Review Article

Recommendations for the Cardiovascular Screening of Athletes

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The sudden death of a young individual is the most tragic event in sports. It is a significant athletic, political, medical and social problem with great impact on public opinion and the media, since this catastrophic event involves individuals who are basically considered apparently healthy and are often treated as heroes.

Despite the known benefits of regular exercise training, an enhanced risk of undesirable events has been described in individuals who take part in mainly high intensity physical activities.[1-4] There is evidence that vigorous physical exertion triggers mechanisms that lead to sudden death.[5-7] Sudden death occurs either during or immediately after the end of sports activity, confirming that participation in competitive sports or high intensity physical activity increases the likelihood of cardiac arrest.[8] Indeed, it has been found that adolescent and young athletes have a 2.8-fold greater risk of sudden cardiovascular death than their sedentary counterparts.[9] The risk-benefit ratio also varies according to the athlete's age, physical capacity, and state of health.[10]

Underlying cardiac disorders are the most common cause of sudden death during sports activities.[11,12] In Europe, the incidence of sudden cardiac death in young people (age <35 years) is estimated to be 2.1 cases per 100,000 athletes per year from cardiovascular causes and 2.3 per 100,000 from all causes,[9] while in the USA the corresponding rate is 0.96 per 100,000 athletes per year.[13] It has been claimed that, in healthy adults (age >35 years) who are joggers or long-distance runners, the incidence of sports-related sudden death ranges from 1:15,000 to 1:50,000.[14] There appears to be a significant predominance of males over females (ratio >10:1), which can be attributed to the particularly higher rate of male participation in competitive sports and high-intensity physical activities.[9] In addition, male gender has been found to be an independent predictive factor for sports-related sudden cardiac death, mainly due to the higher prev-

alence and phenotypic expression of cardiac disorders related to arrhythmias and cardiac arrest, such as cardiomyopathies and coronary artery disease.[15]

Cause and mechanisms of sudden cardiac death in athletes

In young individuals (age<35 years) who participate in sport activities, the most common cardiac disorders that lead to sudden death during exercise, or to other serious cardiovascular complications, are hypertrophic cardiomyopathy and congenital coronary anomalies.[8,11,12] Other less common causes of sudden death in young athletes are a variety of congenital heart diseases, myocarditis, dilated cardiomyopathy, Marfan syndrome, and arrhythmogenic right ventricular cardiomyopathy.[8,11,12] Rarer causes are mitral valve prolapse, aortic stenosis, as well as arrhythmias, conduction system diseases and channelopathies.[8,11,12] In contrast, in adult/senior individuals who are engaged in physical activity, atherosclerotic coronary artery disease is the most common cause of sudden cardiac death during exercise.[8]

The pathophysiological mechanism usually responsible for sudden cardiac death in young individuals is based on an interaction between anatomical and functional disorders that results in electrical instability.[8] Thus, exercise is not itself the cause; rather, it triggers arrhythmias in individuals who have some cardiovascular disorder.[8] Such a substrate can involve either ischaemic or hypertrophic myocardium, or conduction system diseases.[8,16,17] Several factors—such as transient decreases of coronary artery flow, acidosis, hypoxia, haemodynamic disturbances, neurophysiological disorders, or the effect of toxic substances such as drugs—may act on such a substrate and trigger either ventricular extrasystoles, ventricular tachycardia, ventricular fibrillation, or sudden death.[8,16-19] This pathophysiological mechanism appears more often during exercise, especially in the presence of specific environmental conditions. It seems that the exercise characteristics play an important role. Specifically, the risk is higher for those who participate in prolonged, high intensity effort (above the anaerobic threshold), particularly when there are electrolyte disturbances, high temperature (atmospheric temperature ≥32^{o} C and relative humidity ≥50-75%) and when exercise takes place at a high altitude.[20-22]

The risk of sudden death is quadrupled in individuals with sympathetic overactivity.[8] Strenuous exercise stimulates the sympathetic nervous system, increasing catecholamine levels, which enhance the risk of ventricular tachycardia, platelet accumulation and the formation of thrombi or the rupture of atheromatous plaque.[3,17,19] Catecholamines shorten the effective refractory period of healthy or slightly diseased myocardium.[8,19] The mechanisms that lead to potentially malignant or fatal arrhythmias are either increased automaticity or triggered activity. Thus, during physical activity, potentially malignant ventricular extrasystoles sometimes appear as a result of re-entry.[8]

Sudden death during sports can also be due to a non-cardiac cause, such as bronchial asthma, rupture of a cerebral aneurysm, heatstroke, etc.[8,15] In addition, deaths have been reported among athletes from neck[23] and chest injuries, or following a sudden and blunt blow to the precordium (*commotio cordis*).[24]

The abuse of drugs and prohibited substances often causes acute or chronic cardiovascular complications during exercise.[25] Long-term abuse of anabolic steroids, for example, has been implicated in arterial hypertension, arrhythmias, coronary artery disease, and a number of cases of sudden cardiac death in young athletes.[25,26] The doping substances most widely used in sports are anabolic steroids, erythropoietin, growth hormone, and stimulants such as cocaine, cannabis, ephedrine, etc.[25] These substances aim to alter either short- or long-term competitive ability, giving an unfair advantage to the athlete-user with catastrophic consequences for his health. The majority of athletes take a combination of several drugs in high dosages, over long periods of time.

Sedentary individuals who participate occasionally in intensive sports activities seem to have an increased risk of ischaemic events or sudden cardiac death during or after exercise.[1,27] Indeed, sudden cardiac death is often the first manifestation in subjects with silent ischaemia.[5,27]

Protocol for the cardiovascular screening of athletes

Systematic long-term exercise has been proved to improve health by reducing all-cause and particularly cardiovascular mortality. Thus, regular physical activity of moderate intensity has been shown to reduce the incidence of myocardial infarction and sudden death.[1,8] The aim is to provide appropriate recommendations that will ensure the benefits of exercise and reduce the risk. It is important to provide proper sports medicine support for the improvement of physical performance, protection of athletes' health, and prevention or treatment of exercise-related disorders. The strategic plan for the limitation of exercise-induced cardiac disorders, and mainly the prevention

of sudden cardiac death, during sports, is as follows:

a) to establish a common pre-participation cardiovascular screening protocol (for both amateur and professional athletes);
b) to establish diagnostic criteria to determine the most appropriate exercise prescription for individuals with cardiovascular diseases;
c) to equip arenas with smart automatic defibrillators and to train the staff in first aid; and
d) to identify families with a high risk of hereditary cardiac diseases.

Proper and complete regular pre-participation cardiovascular screening contributes to the identification of athletes affected by cardiovascular diseases, so that appropriate interventions may lead to prevention of sudden death.[28] Countries with a great medical and athletic tradition have enacted protocols for the cardiovascular screening of athletes. Both the American Heart Association and the European Society of Cardiology have published guidelines for the cardiovascular screening of athletes, aiming to detect the high-risk athletes and to prevent undesirable events.[15,29] These protocols incorporate mandatory diagnostic methods that complement personal and family history and complete physical examination of athletes. However, in recent years, the results of studies based on the cost-effectiveness ratio of the proposed guidelines for pre-participation cardiovascular screening, doubts about the additional use of echocardiography, and the overuse of diagnostic methods have led to the establishment of new criteria and the use of more easily accessible and effective diagnostic methods. The Sports Cardiology Study Group of the European Society of Cardiology proposed in 2005 a common European protocol for the cardiological screening of athletes.[15] The recommendations were based mainly on the 20-year Italian experience, the applicable legislation, and the experience of specialist cardiologists and sports physicians for all over Europe. These recommendations have also been accepted by the International Olympic Committee.[30,31]

On the basis of these recommendations, we also propose a common cardiovascular screening protocol for all sports federations, for all athletes, both amateur and professional, who engage in sports activities in Greece. The ultimate goal is to store the cardiovascular screening findings in an electronic athletes' Health Identity Card, which will be updated periodically and will be carried throughout the athlete's sport career, being accessible only to authorised physicians of the sports clubs to which the athletes belong. According to the proposed protocol (Figure 1), the athlete's health screening should include a carefully recorded personal and family history, a complete physical examination (looking for findings of Marfan syndrome, auscultation in supine, seated and upright position, palpation of peripheral pulses, and accurate measurement of blood pressure), and the recording of a 12-lead resting ECG. If findings are normal, the health study must be repeated every 1-2 years.[15]

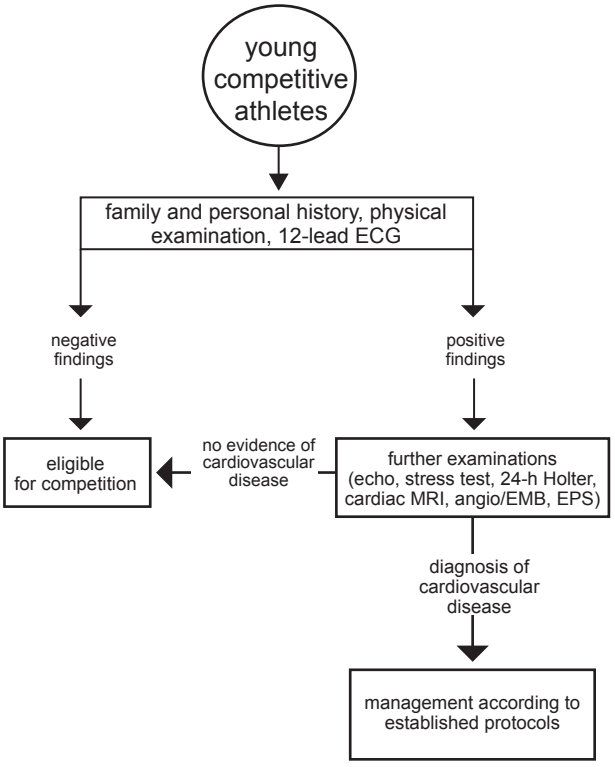

Figure 1. Protocol for the cardiovascular screening of athletes. (From reference 15, reproduced with permission.)

Medical history

Most cardiac disorders related to sudden cardiac death are genetically determined, either autosomal dominant or autosomal recessive, which emphasises the importance of heredity in identifying high-risk athletes. Family history is considered positive when some family member has experienced a heart attack or sudden death at a young age (<55 years in males, <65 years in females), or if there is a family history of cardiomyopathy, coronary artery disease, Marfan syndrome, channelopathies, etc. The personal history is considered positive when the athlete reports symptoms of exertional chest pain or discomfort, syncope or near-syncope, palpitations, dyspnoea or respiratory difficulty, or fatigue not compatible with the degree of physical exertion.[15]

Clinical examination

The physical examination should be detailed and should include all systems. Auscultation of the heart should be performed with the subject in supine and seated positions. Blood pressure should be recorded with the subject seated and the established guidelines should be carefully observed, because of the high incidence of "white coat" hypertension among young athletes.[32] Positive findings include musculoskeletal or ocular disturbances suggestive of Marfan syndrome, diminished or delayed femoral artery pulses, mid- or end-systolic clicks, a second heart sound that is single or widely split, marked murmurs (systolic or diastolic grade ≥2/6), arrhythmias, and hypertension (>140/90 mmHg on more than one measurement).[15]

Electrocardiogram

The resting ECG is a simple method with high sensitivity and specificity (70% and 94%, respectively),[33] which contributes significantly to the identification of asymptomatic patients who require further examination.[11,28,34] A common clinical problem during screening of young athletes is the differential diagnosis between "normal" findings, which are due to anatomical and functional cardiac adaptations to exercise, and pathological findings that are the result of cardiac diseases. Common ECG findings in athletes that are considered to be "physiological" and the consequence of long-term training include sinus bradycardia, first degree atrioventricular block, incomplete right bundle branch block, signs of early repolarisation, and QRS changes indicative of right ventricular hypertrophy.[15,33,34]

In contrast, ECG findings that are considered suspicious and require further examination are negative T waves, ST-segment depression, pathological Q waves, left or right axis deviation, left posterior hemiblock, left anterior hemiblock, complete left or right bundle branch block, long or short QT interval, and findings compatible with Brugada syndrome (Table 1).[15,33,34]

Studies that investigated the cost-effectiveness of the cardiovascular screening of athletes have found the 12-lead ECG to be the most cost-effective examination, compared with medical history, clinical and echocardiographic examinations.[35,36]

Limitations of the cardiovascular screening of athletes

Around 30% of sudden death cases cannot be precluded by medical screening of athletes, even when this includes an ECG examination.[37] There is only a small probability of identifying athletes with early atheromatosis or congenital coronary anomalies.[28,33,38] It is estimated, however, that about 25% of these cases show warning symptoms, usually during exercise, or ECG disturbances at rest or during exercise, that could raise the suspicion of cardiac disease.[15,39] Echocardiographic examination of all athletes has not been found to improve the ability of primary basic cardiovascular screening to identify athletes with hypertrophic cardiomyopathy.[40] In contrast, it has been claimed that the extensive use of echocardiography leads to an increase in false positive or false negative results, a typical example being the identification of athletes with left ventricular hypertrophy who are in the so-called "grey zone".[41-43] In addition, echocardiography has limited diagnostic value in athletes aged under 18 years, since even in cases with hypertrophic cardiomyopathy in adolescents the hypertrophy may not exceed the upper normal levels.[44] For similar reasons, the diagnostic value of the ECG is limited during childhood.[44]

A common finding that arises during pre-participation cardiovascular screening of athletes is the presence of cardiac adaptations to long-term and intensive training. The "athlete's heart" creates problems for differential diagnosis and raises questions about the decision to allow participation in competitive sports or concerning the recommended level of physical activity. Long-term exercise leads to an increase in left ventricular mass, due to either an increase in left ventricular diameter (isotonic exercise), or hypertrophy of the walls (isometric exercise), or both.[45,46] The magnitude of the cardiac adaptations depends upon the characteristics of the physical activity in which each athlete participates.[45,46] The distinction between these exercise-induced changes, called "physiological" hypertrophy, that revert after detraining, and those of cardiac disorders or "pathological" hypertrophy, is of high importance. The identification of a cardiac disease in an athlete usually leads to his disqualification in an attempt to reduce the risk. On the other hand, a false diagnosis of a cardiac disease in an athlete may also lead to disqualification, thus depriving him of the various benefits from sports participation.

Typical examples of clinical dilemmas from the pre-participation screening of young athletes who are in the area between "physiological" and "pathological" are the "grey zone" left ventricular hypertrophy (interventricular septum thickness 13-15 mm), right ventricular dilata-

Table 1. Typical findings from the ECG in athletes due to the presence of cardiovascular disorders. (From reference 15, reproduced with permission).

Disease	QTc interval	P wave	PR interval	QRS complex	ST interval	T wave	Arrhythmias
HCM	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 ≤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 LBBB pattern)
Dilated cardiomyopathy	Normal	(Left atrial enlargement)	(Prolonged ≥0.21 s)	LBBB	Down-sloping (up-sloping)	Inverted in inferior and/ or lateral leads	PVB; (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 ≥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 ≥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);
Pre-excitation syndrome (WPW)	Normal	Normal	Shortened <0.12 s	Delta wave	Secondary changes	Secondary changes	Supraventricular tachycardia; (atrial fibrillation)
Coronary artery disease	(Prolonged)	Normal	Normal	(Abnormal Q waves)	(Down- or up- sloping)	Inverted in ≥2 leads	PVB; (VT);

Less common or uncommon ECG findings are reported in parentheses.
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.

tion, excessive bradycardia (<45 beats/min), left ventricular dilatation (end-diastolic diameter >55 mm), conduction disturbances (second degree Wenckebach atrioventricular block or worse), other arrhythmias, etc.[45,46] Other medical concerns involve the presence of disorders such as mitral valve prolapse, Wolff-Parkinson-White syndrome, atrial septal defect, etc., in relation to the eligibility to participate in competitive sports or even in leisure-time physical activity.[45]

Further examinations in cases of "abnormal" findings

In cases of "abnormal" findings from the first basic cardiovascular screening, the athletes should undergo an echocardiographic study, maximal exercise testing, or other non-invasive examinations according to the indications.[15] In certain cases it is also necessary to carry out invasive examinations, such as coronary angiography, ventriculography, myocardial biopsy, or an electrophysiolog-

ical study. A genetic examination may also be required in the investigation of hereditary cardiac disorders.[44]

Specifically, in athletes with "abnormal" findings from the basic cardiovascular screening, or in those in the "grey zone", the following diagnostic examinations have been proposed:[15,29,34,45-48]

1. In athletes with marked murmurs an echocardiographic-Doppler study is suggested. If it reveals an anatomical cardiac abnormality, maximal exercise testing, chest X-ray, and 24-hour Holter ECG recording should be performed. Athletes with moderate to severe findings may also need transoesophageal echocardiography, cardiac magnetic resonance imaging or, according to the cardiologist's judgement, a haemodynamic study.
2. In athletes with ECG findings indicative of left ventricular hypertrophy, an echo-Doppler examination, maximal exercise testing, and 24-hour Holter ECG monitoring are suggested.
3. In athletes with rhythm disturbances (Lown >II), the screening is accompanied by an echo-Doppler study, a maximal exercise test, and 24-hour Holter ECG monitoring.
4. In athletes with channelopathies, an additional echo-Doppler study, maximal exercise testing, and 24-hour Holter ECG monitoring are suggested. In symptomatic athletes (paroxysmal tachycardias), or in cases with anatomical cardiac disorders, an electrophysiological study may be required.
5. In athletes with conduction disturbances, an echo-Doppler study, maximal exercise testing, and 24-hour Holter ECG monitoring are requested. If there are QRS abnormalities and/or an anatomical cardiac disorder, or second degree atrioventricular block or more severe disturbances, an electrophysiological study is requested.
6. In athletes with syncope, an echo-Doppler study, maximal exercise testing, 24-hour Holter ECG monitoring, and tilt-testing are suggested. A full neurological examination is also required.
7. In athletes who experience chest pain, especially during exercise, a full echo-Doppler study, exercise testing, chest X-ray, and 24-hour Holter ECG monitoring are suggested. In cases of doubt, a dynamic radioisotope myocardial perfusion scan, multi-channel computed tomography, cardiac magnetic resonance imaging, and/or coronary angiography may be needed.
8. In athletes who have mild or moderate hypertension at first measurement, this measurement should be repeated after half an hour's rest and on the following days. If it persists, an echo-Doppler study, 24-hour blood pressure monitoring with a portable device, and a maximal exercise test are recommended. If the findings persist, or in the presence of severe hypertension, further examinations (hormone test, renogram, etc.) may be required.

To conclude, the pre-participation cardiovascular screening of athletes should be considered essential, since it contributes significantly to the prevention of undesirable complications during exercise and to a reduction in sudden cardiac death. This has been confirmed by statistical data from Italy, where an 89% reduction in the cases of sudden death in athletes was observed during the period when mandatory cardiovascular screening was applied.[28]

The aim of the cardiovascular screening of athletes is not to exclude them from sports, but mainly to provide advice concerning the type of exercise that is appropriate, beneficial and safe, as well as to prevent complications in extreme activities. This presupposes the establishment of clear criteria related to the permitted level of physical activity on a case-by-case basis.

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