Sudden cardiac death in athletes

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INTRODUCTION

The impact of prolonged, intensive, and regular training on the cardiovascular system has been investigated for many years. The positive influence of exercise on cardiovascular risk factors is well known. However, since the ancient times of Philippides (or Pheidippides), the first marathoner, who died after strenuous exercise, the question has been raised about possible negative side effects of sport. The epidemiology and prevention of sudden cardiac death (SCD) in athletes is still a subject of ongoing debate. Those rare, tragic events draw public attention and sometimes discredit the positive influence of regular exercise. Therefore, one the most important goals for modern sports cardiology is to minimise the risk of SCD in athletes to an “inevitable rarity”. The proof of the positive impact of exercise on cardiovascular health is well established. Regular physical activity can decrease arterial blood pressure, and improve lipid and glucose level control. Physical activity alters not only the heart anatomy but also promotes physiological pathways on a molecular level [1].

Positive influence on outcomes is seen in the low-risk general population as well as in the high-risk population of patients with recognised cardiovascular disease [2, 3]. The obvious

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positive influence of moderate exercise was often confronted with extreme exercise load in professional athletes. The “U” or “J” shape curve of mortality was postulated in case of the amount of training; nevertheless, even professional athletes participating in the most demanding sports seem to have better prognosis than age- and sex-matched non-athletes [4, 5]. It was also confirmed for many different sports participants in a recent systematic review [6]. Longer life expectancy has been reported in endurance sports such as long distance running but also in some sports that are not perceived as healthy at all. For example, in professional American Football, where some positions require extreme body size and players are often obese, expected lifetime is longer than in the general population, as reported by the Centre for Disease Control and Prevention (http://www.cdc.gov/niosh/pdfs/nflfactsheet.pdf). The explanation of a positive influence of exercise on prognosis exceeds the reduction of cardiovascular risk factor mentioned before. Also, non-cardiac risk reduction was demonstrated in epidemiologic studies concerning athletes, such as lower incidence of colon and breast cancer [7].

**Epidemiology of SCD in Athletes**

The aetiology of SCD in athletes is age-dependent, similarly to in the general population. In individuals > 35 years old the undisputable reason of SCD is early onset of coronary arteries disease (CAD). The incidence of SCD in younger (< 35 years old) athletes varies in different populations and is estimated at 0.5–4/100,000/year. Those large differences may be explained by diverse geographic prevalence of diseases leading to SCD in athletes but also by the methodology of registries. Cardiac societies have recently expressed concern about the quality of available data and addressed the need for large (international) registries [8]. One of the highest incidences was reported in the Veneto region of Italy [9]. Most registries show that prevalence of SCD is slightly higher in athletes then in the general population (which is estimated at 1/100,000), but the data are not univocal. There are several methodological problems with reliable comparison, for instance with estimation of the number of competitive athletes in certain populations to name one. Even if the sporting activity itself does not increase the risk of SCD, it can still be a trigger of life-threatening arrhythmias in prone individuals. Despite the fact that the positive influence of exercise is difficult to discuss, a short-term increased risk of SCD during intensive exercise can be observed. This two-fold higher incidence rate lasting for about an hour after exercise was previously called “the paradox of sport” [10]. All available registries show that SCD is much more possible in male athletes (80–95% of all cases). The other known risk factors of SCD are age and Afro-Caribbean origin. Age is strongly related with the development of CAD, while the most probable explanation of racial differences is the higher prevalence of hypertrophic cardiomyopathy (HCM) in Afro-Caribbeans.

Due to the high percentage of American athletes with African origins, the HCM was and still is cited as the single most important cause of SCD, according to the largest registries from the United States [11, 12]. To the contrary, in the registry from Germany published in 2015 HCM was identified as a reason in only 5% of athletes, and the most common cause of death < 35 years was myocarditis [13]. What is more, very low incidence of sport-related SCD (1.2 per million) was estimated, mainly due to a liberal definition of an athlete in this publication. No nationwide registries have been performed in Poland, but due to geographic and racial similarities, German epidemiology of SCD may correspond better to the Polish situation than North American or Mediterranean. Irrespective of the actual primary cause, the direct reason for cardiac arrest in athletes (both young and > 35 years old) is ventricular arrhythmia. Therefore, widespread knowledge about basic life support and accessibility of automated external defibrillators is crucial, especially in athletic mass events. The French registry from 2011 showed that those two factors were most important in predicting the survival of SCD during exercise in the general population [14].

**Strategies of SCD Prevention in Athletes**

Since the publication of the results of an Italian nationwide program for SCD prevention there has been an on-going discussion between cardiac societies in the United States and Europe on how to perform screening. In general, there is agreement that preparticipation screening should be performed based on standardised medical history and physical examination protocols. The one introduced by the American Heart Association (AHA), which is one of the most often used, has recently been revised and now comprise 14 points (Table 1) [15]. The ongoing debate is about the need to incorporate additional exams, especially electrocardiogram (ECG). So far, the one and only proof for the efficiency of the ECG-based screening protocol from Italy was published in 2006 and showed a significant reduction of SCD from 4 to 0.5 per 100,000 athletes over nearly 20 years of follow-up [9]. The implementation of the screening program in Italy was accompanied with very profound logistic and legislative efforts, as specialisation in sports cardiology was established together with a net of regional sport cardiology institutes. The Italian experience was the main reason for the proposed European recommendations in 2005 [16]. Consequently, cardiologic societies from the United States, for many years, rejected the idea of a nationwide ECG-based protocol. However, the AHA recommendations from 2014 and 2015, Eligibility and Disqualification Recommendations, are less strict in this topic, while the ECG (or echocardiography) “…may be considered in relatively small cohorts of young healthy people from 12 to 25 years of age, not necessarily limited to competitive athletes” [15]. Both American documents present certain arguments against ECG implementation as a screening method: general
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Document content: The page discusses the prevalence and risk factors for sudden cardiac death (SCD) in athletes, highlighting the importance of preparticipation cardiovascular screening. It mentions the American Heart Association questionnaires and the criteria used for interpreting athletes' ECGs. The text also touches on the controversy surrounding the economic impact of such screenings and the potential for false positives.

**Table 1.** The 14-element American Heart Association questionnaire for preparticipation cardiovascular screening of competitive athletes

<table>
<thead>
<tr>
<th>Medical history*</th>
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<tbody>
<tr>
<td><strong>Personal history</strong></td>
</tr>
<tr>
<td>1. Chest pain/discomfort/tightness/pressure related to exertion</td>
</tr>
<tr>
<td>2. Unexplained syncope/syncope†</td>
</tr>
<tr>
<td>3. Excessive and unexplained dyspnea/fatigue or palpitations, associated with exercise</td>
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<tr>
<td>4. Prior recognition of a heart murmur</td>
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<td>5. Elevated systemic blood pressure</td>
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<td>6. Prior restriction from participation in sports</td>
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<td>7. Prior testing for the heart, ordered by a physician</td>
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<tr>
<td><strong>Family history</strong></td>
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<tr>
<td>8. Premature death (sudden and unexpected, or otherwise) before 50 years of age attributable to heart disease in ≥ 1 relative</td>
</tr>
<tr>
<td>9. Disability from heart disease in a close relative &lt; 50 years of age</td>
</tr>
<tr>
<td>10. Hypertrophic or dilated cardiomyopathy, long-QT syndrome, or other ion channelopathies, Marfan syndrome, or clinically significant arrhythmias; specific knowledge of genetic cardiac conditions in family members</td>
</tr>
<tr>
<td><strong>Physical examination</strong></td>
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<tr>
<td>11. Heart murmur†</td>
</tr>
<tr>
<td>12. Femoral pulses to exclude aortic coarctation</td>
</tr>
<tr>
<td>13. Physical stigmata of Marfan syndrome</td>
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<tr>
<td>14. Brachial artery blood pressure (sitting position)§</td>
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</table>

*Parental verification is recommended for high school and middle school athletes.
†Judged not to be of neurocardiogenic (vasovagal) origin; of particular concern when occurring during or after physical exertion.
‡Refers to heart murmurs judged likely to be organic and unlikely to be innocent; auscultation should be performed with the patient in both the supine and standing positions (or with Valsalva manoeuvre), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction.
§Preferably taken in both arms.

Low incidence of SCD, large population requiring screening resulting in high costs of ECG, and even higher costs of medical work-up of athletes with false-positive ECG result. This last point is of the greatest concern for the supporters of ECG implementation. As a result of the success of the Italian screening program, a similar protocol was introduced in Israel in 1997. In 2011 the results of the Israeli registry were presented, which showed similar numbers of deaths in athletes before and after the screening implementation [17]. The authors concluded that ECG is inefficient in reduction of SCD risk; however, the quality of data (newspaper reports) and once again the estimated number of athletes used to assess incidence (unchanged over two decades) were later discussed. In 2010 the result of retrospective analysis of autopsy reports of young individuals in Denmark between 2000 and 2006 were published. Contrary to other publications, it showed that the incidence rate of SCD was lower in athletes (1.2 vs. 3.4/100,000) than in the general population [18]. Based on this data and due to the controversies stated before, despite the recommendations of the European Society of Cardiology (ESC), the Denmark Cardiac Society recommend against any form of cardiovascular screening in athletes.

**ATHLETES’ ECG**

Despite the above-mentioned controversies about the strategies of SCD prevention in athletes, ECG assessment is recommended in many countries, including Poland. In 2007 a large study including ECGs of > 32,000 Italian athletes was presented, which was essential to formulate ESC recommendations for interpretation of athletes’ ECGs [19, 20]. Those recommendations divided ECG findings in two subgroups:
- group 1 — “benign” or exercise related, which are common in athletes (up to 80%) and do not require further investigation [21, 22];
- group 2 — “suspected” or related to underlying serious cardiovascular disease and therefore require further medical work-up.

The authors of the first studies indicated that approximately one in ten athletes have group 1 changes in the ECG. Other studies evaluating proposed ECG criteria showed that this can be the case in as many as one in four athletes [23]. Those numbers confronted with relatively low incidence of SCD indicate high prevalence of false positive findings in athletes ECG, which was the main argument against ECG-based screening. In order to overcome this problem many new studies and registries concerning athletes ECGs were issued. In PubMed there are more than 690 publications dating from 2006 to 2015 when searching with “athletes ECG” as the key words (access date on 20th December 2015). As a result of this intensive research, several modifications of criteria were proposed. The most established modifications, known as the Seattle criteria, were proposed in 2013. In Table 2 key modifications are presented [24–26]. The most important finding in athletes’ ECGs from the group 2 (“suspected”) is pathologic T wave inversion (TWI). Deep, symmetric, negative T waves in two consecutive ECG leads (except for aVR, III and V1) may be one of the first phenotype expressions of cardiomyopathies (HCM or arrhythmogenic right ventricular cardiomyopathy [AVRC]). In a large prospective observation of 12,550 athletes 123 (< 1%) had TWI (defined by authors as > 2 mm in three consecutive leads) [27]. During initial assessment 39 of 123 (31%) were diagnosed with a cardiovascular disorder. What is more important, during eight years of follow-up from the remaining 81 athletes with TWI, one died due to HCM, and three were later diagnosed with HCM, one with dilated cardiomyopathy, and six others developed other cardiovascular disorders. The prevalence of TWI and other group 2 findings is much more common in black athletes, what makes implementation of ECG in preparticipation screening...
even more difficult in this group [28, 29]. The redefinition of ESC athletes’ ECG criteria helped to lower the number of positive findings in Afro-Caribbean athletes from nearly 50% to 18% (Seattle criteria) or 11% (“refined criteria”) (Table 2) [30].

**CARDIOVASCULAR IMAGING IN PREVENTION OF SCD IN ATHLETES**

For many years echocardiography was the most often used modality in the assessment of heart morphology and function in athletes. As in other fields of cardiology, we observe the increasing role of cardiac magnetic resonance (CMR) imaging. Even though recent recommendations from the AHA indicate that echocardiography “may be considered” as a screening method due to the cost-effectiveness discussed above, the implementation of cardiovascular imaging in the protocol is not possible in the whole population of athletes. Some studies showed in relatively small populations that incorporation of echocardiography into a screening protocol did not reveal life-threatening pathologies, but some important, symptomless conditions such as congenital defects can be identified [31, 32]. Still, the role of cardiovascular imaging is very important in athletes undergoing ECG screening. The most important area for imaging is differentiation of the so-called the “grey zone” — overlapping signs of athletes’ heart and cardiomyopathies. Modern echocardiography, including strain analysis, was proven to help in distinguishing HCM or hypertensive hypertrophy and athletes’ heart. Left ventricle (LV) deformation analysis can identify deterioration of systolic function very early, in a subclinical state [33]. Even in extreme examples of physiological remodelling of LV, global longitudinal strain was normally contrary to HCM and hypertensive patients. Furthermore, left atrial strain analysis was proven as a very sensitive marker of LV dysfunction. Left atrium strain was successfully used in the athletic population and helped in differentiation. CMR can also be used in cases of suspected HCM. Resonance can easily identify pathologic hypertrophy in sites difficult to assess in echocardiography (apical HCM). The usage of gadolinium helps to localise places of pathologic fibrosis. Still, while no single method can identify HCM with 100% specificity, a multimodality approach is recommended [34]. The differential diagnosis in difficult cases can require resting and stress echocardiography using tissue Doppler and deformation analysis, followed by CMR. Final diagnosis may require the temporal withdrawal from exercise. Due to its better reproducibility, CMR can be used to minimise the time of deconditioning.

Right ventricle (RV) assessment is an important part of athletes’ heart imaging because the ARVC is, in some registries, the single most common reason for SCD in athletes.

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**Table 2. Comparison of criteria of “suspected” (group 2) findings in athletes’ electrocardiograms**

<table>
<thead>
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<tbody>
<tr>
<td>Negative T wave</td>
<td>&gt; 2 mm in two consecutive leads (V1 excluded)</td>
<td>&gt; 1 mm in two consecutive leads (III, aVR, V1 excluded)</td>
</tr>
<tr>
<td>ST depression</td>
<td>Any ST depression</td>
<td>&gt; 0.5 mm in two consecutive leads</td>
</tr>
<tr>
<td>Pathologic Q waves</td>
<td>&gt; 3 mm depth and &gt; 40 ms in two consecutive leads (III, aVR, excluded)</td>
<td></td>
</tr>
<tr>
<td>QRS right axis deviation</td>
<td>&gt; 110 deg</td>
<td>–</td>
</tr>
<tr>
<td>RVH (Sokolov-Lyon &gt; 10.5 mm)</td>
<td>+</td>
<td>Only with dextrogram &gt; 110 deg</td>
</tr>
<tr>
<td>Right atrium enlargement</td>
<td>&gt; 2.5 mm in II</td>
<td>-</td>
</tr>
<tr>
<td>Left atrium enlargement</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>QRS left axis deviation</td>
<td>&lt; −30 deg</td>
<td>&lt; −30 deg</td>
</tr>
<tr>
<td>Complete LBBB</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Complete RBBB</td>
<td>+</td>
<td>Only with: deep T wave inversion, ST-T elevation or wide R’</td>
</tr>
<tr>
<td>Any IVCD</td>
<td>&gt; 110 ms</td>
<td>&gt; 140 ms</td>
</tr>
<tr>
<td>Prolonged QTc</td>
<td>&gt; 440 ms (men)</td>
<td>QTc ≥ 470 ms (men)</td>
</tr>
<tr>
<td></td>
<td>&gt; 460 ms (women)</td>
<td>QTc ≥ 480 ms (women)</td>
</tr>
<tr>
<td>Short QTc</td>
<td>&lt; 380 ms</td>
<td>&lt; 320 ms</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>≥ 2 ventricular extrasystoles (per 10 s)</td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>&lt; 30/min; pause &gt; 3 s</td>
<td>&lt; 30/min; pause &gt; 3 s</td>
</tr>
<tr>
<td>Other (AF, AFI, WPW, Brugada syndrome)</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

AF — atrial fibrillation; AFI — atrial flutter; ESC — European Society of Cardiology; IVCD — intraventricular conduction delay; LBBB — left bundle branch block; RBBB — right bundle branch block; RVH — right ventricular hypertrophy; WPW — Wolff-Parkinson-White syndrome.
The role of computed tomography in athletes

Multislice computed tomography (CT) is a modality that gives a unique opportunity to noninvasively assess the anatomy of the heart, and even more importantly, the coronary arteries. The coronary artery anomalies were reported as the second most common reason for SCD in young athletes [12]. The most often fatal anomaly is “malignant” course of the right coronary or circumflex artery between the aorta and pulmonary truncus [47]. Nonetheless, CT cannot be perceived as a screening procedure in this population. The development of modern CT scanners has helped to reduce irradiation during the examination, but the potential harmful influence of X-rays in young individuals remains high given the expected low number of positive findings. However, in older athletes CT angiography gives a unique opportunity to assess the degree of atherosclerosis in coronary arteries. CT angiograph has a very high negative predictive value, normal coronary arteries in CT are connected with excellent long-term outcomes. CT can be used for assessment in athletes with risk factors of atherosclerosis, especially those with positive family history of premature CAD. The ongoing MARC trial addresses this issue in the athletic population [48]. Besides the need for radiation, the expected low percentage of positive findings requires thorough cost-effectiveness of CT assessment. While implementation in the low-risk population of professional athletes may be inefficient, it can be useful in the higher risk, previously non-active middle-age population described above. CT has better sensitivity than ECG exercise test, which can be recommended in symptomless individuals before beginning regular physical activity, according to ESC guidelines (IIbC). As reported by Tsiliakis et al. [49], in 50 asymptomatic, > 45 years old marathon runners with negative exercise test, three cases of moderate atherosclerotic changes and one requiring intervention were found in CT [49]. Exercise test can also be used to select candidates for CT. From 940 athletes > 30 years undergoing maximal treadmill exercise test for sport eligibility, 44 had positive or equivocal results [50]. The prevalence of significant coronary lesions was more than two times higher in those athletes (six of 44). In addition, seven cases of non-malignant coronary artery anomalies were found. To conclude, CT coronary angiography seems to be a promising method in the assessment of older athletes, but the proper selection of candidates needs to be established.

Summary

Even though the subject of SCD has been present in medical literature for many years, there remain many questions as yet unanswered. There are no data on the incidence of SCD in athletes in Poland. Even if rare, SCD in young athletes is a tragic event that draws public attention and can be misinterpreted. As postulated by ESC, ECG should be implemented in the preparticipation screening of young athletes, but proper interpretation...
is crucial to avoid unnecessary disqualifications or, even worse, eligibility of individuals with life-threatening conditions. New diagnostic tools can be helpful in the differentiation of athletes from the "grey zone". There is undisputed proof of the positive impact of physical activity on health and longevity, so sport should be a nonpharmacological prescription for the whole population. As the fashion for a healthy lifestyle is reaching "epidemic" proportions, the greatest upcoming challenge for modern sports cardiology is the means of proper assessment of middle-aged individuals to allow safe exercise.

**Conflict of interest:** none declared

**References**


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