Chapter

Sudden Cardiac Death in Young Athletes

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Abstract

Sudden death (SD) is the most dangerous and irreversible outcome of diseases in clinical as well as in sports medicine. Between 1980 and 2011, the Sudden Death in Young Athletes Registry in the USA, which was developed based on mass media information, recorded 2406 cases of sudden death, which were observed in 29 diverse sports. In the USA 80% of all SD occurred in high school/middle school or collegiate student athletes, and 20% were engaged in organized youth, postgraduate. Statistical data vary greatly in different countries: SCD incidence rate in the USA is 7.47 and 1.33 per 1,000,000 exercising male and female school-age athletes, respectively, whereas in Italy, the rate is 2.6 cases in men and 1.1 in women per 100,000 individuals per year who are involved in active competitive sports. The European Heart Rhythm Association (EHRA) position paper concluded that as an overall estimate, 1–2 out of 100,000 athletes between of age of 12 and 35 years old die suddenly each year. It was shown that the risk of SCD is significantly higher in athletes than in nonathletes with the same heart condition in the general population, by more than five times for ARVC, 2.6 times for coronary artery disease, 1.5 times for myocarditis, and more than 2 times for cardiac conduction system diseases.

Keywords: sport, sudden cardiac death, young athletes

1. Introduction

Sudden death (SD) is the most dangerous and irreversible outcome of diseases in clinical [1] as well as in sports medicine [2–7]. SD in the sports definition includes cases of death that occurred immediately during exercise as well as within the first 1–24 hours from the onset of initial symptoms that have led to a change or cessation of physical activity. Most cases of SD in athletes are associated with sporting activity [6, 8]. In 2015 the European Guidelines for the Prevention of Sudden Death classified athletes into a separate group with a special risk of SD [9].

SD is traditionally considered to be associated primarily with heart diseases. But according to the data provided by the US National Collegiate Athletic Association (NCAA) athletes between 2003 and 2013, accidents are the leading cause of death in the SD structure of athletes (50%); however the leading position among somatic diseases undoubtedly belongs to sudden cardiac death (SCD) which constitutes 15% of all SD cases; the other causes of SD, both medical and nonmedical (suicide, homicide) do not exceed 10% [5].

2. The epidemiology of SCD in sports

It is not easy to determine the accurate epidemiology of SCD in sports. Much depends on the selected inclusion criteria for the analysis, the age of the athletes, the level of athletic achievement, sporting experience, type of sports, and other factors. Therefore, studies carried out in different countries show an unequal SCD incidence rate in athletes. Between 1980 and 2011, the Sudden Death in Young Athletes Registry in the USA, which was developed based on mass media information, recorded 2406 cases of sudden death, which were observed in 29 divers sports [6]. In this paper 80% SD occurred in high school/middle school or collegiate student athletes, and 20% were engaged in organized youth, postgraduate.

SCD incidence rate determined in the USA was 7.47 and 1.33 per 1,000,000 exercising male and female school-age athletes, respectively [10]. The statistical data can however vary greatly in some areas. According to Corrado et al. [3], the SCD incidence rate in Italy was 2.6 cases in men and 1.1 in women per 100,000 individuals per year who are involved in active competitive sports. In recent years, with screening of athletes before active exercise, this figure decreased to 0.87 cases per 100,000 per year. In the USA, in children and adolescent athletes, SCD is registered in 0.66 cases per 100,000 exercising male school students and 1.45 per 100,000 male college students and 0.12 per 100,000 female school students and 0.28 per 100,000 female college students (Van Camp et al., [10]). In Ireland [11] the SCD incidence rate in sports was 1 case per 600,000, while in a French study [12], it was 0.26 per 100,000 per year. In a study conducted on Rhoda Island [13], the rate was 0.36 per 100,000 per year in individuals aged up to 30 years and 4.46 and 0.05 per 100,000 per year in men and women older than 30, respectively. The European Heart Rhythm Association (EHRA) position paper concluded that as an overall estimate, 1–2 out of 100,000 athletes between the ages of 12 and 35 years old die suddenly each year [8].

3. SCD and types of sports

The data on sports-associated SCD cases as well as those on epidemiology are quite varied, depending on national sporting traditions, age, gender, and group inclusion criteria (professional sports, school sports, general fitness activity). Most SCD causes in the USA [6], most SCD cases in young athletes in active competitive sports occurred in basketball and football, which accounted for 35 and 30%, respectively; soccer, cross-country/track, and baseball accounted for 8, 7, and 6% of the cases respectively; such sports as wrestling, boxing, swimming, ice hockey, and marathon running accounted for between 1 and 5%; and rugby, triathlon, martial arts, tennis, volleyball, gymnastics, figure skating, golf, and others accounted for less than 1%.

By another study from the USA (Harmon et al. [5]), the highest incidence rates of SCD per athletes were 1 in 8978 in men's basketball, 1 in 23,689 in men's soccer, and 1 in 35,951 in men's football. In women its rates were 1 in 57,611 in swimming and 1 in 77,061 in basketball.

SCDs not associated with commotio cordis (see below) were reported most frequently in children and adolescents involved in ice hockey, football, and basketball [14]. In Spain SCD was observed most often in cyclists (34.4%), soccer players (21.3% in the general group and 33.3% in athletes younger than 35 years), and gymnasts (8%). Fewer deaths occurred in basketball, rowing, marathon running, jogging, and mountain climbing [15]. In Italy [3] the highest number of SCD cases was registered in soccer (40%); 9% of the cases in swimming and rugby; 7% in

cycle racing, running, and volleyball; and 3% of cases in judo, tennis, and gymnastics. It is clear that this rating of dangerous sports is based on a specific regional and temporal sample of published sports-related SCD cases and does not fully reflect all types of sports for which SCD were recorded. SCD cases associated with many other sports periodically come to public attention through the media. The studies by Quigley and Ragosta cited above most frequently recorded SCD when playing golf (31.3 and 23.4%, respectively), cricket (21.5%), and jogging and less often during basketball (10.2%), swimming (8%), and cycling races (6%). In a major study conducted in France [16], SCD was most frequently observed during cycling (30.6%), jogging (21.3%), and soccer (13.05%); in individuals of all ages playing sports and exercising regularly, SCD in other sports did not exceed 5% in this list.

4. Commotio cordis

The SCD cases associated with a blunt blow to the heart area and classified as death caused by heart contusion (contusion cordis) or concussion (commotio cordis) constitute a special group [14, 17–19]. Occurring in the vulnerable phase of the cardiac cycle (the beginning of T wave on ECG), this blow initiates fatal arrhythmias, ventricular fibrillation, or at once asystole. Under normal heart rate (60–80 bpm), this vulnerable period takes up approximately 2–3% of the time or up to 20% if the heart rate increases to 120 bpm or more. Therefore, athletes are more vulnerable to this grave complication during exercise. Young American athletes most frequently experience SCD in lacrosse, then hockey and basketball [14]. There have been reports of SCD occurring from a punch to the heart in martial arts, due to being struck with a hockey puck, or other circumstances. Commotio cordis is the cause of 2 [5] to 20% [6, 7, 14] of SCD cases in young athletes.

5. Gender and age of the victims

According to the US Registry, the age of inclusion in the analysis of SCD and cardiac arrest in athletes was limited to 39 years; 2153 deaths from all causes (89%) occurred in males and 253 deaths (11%) were in females (4). In mortality rate among the 842 athletes with autopsy-confirmed cardiovascular diagnoses, the incidence in males exceeded that in females by 6.5-fold, $P < .001$ ([6], 1172). An analysis of 61 cases of SCD that occurred during exercise in Spain in 1995–2001 revealed that the age of the athletes and those involved in sports reached 65 years (mean age 31.9 ± 14.2 years). In 59 cases vs. 2, the victims were male [15]. Among 60 squash players who died suddenly at the age of 22–66 years (46 ± 10.3), 59 individuals (98.3%) were also male [20]. However, women may dominate in some sports characterized by a relatively small number of SCDs or cardiac arrests, e.g., 90% in volleyball and 73% in softball [6]. The number of arrhythmias and SCD risk increases with age. However, this applies primarily to those who are not engaged in or who have retired from professional and competitive sports [6].

6. Circumstances of SCD and prodromal symptoms

When analyzing the circumstances of SCD in young athletes, it was observed that in 83% of cases, SCD occurred during or immediately after exercise, and only 17% was not associated with any physical activity [6]. In some cases, it was possible to obtain the medical histories of the victims or data on the presence of some

specific diseases or conditions or potential symptoms preceding the fatal episode. In 60 squash players who died suddenly, Northcote et al. [20] were performed an analysis of prodromal symptoms before death. In a decreasing order of symptom frequency, athletes with sudden deaths complained of chest pain, increasing fatigue, non-specific gastrointestinal disorders, a burning sensation in the heart area, feeling short of breath, pain in the ears or neck, non-specific malaise, upper respiratory tract infections, dizziness and/or palpitations, and severe headache. Five of the victims (8.3%) had no significant symptoms before death. Prodromal symptoms were more frequent in athletes than in nonathletes of the same age who died suddenly, 32 vs. 23%, respectively, as observed by Corrado et al. [21]. This suggests that even minor, non-specific health complaints in regularly training athletes must be taken seriously by doctors, coaches, and the athletes themselves, as they may herald the onset of a life-threatening event. Some conditions in athletes, often considered to be undoubtedly life-threatening, such as syncope, to the contrary, are not always associated with a risk of sudden death, although that risk should always be ruled out first. For example, cardiac diseases with a high risk of SCD that required a withdrawal from the sports were revealed only in two (0.4%) of 474 young athletes with syncope [22]; these diseases were hypertrophic cardiomyopathy (HCM) in one case and arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVC) in the other. In our study [23], no diseases possessing a risk of SCD and requiring a withdrawal from sports have been identified in any of the 34 high-level athletes who had a history of syncope.

7. Causes of SCD

Elucidation of the etiological causes of SCD in athletes is one of the most controversial issues in this area. Meanwhile, it is one of the key issues for the development of scientifically based methods for SCD prevention, selection of individuals suitable for sports, and primary and secondary prevention of SCD. Due to new technologies in diagnostics and an increasing number of studies in this area, the opinions on the etiology of SCD have changed considerably. In the 1980s, among all SCD cases in young athletes in the USA, HCM was diagnosed in 36% of athletes who died suddenly, with the maximum left ventricular wall thickness from 15 to 40 mm (mean 23 ± 5 mm) and an average weight of the heart of 521 ± 113 g, followed by (in a descending order) coronary artery abnormalities and borderline left ventricular hypertrophy, interpreted as possible HCM [6]. However, we cannot exclude the possibility that it was exercise-induced cardiac hypertrophy (which is a component of the non-pathological athlete's heart), myocarditis, ARVC, and ion-channel cardiac disease or channelopathies (long or short QT syndrome, Brugada syndrome, idiopathic ventricular fibrillation, catecholaminergic ventricular tachycardia), i.e., diseases that can only be determined by an ECG prior to death. The long QT syndrome (LQTS) is the most dangerous ion-channel cardiac disease in young person and sports accordingly. Modern diagnostic of LQTS (in the absence of secondary causes for QT prolongation) is based on the ESC criteria [9]. At the present days, mutation in 16 various genes have been identified (LQTS1–LQTS16). The LQTS1 most dangerous during sports activity because 90% cardiac events (SCD, cardiac arrest, syncope) occur due adrenergic triggers and in water [24]. Other pathologies, such as mitral valve prolapse, aortic rupture, aortic stenosis, dilated cardiomyopathy, Wolff-Parkinson-White syndrome, rare non-specific myocardial damage (sarcoidosis), and other causes, were recorded in 1–2% of cases each.

A smaller (though with a more extended age range (11–65 years) analysis of sports-associated SCD cases in Spain [15] has demonstrated that in most cases

the cause of SCD in all ages was ischemic heart disease (40.9%), arrhythmogenic cardiomyopathy (as in some cases there was not only right ventricular but biventricular dilatation, and this diagnosis was made) in 16.3% of cases, HCM (6.5%), left ventricular hypertrophy (4.9%), myocardial fibrosis (3.2%), nonatherosclerosis coronary artery abnormalities (3.2%), dilated cardiomyopathy (1.6%), etc. In 16.3% of cases, the cause of death remained unknown. When the observation group was divided into SCD cases occurring before and after 30 years of age, it was revealed that the majority of cases of ischemic heart disease were concentrated in the older age group (23 vs. 2 cases younger than 30 years) and that there was an equal number of cases of HCM, while ARVC, coronary artery abnormalities (so as spontaneous dissection), and all cases with uncertain autopsy results were more frequent among young individuals.

However, in the abovementioned French study [16] of SCD cases in athletes and persons regularly engaged in physical activity aged below 35 years, the percentage of HCM reached 10%, while cases classified as "unexplained death" accounted for 36%; according to the data from the US National Collegiate Athletic Association, published in 2015 [5], the structure of SCD included unexplained death (classified as sudden unexplained death - SUD) in 25% cases, confirmed HCM in 8%, and not otherwise specified HCM in 8%. The most up-to-date information on the subject is probably presented in the 2016 report by the British Registry of SCD in sports [4], where SUD in all age categories constituted 42% and HCM, 6%. Marked changes in the age dynamics of SCD etiology were also noted. In the age group of over 35 years, SUD constituted 28% (idiopathic left ventricular hypertrophy with fibrosis (ILVHF) accounted for the same percentage); at the age of 18–35 years, the proportion of SUD increased to 44% (ILVHF to 14%), and in the youngest group of <18 years, the frequency of SUD was the highest (56%), while ILVHF rates decreased to 10%. Rates of HCM and myocarditis confirmed by autopsy remained virtually unchanged with age at 6–8% for HCM and 1–2% for myocarditis. The frequency of identified ARVC moderately increased with age, from 6% in athletes under 18 years old to 14% at the age of 18–35 and 18% in athletes aged over 35 years.

8. Ethnic differences

There are some ethnic differences in SCD rates depending on its cause. In general, for over 27 years of observation in the USA, white males dominated in a large cohort of athletes who died suddenly (46%), followed by African Americans and other minority (43%), and white and black and other minority females (8 and 3%) [6]. However, an analysis of specifically cardiovascular SCD in those who died from HCM and coronary artery abnormalities revealed significantly higher (more than twofold) rates in African Americans, while Caucasians were still at the top of the list for ARVC and primary electrical diseases (channelopathy). In the European study [21], the range of diseases identified in athletes suddenly dying was almost the same, yet there were significant differences in the frequency of the main variants of myocardial damage; ARVC was detected in 24% of cases, HCM in 2%, and myocarditis in 10%. If the proportion of the three major variants of myocardial damage (ARVC, HCM, and myocarditis), detected in suddenly dying young American and Italian athletes, is compared, similar aggregate values are obtained, namely, 38% in Italy and 46% in the USA. Taking into account all potential ethnic differences or autopsy reports, there may be a different interpretation of similar pathomorphological changes.

Nevertheless, it is obvious that the main risk group for SCD in athletes includes those with life-threatening cardiac arrhythmias and myocardial changes. However,

the risk of SCD is significantly higher in athletes than in nonathletes with the same heart condition in the general population—by more than 5 times for ARVC, 2.6 times for coronary artery disease, 1.5 times for myocarditis, and more than 2 times for cardiac conduction system diseases [6].

9. SCD prevention in athletes

Solutions to this problem vary from country to country. In the USA, a group of American Heart Association (AHA) experts has proposed 12 steps that can help in the prevention of SCD in athletes at the initial screening stage [25]. These include the following conditions and medical history features:

Medical history:

1. Chest pain/discomfort on exertion
2. Sudden fainting/presyncope
3. Vertigo (dizziness) on exertion
4. Heart murmurs
5. High blood pressure (> 140/90 or more on the first measurement)

Family history:

1. Sudden death of the first-degree relatives aged under 50 years (first of all parents, brothers, sisters, and grandparents)
2. Cardiovascular disease in close relatives under 50 years
3. Cardiomyopathy, LQTS, Marfan syndrome, ARVC, or other conditions with a risk of life-threatening arrhythmias or coronary artery disease in relatives

Physical examination:

1. Femoral pulse
2. Marfan syndrome manifestations
3. Sitting BP measurements

It is noteworthy that an ECG is not included in this screening list. Supporting this approach, the guideline authors note that the rates of SCD in athletes in the USA and Italy (where an ECG is a compulsory component of the medical checkup in athletes before training) are about the same. A prospective cohort study in individuals aged below 36 years engaged in competitive sports was conducted in the Italian region of Veneto between 1979 and 1999. The most frequent cause of SCD in the study was ARVC (24%), followed by ischemic heart disease of atherosclerotic etiology (20%), abnormal outlet of coronary arteries (14%), and mitral valve prolapse (12%) [2]. Among older athletes (> 35–40 years), more than half of the cases of SCD were associated with ischemic heart disease, as in the general population.

Some other American studies support the use of an ECG as part of a medical checkup of athletes at the early stages. A large study of 5615 young athletes conducted in Nevada (USA) demonstrated that the sensitivity of an ECG in the identification of serious cardiovascular pathology was 70% compared to 3% in the group of athletes where only a medical history and physical examination were used [26]. The specificity of ECG was 97.4%. Only 0.4% (22 of 5615) were withdrawn from sporting competitions. The estimated "cost" of a life saved by using only clinical and medical history data in this study was USD 84,000, while by adding an ECG, it may be reduced almost twofold (USD 44,000).

In the Japanese study [27], the researchers evaluated ECG screening results in 68,503 school students, and the SCD incidence in adolescents involved in competitive sports was on average 1.32 per 100,000 per year. Three deaths occurred in children without preceding syncope or SCD cases in the family history. In one 14-year-old boy, HCM had been identified earlier, at the pre-screening stage, and he was withdrawn from the sport, but he still died suddenly while jogging. In two other cases (13- and 16-year-old boys), SCD occurred while playing handball and basketball, and both had a normal ECG, and no pathological changes were identified during autopsy. The estimated "cost" of a life saved by using ECG screening in this study was USD 8000 (26).

Together with history and physical examination, the mandatory instrumental part of the cardiac examination in members of Russian junior national teams (less 18 years old) consists of a 12-lead resting ECG (with using original normal ECG criteria, which were elaborated at 500 young elite athletes) [28], EchoCG, and bicycle ergometry or treadmill test. A more thorough examination (Holter monitoring, analysis of heart rate turbulence, ventricular late potentials, magnetic resonance therapy, tilt test, etc.) depends on the changes detected at the preliminary stage, as well as medical history features, such as syncope, sudden death in the family, ECG changes, etc.

Despite a rather sizable document, it seems to us that for so-called elite athletes in high-level sports, it would be beneficial to include Holter monitoring, for special indication in athletes with syncope, arrhythmias, palpitation, and pathological changes of ECG—long or short QT and others [29, 30].

The European experience, which formed the basis for the International Olympic Committee recommendations, includes gathering a detailed medical history with an emphasis placed on the identification of complaints of potentially arrhythmogenic origin (palpitations, heart pain, etc.), syncope, cardiovascular disease, and cases of SCD in the family, especially at a young (under 50 years) age, and physical and ECG examinations, especially focusing on abnormal heart murmurs, alterations in blood pressure, ECG criteria of heart chamber hypertrophy, signs of myocardial ischemia, shortening or lengthening of the QT and PR intervals, and ventricular and supraventricular tachyarrhythmias [2]. The use of such screening, including an ECG in assessing the risk of SCD for 25 years in Italy, has shown that the incidence of SCD in young athletes aged 12–35 years engaged in competitive sports declined from 3.6 SCD cases per 100,000 per year (one death per 27,777 athletes) in 1979–1981 to 0.4 deaths per 100,000 per year (one death per 250,000 athletes) in 2003–2004. In general, SCD in athletes included in the screening decreased by 89%, whereas the incidence of SCD in the population not covered by the screening has not changed during the period [2]. This was due primarily to an increase in early detection and withdrawal from competitive sports of young people suffering from HCM, ARVC, and dilated cardiomyopathy (from 4.4% in 1979 to 9.4% in 2004). ECG changes may be the only early marker of a risk of life-threatening arrhythmias and SCD in athletes. However, the interpretation of ECG in athletes has its own peculiarities; any potentially life-threatening changes may be affected by conditions specific

only to sports. For instance, the QT interval is longer in athletes [31]; its shortening was revealed when using some anabolic agents in athleticism [32]. The emergence of new, noninvasive methods of electrocardiological diagnostics seems to be promising for risk group stratification in sports. Certain features of the QT interval frequency adaptation [33] and microvolt T-wave alternans [34, 35] may aid in the stratification of athletes with electrical instability of the heart and an increased risk of life-threatening arrhythmias and SCD, and they may differentiate pathological and non-pathological transformations of the athlete's heart. The 2015 European Society of Cardiology Guidelines for the prevention of SCD proposes the following algorithm of SCD prevention in athletes [9]:

Prevention of sudden cardiac death in athletes (ESC).

Recommendations	Class	Level	Reference
Careful history taking to uncover underlying cardiovascular disease, rhythm disorder, and syncopal episodes or family history of SCD is recommended in athletes	I	C	This panel of experts
Upon identification of ECG abnormalities suggestive of structural heart disease, echocardiography and/or CMR imaging is recommended	I	C	This panel of experts
Upon identification of ECG abnormalities suggestive of structural heart disease, echocardiography and/or CMR imaging is recommended	IIa	C	This panel of experts
Physical examination and resting 12-lead ECG should be considered for pre-participation screening in younger athletes	IIa	C	This panel of experts
Middle-aged individuals engaging in high-intensity exercise should be screened with history, physical examination, SCORE, and resting ECG	IIa	C	[36]
Staff at sporting facilities should be trained in cardiopulmonary resuscitation and on the appropriate use of automatic external defibrillators	IIa	C	[37, 38]

ESC = European Society of Cardiology, CMR = cardiac magnetic resonance, ECG = electrocardiogram, SCD = sudden cardiac death, SCORE = systematic coronary risk evaluation, Class = class of recommendation (I, IIa, IIb, III), Level = level of evidence (A, B, C), Reference = reference(s) supporting recommendations.

The main fatal arrhythmia leading to death is ventricular fibrillation. If this develops, the most effective method for treatment is electric defibrillation. As was shown above, the majority of SCD cases in athletes occur during engagement in sports [2, 6], in contrast to similar data from nonathletes where up to 80% of SCD cases are registered at home [29, 30]. This enables the creation of a system of more effective medical aid in the first few minutes after cardiac arrest during physical activity. According to the US National Registry of Sudden Death, in cases of sudden death associated with exercise in young people over the period from 2000 and 2006, the percentage of survival in the latter 3 years of the study almost doubled compared to the first 3 years, reaching 14–17% [39]. And only in 2006, similar rates of successful recovery after cardiac arrest were achieved by using automatic external defibrillators (AED), which are publicly available, and electrical defibrillation performed by specialized emergency teams [39]. There were many reports of successful defibrillation in cardiac arrest in athletes during physical activity or competition [19].

Labor costs, effectiveness, and economic costs of comprehensive preventive screening in 785 athletes aged 5–65 years who are engaged in high-intensity sports [38] were also evaluated. As a result of this screening, newly diagnosed

cardiovascular diseases were identified in 2.8% of athletes; economic costs were USD 199 per athlete. The researchers consider such a screening to be warranted and affordable. The guidelines also highlight the importance of training coaches and staff in sports centers on the actions needed in case of emergency, performing cardiopulmonary resuscitation and the use of AED, both in athletes and spectators during major competitions [37].

Regular physical activity in the young is the most effective prophylactic for all cardiac diseases, but SCD in young athletes remains rare but a very tragic event for the family, friends, and society, which can arise deep negative resonance media about sports. Prevention of SCD in the young athletes is based on careful pre-participation screening of young athletes for identifying diseases with risk of SCD during sports activity and to elaborate a detailed plan of the first aid during and after cardiac events in sports competition and any sports activity, it is necessary to perform careful pre-participation screening of young athletes for identifying diseases with high risk of SCD during sports activity and to elaborate a detailed plan of the first aid after cardiac events during sports competition and any sports activity.

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