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REVIEW

Controversies in cardiovascular medicine

Risk of sports: do we need a pre-participation screening for competitive and leisure athletes?

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Sudden cardiac arrest is most often the first clinical manifestation of an underlying cardiovascular disease and usually occurs in previously asymptomatic athletes. The risk benefit ratio of physical exercise differs between young competitive athletes and middle-age/senior individuals engaged in leisure-time sports activity. Competitive sports are associated with an increase in the risk of sudden cardiovascular death (SCD) in susceptible adolescents and young adults with underlying cardiovascular disorders. In middle-age/older individuals, physical activity can be regarded as a 'two-edged sword': vigorous exertion increases the incidence of acute coronary events in those who did not exercise regularly, whereas habitual physical activity reduces the overall risk of myocardial infarction and SCD. Although cardiovascular pre-participation evaluation offers the potential to identify athletes with life-threatening cardiovascular abnormalities before onset of symptoms and may reduce their risk of SCD, there is a significant debate among cardiologists about efficacy, impact of false-positive results and cost-effectiveness of routine screening. This review presents an appraisal of the available data and criticisms concerning screening programmes aimed to prevent SCD of either young competitive athletes or older individuals engaged in leisure-time sports activity.

Keywords cardiomyopathy • coronary artery disease • congenital coronary anomalies • electrocardiogram • exercise testing • screening • sudden cardiac death

Introduction

Regular physical exercise is recommended by the medical community because it is associated with a decrease in all cause-mortality, particularly from cardiovascular causes.[1] Several epidemiological and clinical studies have provided solid scientific evidence that habitual aerobic physical activity reduces the risk of acute myocardial infarction and sudden cardiac death (SCD).[2] On the other hand, vigorous exertion may acutely and transiently increase the risk of acute coronary events and sudden cardiac arrest in susceptible individuals.[3–5] For centuries, it was a mystery why SCD should occur in athletes, who had previously achieved extraordinary exercise performance without complaining of any symptoms. It is now clear that the most common mechanism of SCD during sports activity is an abrupt ventricular tachyarrhythmia as a consequence of a wide spectrum of cardiovascular diseases.[3–10] The culprit disease is often clinically silent and unlikely to be suspected or diagnosed on the basis of spontaneous symptoms of the athlete. Systematic pre-participation screening of all subjects embarking in sports activity has the potential to identify those athletes at risk and to reduce mortality.[11,12] There is, however, a significant debate among cardiologists in Europe and the USA about the efficacy, the impact of false-positive results, and cost-effectiveness of routine pre-participation cardiovascular evaluation of athletes.[13,14]

This article presents an appraisal of the available data and criticisms concerning pre-participation screening programmes with the target of reducing the cardiovascular risk of either competitive athletes or individuals engaged in leisure-time sports activity. For the purpose of the article, *leisure athletes* are defined in opposition to

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competitive athletes. According to Maron *et al.*,[15] a *competitive athlete* is a young (usually ≤35 years) subject who participates in an organized team or individual sport that requires systematic training and regular competition against others and that places a high premium on athletic excellence and achievement. Conversely, *leisure athletes* are individuals, most frequently middle-aged/senior (usually >35 years), participating in a variety of informal recreational sports, within a range of exercise levels from modest to vigorous, on either a regular or an inconsistent basis, which do not require systematic training or the pursuit of excellence. Because leisure-time athletes may be involved in physical activity—either for intensity or duration—not unlike competitive athletes, this classification may be useless in individuals with cardiovascular disorders, in whom risk assessment and sports eligibility mainly depends on the athletic performance. However, the distinction between *young competitive* vs. *middle-aged/senior leisure* athletes herein appears appropriate to address the available data on screening efficacy and cost-effectiveness, which mostly differ in relation to age-related heart diseases.

Table 1 Incidence of sudden cardiac death/arrest in young people and athletes according to different reporting systems

Study population	Ref.	Study design and reporting system	Incidence (person-years)
US Military (age 18–35)	Eckart *et al.*[21]	Retrospective, mandatory	1:9000
Italian Athletes (age 12–35)	Corrado *et al.*[10]	Prospective, mandatory	1:25,000
US Adolescents (age 12–19)	Atkins *et al.*[20]	Prospective, EMS	1:27,000
US Children (age 10–14)	Chugh *et al.*[22]	Prospective, EMS/ Hospitals	1:58,000
US Athletes (age 12–35)	Maron *et al.*[19]	Retrospective, public media reports	1:160,000

EMS, emergency medical service.

Risk of sudden death in the athlete

The risk of SCD varies in the different athletes series reported in the literature. It generally increases with age and is greater in men.[8–10] In apparently healthy adults (>35 years), joggers, or marathon racers, the estimated rate of SCD ranges from 1:15,000 to 1:50,000.[3,4,10,16] In comparison, a significantly lower incidence of fatal events have been reported in young (≤35 years) competitive athletes (YCAs). A prospective study in Italy showed an annual incidence of SCD of ∼3 per 100,000 YCAs,[9] whereas the prevalence of fatalities among US high-school and college athletes has been estimated to be <1 in 100,000 participants per year.[17–19] Compared with US high school and college participants, the Italian athletic population includes older athletes (age range 12–35 vs. 12–24 years) and a significantly higher proportion of men (85 vs. 65%). This partly explains why the mortality rates found in the Italian investigations are significantly higher than those reported in the USA. In addition, while the Italian data were systematically gathered from a well-defined geographic area (the Veneto region of Italy) according to a prospective study design, the US SCD rates were mostly based on retrospective analysis of data from public media reports and insurance claims, which unavoidably led to an incorrectly low number of events and underestimation of mortality. The accuracy of the determination of incidence rates of SCD among US athletes is further questionable, because denominator data did not reflect the real number of active athletes in each year, but the total participation figures divided by an estimate of the average number of sports, in which each high school and college athlete participated.[17–19] Other studies with more rigorous data collection and denominator estimates reported an incidence of either SCD or sudden cardiac arrest of young athletes in the USA quite similar to the incidences found in the Veneto region of Italy in the pre-screening period (*Table 1*).[12,20–22]

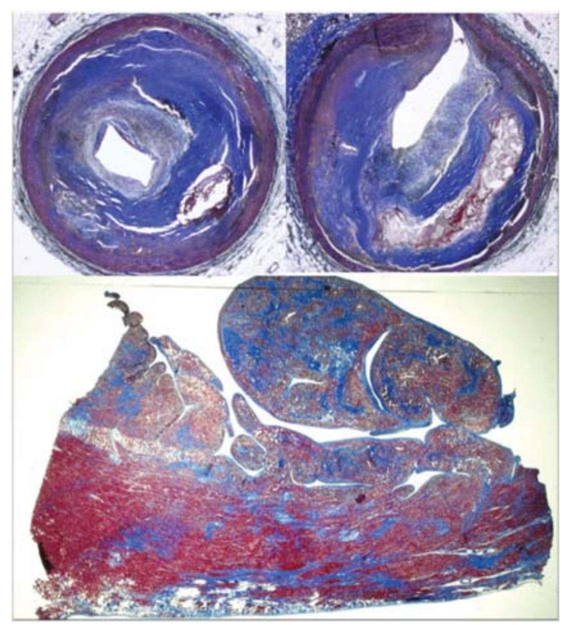

Figure 1 Sudden death of a middle-aged athlete. Obstructive atherosclerotic coronary artery disease of both left (anterior descending branch) and right coronary arteries (*A* and *B*). Histology of the myocardium shows replacement type fibrosis due to previous myocardial infarction (*C*). Heidenhain trichrome.

Atherosclerotic coronary artery disease accounts for the vast majority of fatalities in adults (>35 years) (*Figure 1*), while the most common causes of SCD in younger athletes are genetic or congenital cardiovascular abnormalities, including cardiomyopathies and coronary artery anomalies (*Figure 2*). Hypertrophic cardiomyopathy (HCM) has been reported to account for more than one-third of fatal cases in the USA,[8,17,19] and arrhythmogenic right ventricular cardiomyopathy (ARVC) for approximately one-fourth in the Veneto Region of Italy.[6,7,9,11,12] Two to five per cent of young people and athletes who die suddenly have no evidence of structural heart disease and the cause of their cardiac arrest in all likelihood is related to a

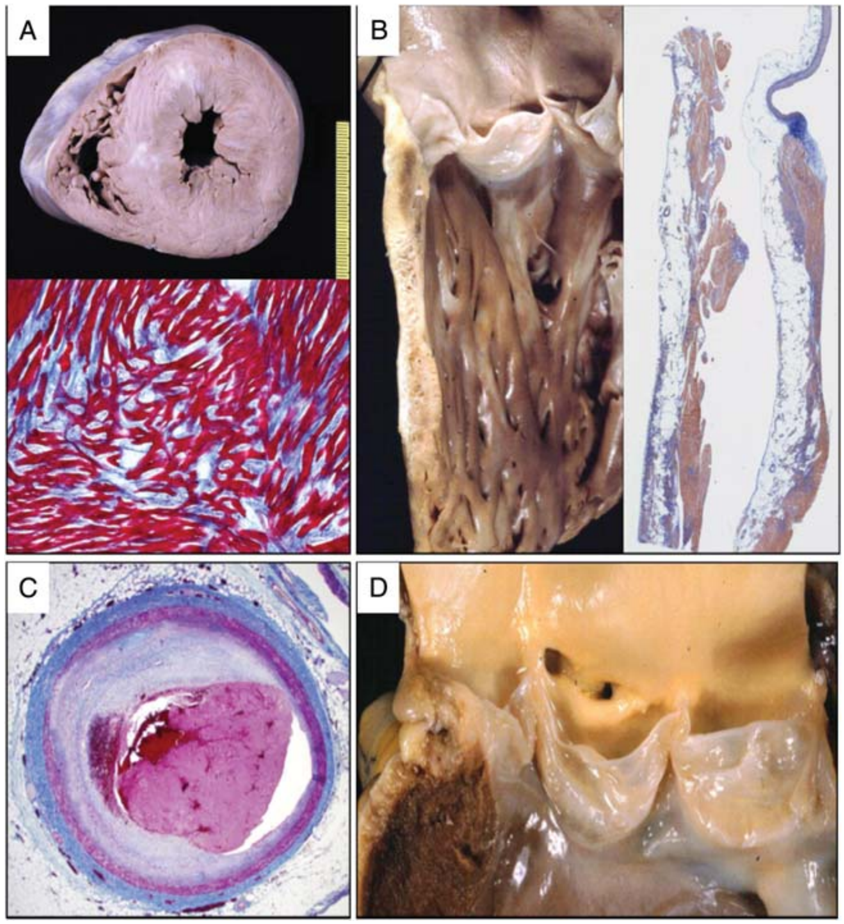

Figure 2 Leading causes of sudden cardiovascular death in young competitive athletes. (*A*) Hypertrophic cardiomyopathy: short-axis cut of the heart specimen showing asymmetric septal hypertrophy with multiple septal scars (top); histology of the interventricular septum revealing typical myocardial disarray with interstitial fibrosis (bottom) (Heidenhain trichrome); (*B*) Arrhythmogenic right ventricular cardiomyopathy: section of the heart specimen along the right ventricular infundibulum (left); panoramic histological view of the right infundibular free wall showing wall thinning with fibro-fatty replacement (right) (Heidenhain trichrome); (*C*) Atherosclerotic coronary artery disease: histology of the proximal tract of the left anterior descending coronary artery showing a non-obstructive fibrous plaque complicated by luminal thrombosis due to endothelial erosion (Heidenhain trichrome); (*D*) Congenital coronary anomaly: gross view of the aortic root showing both coronary ostia located in the right coronary sinus, with left coronary artery arising from the right aortic sinus of Valsalva and running between the aorta and the pulmonary trunk.

primary electrical heart disease such as inherited cardiac ion channel defects (channelopathies), including long and short QT syndromes, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia.[23] Sudden death may also be caused by a non-arrhythmic mechanism—e.g., spontaneous aortic rupture complicating Marfan's syndrome or bicuspid aortic valve as well was by diseases not related to the heart—e.g., bronchial asthma or rupture of a cerebral aneurysm.[2] Blunt, non-penetrating, and often innocently appearing blows to the precordium may trigger ventricular fibrillation without structural injury to ribs, sternum, or heart itself (commotio cordis).[8]

The risk-benefit ratio of physical exercise differs between adults and YCAs because of the different nature of cardiovascular causes of death.[2,3,10] Several epidemiological studies have assessed the relationship between physical exercise and the risk of acute myocardial infarction/SCD in the middle-aged/senior individuals engaged in leisure sports activity, in which physical exercise can be regarded as a 'two-edged sword'.[1–3,5,10] The available evidence indicates that vigorous exercise acutely increases the incidence of both cardiac arrest and acute myocardial infarction in those who do not exercise regularly. In comparison, epidemiological studies support the concept that habitual sports activity may offer protection against cardiovascular events over the long-term.[1–3,10] Adolescent and young adults involved in competitive sports activity have an estimated risk of SCD approximately three times greater than that of their non-athletic counterpart.[9,12] Sports activity acts as a trigger of arrhythmic cardiac arrest in those athletes with predisposing cardiovascular conditions.

Sudden cardiac death shows a clear gender predilection with striking male predominance (male to female ratio up to 10:1).[9] This predominance of fatal events in male athletes has been traditionally explained because females participate less commonly in competitive sports programmes than males. On the other hand, males have a higher prevalence and/or greater phenotypic expression of potentially 'lethal' cardiovascular diseases, such as HCM, ARVC, and premature coronary artery disease in the age range of competitive sports.[8,9,11]

Pre-participation screening of competitive athletes

The primary purpose of pre-participation screening is to identify the cohort of athletes affected by unsuspected cardiovascular diseases and to prevent SCD during sports by appropriate interventions.[13,25] The American College of Cardiology (ACC) states that the ultimate goal of athletic screening is the detection of silent cardiovascular abnormalities that can lead to SCD.[25] Thus, from a screening perspective, the prevalence of cardiovascular conditions with the potential for SCD among adolescents and young adults is of the utmost important. In contrast to the disparities on SCD rates, the overall prevalence of cardiovascular diseases that predispose to SCD in young athletes has been estimated to range from 0.2 to 0.7% (*Table 2*).[12,26–28]

The vast majority of 'at risk-athletes' does not experience premonitory symptoms and, thus, pre-participation screening represents the only strategy capable of identifying the underlying cardiovascular disorder.[13,25] The importance of early identification of clinically silent cardiovascular diseases at a pre-symptomatic stage relies on the concrete possibility of SCD prevention by lifestyle modification, including restriction of competitive sports activity (if necessary), but also by prophylactic treatment with drugs and implantable defibrillator.[25]

Both the American Heart Association (AHA) and the European Society of Cardiology (ESC) consensus panel recommendations agree that cardiovascular screening for YCAs is justifiable and compelling on ethical, legal, and medical grounds[13,14]. However, there is a considerable discordance in the consensus guidelines on the pre-participation screening protocols used among European and US cardiologists/sports medicine physicians.

ECG screening

The AHA recommends pre-participation cardiovascular evaluation by means of history (personal and family history) and physical examination alone, although this screening protocol has a recognized limited power (<10%) to detect potentially lethal cardiovascular abnormalities.[14] Glover and Maron[29] found that of 134 high school and collegiate athletes who suffered from SCD after they underwent a pre-participation screening, only 3% were suspected of having cardiac disease and, eventually, <1% received an accurate diagnosis. Twelve-lead ECG enhances the sensitivity of the screening process by allowing early detection of cardiovascular conditions distinctively manifesting with ECG abnormalities, such as cardiomyopathies, pre-excitation syndromes, and cardiac ion channel disorders[13,25] (*Table 3*). Based on published series from the USA and Italy, these ECG detectable conditions are present in approximately two-thirds of YCAs with SCD.

Table 2 Prevalence of cardiovascular diseases at risk for sudden cardiovascular death in young athletes

Ref.	Population	Prevalence (%)
Fuller *et al.*[26]	5617 high school athletes (USA)	0.4
Corrado *et al.*[12]	42,386 athletes age 12–35 (Italy)	0.2
Wilson *et al.*[27]	2720 athletes and children age 10–17 (UK)	0.3
Bessem *et al.*[28]	428 athletes age 12–35 (Netherlands)	0.7
Baggish *et al.*[31]	510 collegiate athletes (USA)	0.6

Italy is the only country in the world where law mandates that every subject engaged in competitive sports activity must undergo a clinical evaluation to obtain eligibility.[11,12] A nationwide mass pre-participation screening programme, essentially based on ECG, has been in practice since 1982 (*Figure 3*).[12]

The efficacy of ECG screening in the identification of cardiomyopathies has been demonstrated in a large population-based prospective study in the Veneto region of Italy.[11,12] Among 33,735 athletes undergoing ECG screening at the Center for Sports Medicine in Padua, 22 (0.07%) were identified with HCM, based predominantly on an abnormal ECG.[11] An absolute value of ECG screening sensitivity for HCM cannot be derived from this study because systematic echocardiographic findings were not available; however, this 0.07% prevalence of HCM is similar to that (0.10%) observed in a population-based study in the USA, using echocardiography.[30] This indicates that an ECG may be as sensitive as an echocardiogram in detecting HCM in the young athletic population. It is noteworthy that among the 22 athletes with HCM who were detected by ECG screening, only 5 (23%) would had been identified on the basis of a positive medical history or abnormal physical findings alone. Thus, the estimated sensitivity of ECG screening for HCM is 77% greater than that of a screening protocol which does not include the ECG.[11] A recent US study on 510 student athletes showed that the addition of ECG to history and physical examination improved the detection of echocardiographically documented cardiac abnormalities from 5 to 10 of 11, thereby improving the overall sensitivity to 90.9%.[31] Instead, the addition of an echocardiogram to the basal protocol does not seem to significantly improve the accuracy of ECG screening in identifying HCM.[32]

Impact on mortality

A subsequent Italian study provided the most compelling evidence of efficacy of ECG screening to save lives by identifying and disqualifying athletes with at-risk heart diseases. A time-trend analysis of the incidence of SCD in YCAs in the Veneto region of Italy over 26 years (1979–2004) showed a sharp decline of mortality rates after the introduction of the nationwide screening programme.[12] Fifty-five SCDs occurred in screened athletes (1.9 deaths per 100,000 person-years) and 265 deaths in unscreened non-athletes (0.79 deaths per 100,000 person-years). The annual incidence of SCD in athletes decreased by 89%, from 3.6 per 100,000 person-years in the pre-screening period to 0.4 per 100,000 person-years in the late-screening period (*Figure 4*).

Table 3 ECG features of cardiac diseases detectable at pre-participation screening in young competitive athletes

Disease	QTc interval	P-wave	PR interval	QRS complex	ST interval	T-wave	Arrhythmias
Hypertrophic cardiomyopathy	Normal	(left atrial enlargement)	Normal	Increased voltages in mid-left precordial leads; abnormal 'q' waves in inferior and/or lateral leads; (LAD, LBBB); (delta wave)	Down-sloping (up-sloping)	Inverted in mid-left-precordial leads; (giant and negative in the 'apical' variant)	(atrial fibrillation); (PVB); (VT)
Arrhythmogenic right ventricular cardiomyopathy/dysplasia	Normal	Normal	Normal	Prolonged $>$110 ms in right precordial leads; epsilon wave in right precordial leads; reduced voltages $\leq$0.5 mV in frontal leads; (RBBB)	(up-sloping in right precordial leads)	Inverted in right precordial leads	PVB with a LBBB pattern; (VT with a LBBB pattern)
Dilated cardiomyopathy	Normal	(left atrial enlargement)	(prolonged $\geq$0.21 s)	LBBB	Down-sloping (up-sloping)	Inverted in inferior and/or lateral leads	PVB; (VT)
Myocarditis	(prolonged)	Normal	Prolonged $\geq$0.21 s	(abnormal 'q' waves)	Down- or up-sloping	Inverted in $\geq$2 leads	(atrial arrhythmias); (PVB); (2nd or 3rd degree AV block); (VT)
Long QT syndrome	Prolonged $>$440 ms in males; $>$460 ms in females	Normal	Normal	Normal	Normal	Bifid or biphasic in all leads	(PVB); (torsade de pointes)
Brugada syndrome	Normal		Prolonged $\geq$0.21 s	S1S2S3 pattern; (RBBB/LAD)	Up-sloping 'coved-type' in right precordial leads	Inverted in right precordial leads	(polymorphic VT); (atrial fibrillation) (sinus bradycardia)
Lenègre disease	Normal	Normal	Prolonged $\geq$0.21 s	RBBB; RBBB/LAD; LBBB	Normal	Secondary changes	(2nd or 3rd degree AV block)
Short QT syndrome	Shortened $<$300 ms	Normal	Normal	Normal	Normal	Normal	Atrial fibrillation (polymorphic VT)
Preexcitation syndrome (WPW)	Normal	Normal	Shortened $<$0.12 s	Delta wave	Secondary changes	Secondary changes	Supraventricular tachycardia; (atrial fibrillation)
Coronary artery diseases	(prolonged)	Normal	Normal	(abnormal 'q' waves)	(down- or up-sloping)	Inverted in $\geq$2 leads	PVB; (VT)

Less common or uncommon ECG findings are reported in brackets; coronary artery diseases, either premature coronary atherosclerosis or congenital coronary anomalies; QTc, QT interval corrected for heart rate by Bazett's formula; LBBB, left bundle branch block; RBBB, right bundle branch block; LAD,. left-axis deviation of $-30°$ or more; PVB, either single or coupled premature ventricular beats; VT , either non-sustained or sustained ventricular tachycardia. *Adapted from Corrado et al.*[13]

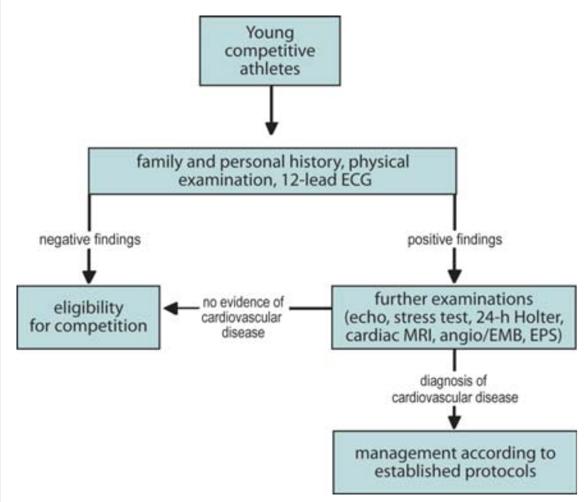

Figure 3 Flow diagram illustrating the modality of pre-participation cardiovascular screening recommended by the European Society of Cardiology section of Sports Cardiology. The screening modality is substantially based on the Italian protocol of pre-participation cardiovascular evaluation. First line examination includes family history, physical examination, and 12-lead ECG; additional tests are requested only for subjects who have positive findings at the initial evaluation. Athletes recognized to be affected by cardiovascular conditions potentially responsible for sudden death in association with exercise and sport participation are managed according to the available recommendations for sports eligibility. The screening starts at the beginning of competitive athletic activity, which for the majority of sports disciplines corresponds to an age of 12–14 years. Because the phenotypic manifestations both ECG abnormalities and arrhythmic substrates of most inherited heart diseases are age-dependent and occur during adolescence or young adulthood, screening of children is expected to have a low sensitivity for detection of cardiomyopathies and cardiac ion channel diseases, except for long QT syndrome. Of importance, there is the need of repeating the screening on a regular basis every 1–2 years, mostly in teenagers, in order to timely identify delayed phenotypic manifestations, disease progression, or substrate worsening over the time. In Italy, screening for cardiac disease is part of a more comprehensive medical evaluation that includes a general clinical history, physical examination, orthopaedic examination, spirometry, and urinalysis. In addition, athletes undergo a Montoye step test, which is limited to evaluation of heart rate recovery after exercise, although it may occasionally unmask effort-dependent arrhythmias. Exercise-induced ST-T abnormalities are appropriately assessed by maximal exercise testing, which is reserved to competitive athletes ≥35 years. Angio/EMB, contrast angiography/endomyocardial biopsy; EPS, electrophysiological study with programmed ventricular stimulation; MRI, magnetic resonance imaging. *Modified from Corrado et al.*[13]

These data have generated a number of concerns.[33,34] The main criticism is that the study was not a randomized trial comparing screening vs. non-screening of YCAs, and, thus, definitive conclusions that the reduced mortality was solely the consequence of the screening process could not be drawn. However, the strong cause–effect relationship between ECG screening and the substantial reduction of SCD in this prospective, population-based investigation is supported by the following findings: (i) there was a coincident timing between decline of SCD in YCAs and screening implementation in Italy; (ii) most of the reduced incidence of SCD was due to fewer deaths from cardiomyopathies (HCM and ARVC), and it was accompanied by the concomitant increase in the proportion of YCAs who were identified with these cardiomyopathies and disqualified from competition at the Center for Sports Medicine in Padua during the same time interval; and 3) during the study period, the incidence of SCD did not change among the unscreened non-athletic population of the Veneto region of the same age range.[12] Although additional factors—environmental, socio-economic, or medical/surgical—may have contributed to mortality reduction over the time, such factors are expected to impact mortality similarly in screened athletes and unscreened non-athletes, and hence are unlikely to explain the declining trend in SCD selectively recorded in the screened athletic population.[12]

It has been reported that during the time interval 1993–2004 the annual rate of SCD among screened Italian athletes was roughly similar to that of unscreened US high school and college competitors (0.87 vs. 0.93 per 100,000 athlete-years, respectively; $P = 0.88$).[19] Thus, it has been argued that SCD in YCAs is a low event-rate phenomenon which is unlikely to be influenced by pre-participation ECG screening. However, as discussed above in the 'Risk of sudden death in the athlete' section, the two athletic populations were clearly non-comparable with regard to age and gender, the Italian athletes being much older and including more males. Moreover, the US mortality rates were unavoidably underestimated because of the lack of a reliable reporting system and the retrospective data collection mostly based on reviews of public media reports.[19]

False-positive results

Changes in the ECG of trained athletes usually develop as a consequence of the heart's adaptation to sustained physical exercise ('athlete's heart').[2,34] There is a misconception that such physiological ECG changes overlap significantly with ECG abnormalities seen in cardiovascular diseases that cause SCD in the young.[14,35] Therefore, the ECG has been traditionally considered to be a poor screening test in the athlete, because of its presumed high level of false-positive results.[14,35] Several studies disprove this general idea that ECG is a non-specific and non-cost-effective test. Among 42,386 athletes initially screened by history, physical examination, and ECG, 3914 (9%) had positive findings as to require further examination, 879 (2%) were diagnosed with cardiovascular disorders and 91 (0.2%) were ultimately disqualified due to potentially lethal heart diseases.[12] The percentage of false-positive results, i.e., athletes with a normal heart but positive screening findings, was 7% for all cardiovascular disorders and 8.8% for heart diseases at high risk of SCD during sports. Likewise, ECG screening of highly trained competitive athletes in the UK was associated with a rate of false-positive results of only 3.7%.[28]

On the other hand, recent data in black athletes have shown a higher prevalence of ECG abnormalities, indicating a varying ECG specificity among athletes of different ethnicity.[36] An increase in the accuracy of ECG screening is expected as new studies

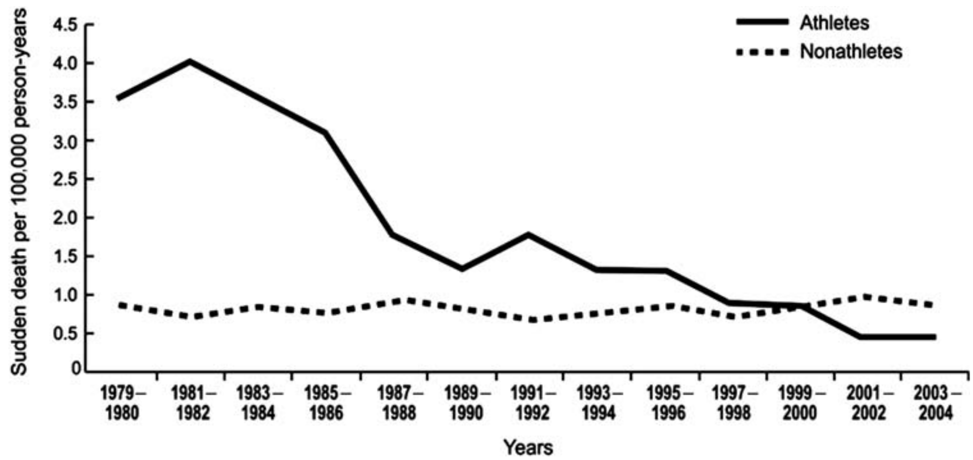

Figure 4 Annual incidence rates of sudden cardiovascular death per 100,000 person, among screened competitive athletes and unscreened non-athletes 12–35 years of age in the Veneto Region of Italy, from 1979 to 2004. During the study period (the nationwide pre-participation screening programme was initiated in 1982), the annual incidence of sudden cardiovascular death declined by 89% in screened athletes (*P* for trend <0.001). In contrast, the incidence of sudden cardiovascular death did not demonstrate consistent changes over that time in unscreened non-athletes. *Modified form Corrado et al.*[12]

emerge and are translated into updated guidelines for ECG interpretation in the athlete, like the recent recommendations of the ESC Section of Sports Cardiology.[37] The document provides cardiologists and sports medicine physicians to distinguish between physiological and potentially pathological ECG patterns. Defining which ECG changes are physiological (common and training-related ECG abnormalities) and which are pathological (uncommon and training-unrelated ECG abnormalities) (*Figure 5*) has significant favourable effects on the athlete's cardiovascular management, including clinical diagnosis, risk stratification, and cost savings. The effect of the use of the proposed *modern* criteria is to substantially increase the ECG specificity (by ~70%), primarily in the important group of athletes who exhibit pure voltage criteria for left ventricular hypertrophy and early repolarization abnormalities, but with the important requisite of maintaining sensitivity for detection of cardiovascular diseases predisposing to SCD during sports.

Costs of screening

Unlike older patients with coronary artery diseases or heart failure, young athletes/patients with a genetic disease at risk of SCD are likely to survive for many decades with normal or nearly normal life expectancy if detected by pre-participation cardiovascular evaluation, thanks to restriction from competition and prophylactic therapy against life-threatening arrhythmias.[11,13,25,38] This large amount of life-years saved favourably influences analysis of cost-effectiveness of the screening process, with cost estimates per year of life saved consistently below $50,000,[39–41] which is the traditional threshold to consider a health intervention as cost-effective. A recent US analysis estimated that adding ECG to history and physical examination in the screening protocol of athletes aged 14–22 years saves 2.06 life-years per 1000 athletes, at a cost of $42,000 per life-year saved.[41]

The benefit of pre-participation evaluation goes beyond the detection of index athletes with an inherited heart disease because it enables cascade screening of relatives, which results in a multiplier effect for identifying other affected family members, thus saving additional lives.[25,38]

Strategies for implementing nationwide screening programmes depend on the particular socio-economic and cultural background as well as on the specific medical systems in the different countries. In Italy, screening is feasible thanks to the National Health System, which has been developed in terms of healthcare and prevention services, and to the limited costs of cardiovascular evaluation in the setting of a mass-programme.[13] The cost of performing a pre-participation cardiac history, physical examination, and ECG by qualified physicians has been estimated to be ~30€. The costs of screening are covered by the athlete or by the athletic team, except for athletes <18 years, for whom the expense is supported by the National Health System. Moreover, the cost of further evaluation of athletes with positive findings at first-line examination is less than expected on the basis of the *presumed* low specificity of athlete's ECG. The percentage of athletes requiring additional testing, mainly echocardiography, has been found to be ~9%, with a modest proportional impact on cost.[11,12]

Cost for developing the necessary infrastructure and for training of specialized physicians should also be taken into account whenever calculating the overall screening cost. In Italy, those physicians, who are primarily responsible for ECG screening and eligibility for competitive sports, attend postgraduate residency training programmes in sports medicine (and sports cardiology) for 4 years ('full-time'). Such specialists work in sports medical centres, specifically devoted to periodical evaluation of athletes.

Individual cost

Disqualification from competition of a young athlete diagnosed with a heart disease may be associated with important *individual*

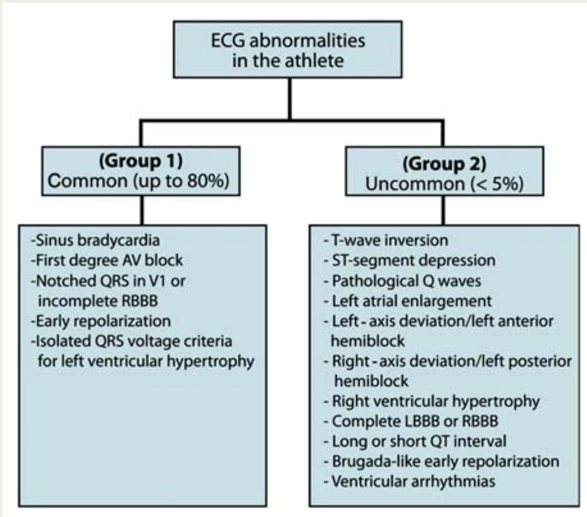

Figure 5 Classification of ECG abnormalities in the athlete. *Common ECG abnormalities*: up to 80% of trained athletes exhibit ECG changes such as sinus bradycardia, first degree AV block, early repolarization, incomplete right bundle branch block and pure increase of QRS voltages (*Group 1*). Such common ECG changes are the consequence of the physiological cardiovascular adaptation to sustained physical exertion and do not reflect the presence of an underlying cardiovascular disease. Therefore, they are not associated with an increase in cardiovascular risk and allow eligibility to competitive sports without additional evaluation. *Uncommon ECG abnormalities*: this subset includes uncommon ECG patterns (<5%) such as ST-segment and T-wave repolarization abnormalities, pathological Q-waves, intraventricular conduction defects, and ventricular arrhythmias (*Group 2*). These ECG abnormalities are unrelated to athletic conditioning and should be regarded as an expression of possible underlying cardiovascular disorders, notably cardiomyopathies and cardiac ion channel diseases, and, thus, associated with an inherent increased risk of sudden arrhythmic death. AV, atrioventricular; RBBB, right bundle branch block; LBBB, left bundle branch block. *Modified form Corrado et al.*[37]

costs in terms of health, contentment, and even future opportunity for professional sports. The risk of SCD during sports inherent to many cardiovascular disorders is still unknown, difficult to assess, and relatively low. A number of disqualified athletes would not die or experience any other consequences due to their physical activity. The screening perspective, however, is that the risk of SCD associated with competitive sports in the setting of potentially life-threatening cardiovascular disease is a controllable factor, and the devastating impact of even infrequent fatal events in the young athletic population justifies appropriate restriction from competition.[25,26]

Screening athletes for cardiomyopathies and ion channel disorders is expected to be most productive in preventing athletic-field SCD, while the exclusion from competition of other young athletes with non-lethal diseases is more arbitrary and likely not as productive.[13,25] The prevalence of Italian athletes who were diagnosed and disqualified because of cardiovascular diseases was ~2%; however, true potentially lethal conditions, such as cardiomyopathies, rhythm and conduction disturbances, long QT syndrome, valvular heart disease, coronary artery disease, and Marfan syndrome were identified in a smaller subgroup not exceeding 0.2%[12] (*Table 3*). This has significant implications for optimizing sports eligibility guidelines and management of YCAs with cardiovascular diseases in the future. The main objective should be to reduce the number of unnecessary disqualifications and to adapt (rather than restrict) sports activity in relation to the specific cardiovascular risk.

Other preventive strategies

The screening ability to detect YCAs with either premature coronary atherosclerosis or congenital coronary anomalies is limited by the scarcity of baseline ECG signs of myocardial ischaemia.[11,13,25,42] Moreover, SCD during sports may be the result of non-penetrating chest injury (commotio cordis) which cannot be prevented by screening.[8] This justifies the growing efforts to implement additional prevention strategy based on early external defibrillation of sudden cardiac arrest.[43] The presence of a free-standing automated external defibrillator (AED) at sporting events may be a valuable intervention for conditions unrecognized by screening. However, AED should not be considered neither as a substitute of pre-participation evaluation nor a justification for participation in competitive sports of athletes with at risk-heart diseases. Chances for on-field successful resuscitation are remote, even if cardiopulmonary resuscitation is started immediately and defibrillation equipment is readily available. Drezner *et al.*[44] reported that only 11% of athletes with underlying cardiomyopathy survived from athletic-field cardiac arrest despite a witnessed collapse, timely cardiopulmonary resuscitation, and prompt defibrillation.

Pre-participation screening of leisure athletes

The risk of sports-related acute cardiovascular events, including SCD, increases exponentially among individuals >35 years and is almost exclusively related to the development and progression of atherosclerotic coronary artery disease.[10] The growing number of middle-aged/senior subjects engaged in leisure-time sports activity, outside the competitive sports community, makes the pre-participation screening of this athletic population an emerging task, with specific problems in terms of feasibility, logistics, and costs.

The identification and management of coronary artery disease in asymptomatic adults and elderly is a controversial issue. So far, no strategies have been adequately studied to evaluate their ability to reduce the risk of exercise-related acute cardiovascular events in this group of athletes.[2]

Several epidemiological studies reported the association between ECG abnormalities and an increased relative risk (1.5–2.5 fold) of mortality from coronary artery disease.[45,46] Despite its recognized prognostic value, the utility of ECG for screening asymptomatic subjects without known coronary atherosclerosis is limited. Up to half of individuals with angiographically normal coronary arteries show ECG changes, approximately one-third of those with coronary artery disease show normal basal ECG findings, and, most importantly, the vast majority of coronary events occurs in the absence of prior ECG abnormalities.[47,48]

Thus, basal ECG results in an unacceptably large number of false-negative and false-positive results in athletes >35 years and is not suitable as a single test for screening this athlete's age-group.

Exercise testing screening

Because of its established prognostic value, widespread availability and low cost, exercise testing is widely deemed the best available test for screening asymptomatic adults prior to an exercise programme. Several studies reported an increase in the relative risk of coronary death (range 2–5), for those asymptomatic subjects with a positive exercise testing.[49–51] However, the test accuracy for detection of coronary artery disease is expectedly limited among the general population because of the relatively low disease's prevalence.[52,53] The test performance increases with a greater pre-test probability of coronary atherosclerosis, so that subgroups of asymptomatic individuals with risk factors who would most benefit from screening by exercise testing have been defined.[50,51,54] These subgroups include men with advanced age, multiple coronary risk factors, or diabetes; instead, the test prognostic value has not been demonstrated in asymptomatic healthy women. There is evidence that the risk of cardiac events related to underlying coronary artery disease further depends on the level of fitness/habitual physical activity as well as on the intensity of the intended physical exercise.[55–57] However, the predictive value of exercise ECG test for cardiovascular events occurring specifically during exercise is very limited. Siskovick *et al.*[49] reported a 18% sensitivity and 92% specificity of a positive exercise testing to predict an exercise-related cardiovascular event in asymptomatic, hypercholesterolaemic men (35–59 years).

Although there are no solid scientific data to guide the use of exercise testing for screening, several Associations of Cardiology and Sports Medicine have addressed this important issue by consensus.[58–60] Despite slight differences, the common denominator of current recommendations is that individuals who appear to be at a greater risk of suffering from underlying coronary artery disease (for instance those with diabetes mellitus[61–63]) should be considered for exercise testing prior to the beginning a vigorous exercise training programme. In contrast, the US Preventive Services Task Force states that there is insufficient evidence to determine the benefits of pre-participation exercise testing prior to exercise programmes.[64]

European Society of Cardiology Recommendations

Most recent recommendations of cardiovascular evaluation of middle-aged/senior individuals engaged in leisure sports activity have been proposed by the ESC sections of Sports Cardiology

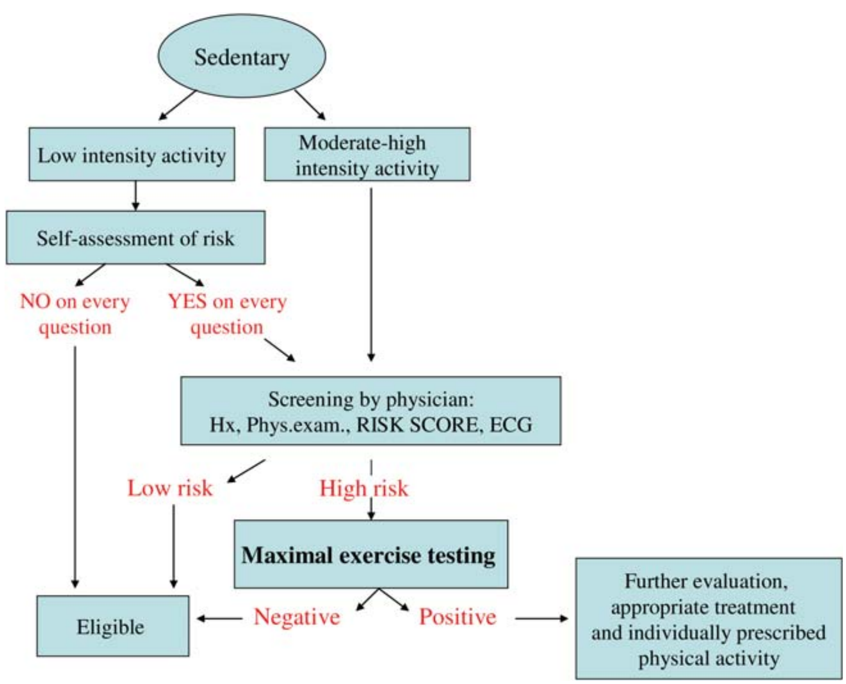

Figure 6 Specific pre-participation screening work-up for sedentary middle-aged/senior individuals. Sedentary individuals are defined as individuals whose energy expenditure during physical exercise accumulates to <2 MET-h/week. This low activity has been associated with higher coronary event rates and a poorer prognosis. The recommendations consider low cardio respiratory fitness equivalent of having a high risk according to score. The intensity of the intended physical exercise programme, assessed by the individual or by a non-physician is classified as follows:(i) low intensity, corresponding to 1.8–2.9 METS; (ii) moderate intensity, corresponding to 3–6 METS; (iii) high intensity, including individuals participating/willing to participate in masters events such as long-distance cycling, city marathons, long distance cross country skiing and triathlons, corresponding to an effort >6 METS.

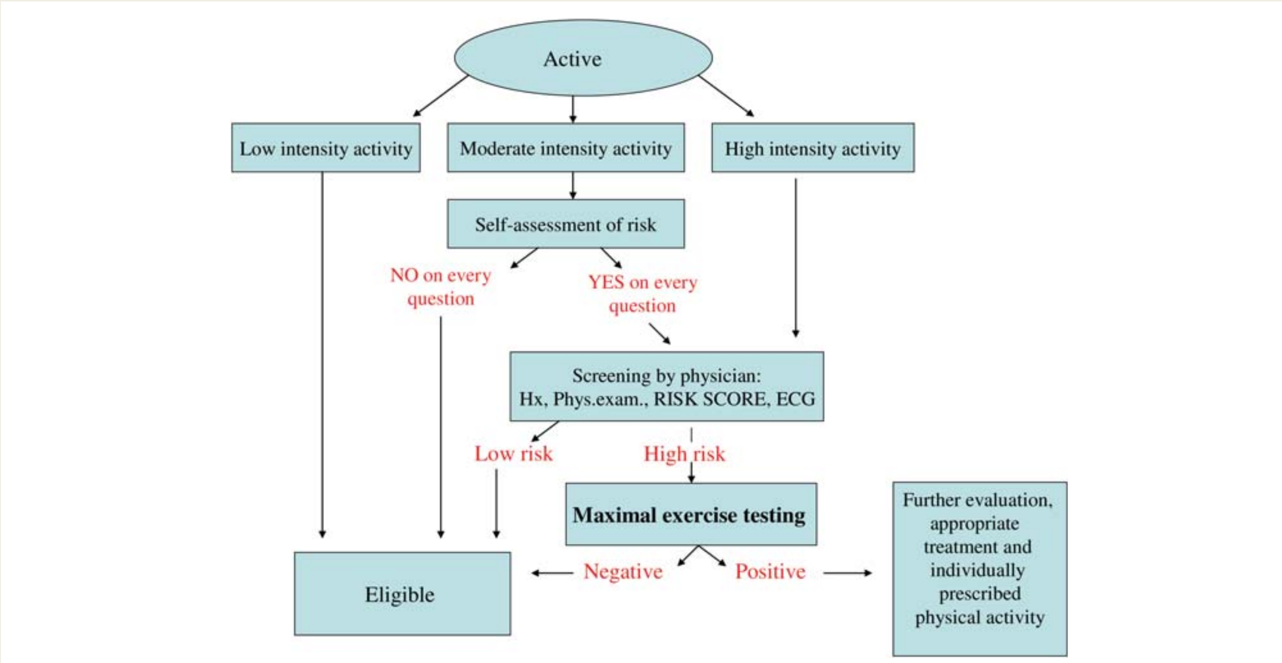

Figure 7 Specific pre-participation screening work-up for regularly active middle-aged/senior individuals. Active individuals are defined as those accumulating ≥2 MET-h/week, even intensive, though non-competitive sport activities. Classification of intensity of the intended physical activity as in *Figure 6*.

and Exercise Physiology of the European Association of Cardiovascular Prevention and Rehabilitation.[60] *Figures 6* and *7* summarize the specific work-up of cardiovascular evaluation recommended as appropriate for either sedentary or regularly active individuals, based on the individual risk profile and the type or intensity of intended physical exercise.[60] The recommended first line evaluation consists of a self-assessment (by the individual or by non-physician health-related professionals) of the habitual physical activity level and the risk factors, using validated questionnaires such as the AHA pre-participation Questionnaire[65] or the simpler revised Physical Activity Readiness Questionnaire.[66] If indicated, subsequent thorough risk assessment is performed by a qualified physician, using the ESC Systematic Coronary Risk Evaluation (SCORE).[67–69] According to the SCORE system, the assessment of cardiovascular risk of coronary death within 10 years is based on age, sex, blood pressure, blood cholesterol, and smoking history.[67–69] Maximal exercise testing (and possibly further cardiological evaluations) is reserved to those individuals embarking in moderate/intense physical activity who show an increased risk for coronary events.[63]

Whether further evaluation and successful treatment of an asymptomatic individual with a positive exercise test by interventional/non-interventional therapies can improve outcomes, thereby validating the screening clinical utility, remains to be established. Screening with exercise testing is likely to be cost-effective in older patients with coronary risk factors, while it is not justified in low-risk subgroups.

Conclusions

The available evidence, based on the long-running Italian experience, indicates that ECG screening has to be considered an efficient health strategy for prevention of SCD of YCAs. It meets the most important Wilson and Jungner's criteria[70] for appraising the validity of a screening strategy: (i) safe sports activity represents an important health issue; (ii) still asymptomatic athletes with at risk-heart diseases are successfully identified; (iii) an effective management strategy based on restriction of life-threatening training/competition and subsequent clinical treatment of at risk-athletes does exist; (iv) and early identification/management of the underlying disease favourably modifies the outcome and leads to substantial mortality reduction.

It is noteworthy that a 25-year interval was required to generate the Italian data showing the actual success of the pre-participation ECG screening programme. Until data from other studies of comparable prospective study design, size of the study athletic cohort, and follow-up duration are obtained, the existing data provide good evidence that pre-participation screening does work. If one accepts the principle, sanctioned by both the AHA and the ESC, that cardiovascular screening for YCAs is justifiable and compelling, the available evidence suggests to adopt a screening protocol including ECG, which is the only screening tool proved to be effective. Hence, pre-participation ECG screening of YCAs has been recommended by the ESC,[13] by the International Olympic Committee ('Lausanne

Table 4 Pre-participation athletic screening of young competitive athletes in European countries

Country	Medical/sports Associations	Target athletic population	Screening protocol
Luxemburg	National Sports Ministry, Olympic Medical Committee, National Association of Sports Physicians	Competitive athletes of all sports	History, physical examination, ECG (required)
Sweden	National Board of Health and Welfare, National Federation of Sports	Elite athletes of all sports	History, physical examination, ECG (recommended)
Norway	Norvegian Football Association Medical Committee	Professional football players	History, physical examination, ECG, echocardiography (required)
Germany	German Association of Sports Medicine, National Sports Federations	Elite athletes of all sports	History, physical examination, ECG, echocardiography, exercise testing (required)
Poland	Ministry of Sports and Tourism, Ministry of Health, Polish Cardiac Society, Sports Federations	Competitive athletes (age <23 years) of all sports and national team members	History, physical examination, ECG (required)
France	National Sports Ministry	Professional athletes of all sports	History, physical examination, ECG, echocardiography, exercise testing (required)
	French Society of Cardiology	Competitive athletes of all sports	History, physical examination, ECG (recommended)
Scotland	Government, Department of Health	Football, competitive athletes >16 years old	History, physical examination, ECG (required)
England	British Lawn Tennis and Football Associations	Competitive athletes	History, physical examination, ECG (required)
Greece	Hellenic College of Sports Medicine, National Sports Federations	Competitive athletes of all sports	History, physical examination, ECG (recommended)
Belgium	National Sports Federations	Athletes of cycling and motocross sports	History, physical examination, ECG (required)
Spain	High Sports Government Council	Competitive athletes of all sports	History, physical examination, ECG (recommended)
The Netherlands	Working group of Cardiovascular Prevention and Rehabilitation, National Olympic Committee, National Sports Federations, Netherland Society of Cardiology	Elite competitive athletes (age <35 years) of all sports	History, physical examination, ECG (required)
		Professional football players	History, physical examination, ECG, echocardiography (required)
		Elite athletes of cycling, motor and flying sports and diving	History, physical examination, ECG (required)

Adapted from Corrado *et al.*[72]

Recommendations'),[71] and by most European Cardiologic Societies and Sports Medical Federations (*Table 4*).[72]

The AHA 2007 Update on pre-participation athletic screening again recommends the traditional history/physical exam protocol without ECG. Most importantly, the document does not dispute the incremental value to ECG screening, but concludes that it is not applicable to the US system because of the logistics, manpower, and financial resources required for a national screening programme.[14]

On the other hand, the utility of screening middle-aged/senior individuals engaged in leisure sports by exercise testing to detect coronary artery disease remains to be determined. This explains the large discordance between the screening recommendations and the lack of uniformity in clinical practice. Because many sports-related SCDs occur in adult and elderly people, prevention by the introduction of a feasible screening protocol remains a clinical challenge. According to the guidelines of the ESC, ACC/AHA, and the American College of Sports Medicine, exercise testing screening prior to initiating a vigorous exercise training should be reserved to those asymptomatic individuals with an increased risk of coronary artery disease, assessed using available risk score systems. Although this strategy has not been rigorously evaluated to reduce exercise-related cardiovascular morbidity and mortality, it appears to be prudent in the light of our current understanding of the risks and benefits of exercise in this age group.

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