalities on resting ECG [38]. A recent analysis model suggested that, with the optimal use of the ECG, the negative predictive value approaches 100% for the detection of HCM, LQTS, and Wolff–Parkinson–White (WPW) syndrome [39]. Studies also report that abnormal ECG patterns may be present prior to the morphologic changes of cardiomyopathy found on advanced imaging [40]. Thus, athletes with distinctly abnormal ECGs should undergo regular clinical surveillance with repeat cardiac imaging.

FALSE-POSITIVE RESULTS

Early concerns surrounding ECG screening stem from studies showing false-positive rates between 15 and 40% [40,41]. However, false-positive rates are contingent upon the criteria used to interpret the ECG. Modern ECG interpretation criteria account for physiologic adaptations to exercise, such as increased vagal tone or left ventricular chamber enlargement. Guidelines from both the European Society of Cardiology (2010) and a US-led consensus statement (2011) provide updated ECG interpretation criteria for physicians performing ECG screening in athletes [42,43■■]. These statements detail the difference between normal physiologic changes in response to exercise and findings suggestive of an underlying pathological disease. Using modern criteria guidelines, false-positive rates have been markedly reduced. Marek *et al.* [44■] performed a large ECG screening study in over 32 500 adolescents, with only 2.5% of individuals having an abnormal ECG. In a study of 2720 competitive athletes and physically active school children in the United Kingdom, Wilson *et al.* [8] reported a false-positive rate of less than 2% by ECG alone. In college athletes, application of the 2010 ESC criteria reduced the rate of false-positive evaluations by 41% [45].

COST CONSIDERATIONS

Issues surrounding total cost and cost-effectiveness are an important consideration in the development of any screening strategy. Cost-effectiveness

Table 3. Cost-effectiveness models for cardiovascular screening

Study	Type of study	Assumptions		Cost	Comments
		False-positive rate	Prevalence of disease		
Wheeler (2010) [47]	Decision-analysis model	FP rate of H and P + ECG 5%	Overall risk of SCD 2.4/100 000 athletes per year	ICE of adding ECG to H and P is $42 000/LY saved	ECG screening alone is cost-effective. The addition of an ECG to baseline practices saved 2.1 life-years per 1000 athletes screened and focused H and P + ECG saved 2.6 life-years per 1000 athletes screened.
Leslie (2012) [46]	Simulation model screening for HCM, WPW, and LQTS at age 14	FP rate of 15%	2/1000	$91 000/LY	High false-positive rate and relatively low prevalence of disease compared with other studies. Alternative assumptions for HCM prevalence and mortality for WPW would reduce CE to <$50 000 per LY gained.
Schoenbaum (2012) [48■]	Decision-analysis model	FP rate of ECG 5%, H and P + ECG 9%	1/1000	ICE of ECG alone $37 700/QALY, H and P + ECG $68 800/QALY	Low prevalence of disease used in study. If 1.45/1000 were used, H and P + ECG would have an ICE of <$50 000 per LY gained.

CE, cost-effectiveness; ECG, electrocardiogram; FP, false-positive; H and P, history and physical; HCM, hypertrophic cardiomyopathy; ICE, incremental cost-effectiveness; LQTS, long QT syndrome; LY, life-year; QALY, quality-adjusted life-year; SCD, sudden cardiac death; WPW, Wolff–Parkinson–White.

estimates are driven by the sensitivity and specificity of the screening tool to detect disease and the prevalence of the disease itself. Typically, medical interventions are cost-effective when incremental cost-effectiveness (ICE) ratios are below $50 000 per quality-adjusted life-year gained.

Recent modeling studies have demonstrated that screening by history and physical examination alone is the least cost-effective strategy, and that adding an ECG to history and physical examination or screening by ECG alone satisfies or approaches cost-effectiveness standards (Table 3) [46,47,48▪]. Wheeler *et al.* estimated that the addition of ECG resulted in 2.1 life-years saved per 1000 athletes screened, with an incremental cost-effectiveness ratio of $42 000 per life-year saved for ECG screening compared with history and physical examination alone. The cost-effectiveness ratio for history and physical versus no screening was $199 000 per life-year saved.

In another comprehensive cost-effectiveness analysis, Schoenbaum *et al.* compared history and physical, history and physical plus ECG, and ECG alone. The ICE for a history and physical plus ECG was $68 800 per quality-adjusted life-year (QALY), while the ICE for an ECG alone was $37 700 per QALY. The authors chose a conservative estimate of 0.1% for the prevalence of underlying cardiovascular disease in athletes, although the reported prevalence of disorders associated with SCD in athletes is 0.2–0.7% [5–11]. The addition of ECG to history and physical would have met the ICE threshold of $50 000 if the analysis had used any prevalence of disease greater than 0.145%.

LIMITATIONS OF ELECTROCARDIOGRAM SCREENING

Although ECG improves disease detection, it does not identify every cardiac condition predisposing young athletes to SCD. Specifically, anomalous coronary arteries, premature atherosclerotic coronary artery disease, and aortic root dilatation will go largely undetected. Thus, any primary prevention strategy must be combined with secondary prevention, emergency response planning, and prompt availability of automated external defibrillators (AEDs) to effectively respond to a cardiac emergency in the athletic setting [49–51].

THE NEED FOR TRAINING AND INFRASTRUCTURE

There are practical concerns for the widespread implementation of ECG screening in the United States and many other countries. The most pressing issue is the absence of a physician infrastructure to appropriately interpret ECGs and guide secondary evaluations for abnormal findings [52]. Pediatric cardiologists were assessed for their accuracy of ECG interpretation in preparticipation screening by reviewing a series of ECGs and determining sports eligibility [53]. In this study, they appropriately permitted or restricted sports participation in 78% of cases [53]. This suggests that training and education are critically needed for physicians who interpret ECGs in athletes. An example of the effect of education was highlighted in a recent study of 60 primary care physicians and cardiologists who were asked to interpret ECGs from healthy athletes randomized with ECGs representing cardiac conditions associated with SCD [54▪▪]. Physicians interpreted the ECGs both before and after the use of a simple criteria tool to guide ECG interpretation [54▪▪]. At baseline, primary care physicians appropriately categorized 74% of ECGs as normal or abnormal, and cardiologists 85% [54▪▪]. With the ECG interpretation tool, both primary care and cardiology physicians significantly improved their ability to accurately classify the ECGs (91 and 96%, respectively), even in resident physicians with little to no experience [54▪▪].

As this study demonstrates, more formal training programs will undoubtedly lead to improved interpretation competency. To enhance physician interpretation of athlete ECGs, sports cardiologists and sports medicine physicians from organizations including the American Medical Society for Sports Medicine (AMSSM), European Society of Cardiology (ESC) Sports Cardiology Section, the Pediatric and Congenital Electrophysiology Society (PACES), and FIFA met to develop a comprehensive online training module for ECG interpretation in athletes, which will be freely available worldwide (expected launch in January 2013). Efforts have also focused on designing formal curricula among European sports cardiology programs [55].

More research and education are needed to better understand the management of athletes with identified cardiac pathology. A recent 10-year study by Johnson *et al.* [56▪] of patients with LQTS demonstrates the benefits of early detection and active management to mitigate the risk of SCD events. A total of 353 patients with LQTS, including 130 athletes who chose to continue competitive sports, received extensive counseling and tailored therapy including beta-blockade, left cardiac sympathetic denervation, and an implantable cardioverter defibrillator (ICD), and were followed for a mean of 5.1 years. No athlete died and the overall rate of an ICD terminating ventricular fibrillation was 0.003 (or 1 event in 331 athlete years) [56▪].

Although the findings in this study are not transferable to other diseases, it highlights the need for evidence-based management and eligibility decisions.

CONCLUSION

The goal of cardiovascular screening is to identify athletes with intrinsic cardiac disorders at risk for SCD and to maximize their health and safety on the playing field. Cardiovascular screening is universally recommended, but agreement on a single screening protocol remains elusive. The customary US screening program is rooted in the symptom identification for disease processes, in which the majority of individuals are asymptomatic. Cardiovascular screening inclusive of ECG is more likely to be cost-effective and to meet the objectives of the preparticipation examination. Available evidence suggests that a screening protocol inclusive of ECG, performed with proper ECG interpretation and adequate cardiology resources for the secondary evaluation and management of abnormal findings, merits the highest consideration for the prevention of SCD in athletes.

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None.

Conflicts of interest

There are no conflicts of interest.

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