Preparticipation screening of elite and recreational athletes

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Abstract
Regular physical activity is associated with appreciable cardiovascular benefits but, paradoxically, vigorous exertion increases the risk of sudden cardiac death (SCD) in athletes by 2- to 3-fold compared with nonathletes. The exact incidence of sports-related SCD remains unclear owing to differing methodology and heterogeneous population comparisons. Younger athletes are most commonly affected by underlying inherited/congenital cardiac disease whereas in older athletes aged >35 years coronary artery disease (CAD) predominates by far. However, different regional distribution patterns of cardiac diseases as a result of heterogeneous ethnic population compositions have to be taken into account. Preparticipation screening with personal/family history, physical examination and resting electrocardiogram has the potential to detect many causes of SCD, which reduces its incidence. However, in older athletes, this screening modality is of limited value because of the high prevalence of CAD. Therefore, an individualised screening approach is adopted for athletes aged >35 years according to their risk profile and the intended level of physical activity. As cardiovascular screening cannot detect all individuals at risk, particular focus should be put upon secondary prevention measures, including education about adequate cardiopulmonary resuscitation and availability of automated external defibrillators at sporting facilities. In this review, we summarise the current state of knowledge of SCD in athletes of different age groups with regard to epidemiology. Furthermore, we discuss primary and secondary prevention strategies such as cardiovascular screening recommendations and on-site prevention.

Key words: sudden cardiac arrest; athletes; cardiovascular screening

Introduction
Participation in regular physical activity has appreciable cardiovascular benefits such as a decrease in all-cause and cardiovascular mortality as well as a decrease in metabolic disorders [1–4]. Paradoxically, athletes with underlying cardiovascular diseases are at greater risk of sports-related sudden cardiac death (SrSCD). Data from Italy have shown an almost 3-times greater risk of sudden cardiac death (SCD) among competitive athletes compared with their sedentary counterparts [5]. Intense physical activity is not per se the cause of the increased mortality – it rather acts as a trigger for sudden cardiac arrest (SCA) in the presence of underlying cardiovascular diseases [5, 6]. The mechanism is typically ventricular arrhythmia, probably due to exercise-induced high levels of catecholamines, dehydration, electrolyte disturbances and increased platelet aggregation [7–9]. Unusually high exercise intensities increase the relative risk of SrSCD, especially in recreational athletes with a low physical fitness or in individuals who are in the early phase of returning to exercise [10, 11]. As an increasing number of “older athletes” are participating in competitive sporting events (e.g., marathon running), the incidence of SrSCD in older adults is expected to rise [8, 12]. It can be assumed that the majority of those older athletes have not undergone preparticipation cardiovascular screening (PPS) beforehand. Furthermore, a great number of so-called ‘ambitious recreational athletes’ are pushing themselves too hard above their usual limits during competition. Therefore, the awareness of SrSCD as an important issue of public health in general has to be broadened within the society.

The present review focuses on the incidence and aetiology of SrSCD in elite and recreational athletes of different ages and provides insight into prevention strategies such as PPS and on-site prevention.

Abbreviations
AED = automated external defibrillator
AHA = American Heart Association
ARVC = arrhythmogenic right ventricular cardiomyopathy
CAD = coronary artery disease
CPR = cardiopulmonary resuscitation
ECG = electrocardiogram
ESC = European Society of Cardiology
PPS = preparticipation screening
SCA = sudden cardiac arrest
SCD = sudden cardiac death
SrSCD = sports-related sudden cardiac death
Incidence of sudden cardiac death

The exact incidence of SrSCD is debatable. An annual incidence of about 0.7–3.0 per 100,000 athletes can be assumed in young competitive athletes <35 years of age, although a wide range of incidences has been described (table 1). Differences between current estimates are due to differing methodology and comparison of heterogeneous populations. Factors affecting case identification include the definition of an athlete, methods of data acquisition, lack of mandatory reporting requirements in most settings, the inclusion or exclusion of cases based on time and location of the event, inclusion of all cardiac events (including survivors) versus only those resulting in death and the population examined [13]. The US Registry for Sudden Death in Athletes calculated the incidence of SCD for US athletes aged 8–39 as 1:164,000 [14]. In a prospective, observational study in Italy from 1979 to 1999 that analysed regional registry data with mandatory reporting systems, the reported rate of SCD was 1:43,478 in athletes aged 12–35 [5]. The disparity in incidence numbers between Italy and the USA may be due to the differing ethnic populations. However, different methods of measuring incidence with retrospective cohorts based on media reports and registries versus a prospective mandatory reporting system with a reliable denominator may also play an important role [13]. A study analysing the incidence of SCD associated with half-marathon and marathon races came to a very low incidence rate with 0.5 per 100,000 [15], whereas data from US college athletes demonstrated an overall incidence rate of 1:43,770 with further identification of high-risk subgroups such as men (1:33,134), African-Americans (1:17,696) and basketball athletes (1:11,394) [16]. The above mentioned high-risk subgroups men and African-Americans were also identified by other studies [5, 14, 17].

The incidence of SCD in older athletes aged >35 years is expected to rise as a growing number of older individuals takes part in organised sports and competitive sports events. However, prospective national registries examining the incidence and aetiology of SrSCD not only in young competitive athletes but also in elderly recreational sports participants are rarely established. By definition, a “competitive athlete” is a subject who participates in an organised team or individual sport that requires extensive and intensive systematic training and regular competition against others, whereas a “recreational athlete” is an individual who participates in informal recreational sport without competition against others, on either a regular or an inconsistent basis. A prospective 5-year study of SrSCD in the general population of France reported an incidence of 4.6 SrSCDs per 1 million residents of France per year. The overall average age was 47 ± 16 years with most of the cases occurring in male athletes [18]. The striking male predominance is in accordance with our own ongoing prospective registry in which SrSCDs in the general population in Germany are covered (www.scd-deutschland.de). After 30 months of observation, 97% of the 144 cases detected occurred in men and the overall mean age was 47 ± 16 years. These findings emphasise that men are at significantly higher risk compared with women and that the focus has to be put on recreational older athletes as well.

Aetiology of sudden cardiac death

The aetiology of SCD varies greatly in different studies that were conducted in different parts of the world. The most common causes in young athletes <35 years of age are genetic or congenital cardiovascular abnormalities. Hypertrophic cardiomyopathy accounted for the majority of fatal cases in several North American studies, whereas arrhythmogenic right ventricular cardio-

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SCA = sudden cardiac arrest; SCD = sudden cardiac death; M = male; F = female

Table 1: Incidence studies of SCD/SCA in different cohorts.
myopathy (ARVC) was responsible for up to one quarter of SrSCDs in the Veneto region [14, 19–21]. The high rate of ARVC may be explained by the fact that Italy introduced systematic preparticipation screening with a 12-lead electrocardiogram (ECG), resulting in efficient detection of hypertrophic cardiomyopathy [22]. Thus, other cardiovascular disease entities such as ARVC became responsible for a greater proportion of SCDs in Italian athletes. Other causes of SrSCD in younger athletes include coronary artery anomaly (CAA), which may be the third most common cause, dilated cardiomyopathy and to a lesser extent myocardial bridging [12, 14]. In 2%–10% of young athletes who die suddenly and have no evidence of structural heart disease, inherited cardiac ion channelopathies including long and short QT syndrome, Brugada syndrome and catecholaminergic polymorphic ventricular tachycardia may be the cause of cardiac arrest [14, 17, 21]. Myocarditis, typically caused by viral infections, is considered to be the cause of death in around 3%–8% of athletes, but may be underestimated in certain subpopulations [14, 17]. Myocarditis frequently escapes discovery by established screening procedures because its manifestation follows infections of other organs, which spread to the heart and which are unlikely to be present when screening is performed. Interestingly, a Danish study group found myocarditis to be the most common structural cause of cardiac death in the 1–18-year-old group [23]. In our prospective registry, myocarditis predominated in young athletes and the mean age in subjects with a proven myocarditis was 24.5 ± 10.4 years. Thus, myocarditis may be more common in young athletes and might also be a triggering co-factor in fatal cases diagnosed with other structural cardiac diseases during autopsy.

In older athletes, coronary artery disease (CAD) is the most common cause of SrSCD, identified in more than 80% of cases [8, 24–26]. Interestingly, a recent study has found that CAD already represents the main risk factor for SCD in the age group 25–35 years [27]. The surprisingly high frequency of premature CAD was also observed in a prospective study by Corrado et al. and confirmed by a study by Solberg et al. [5, 28]. These findings may raise questions about the traditional age cut-off of 35 years separating younger from older athletes.

**Cardiovascular screening**

By means of standardised cardiovascular screening, many potential causes of SCD can be detected and treated in the early stages, which leads to a reduction in the incidence of SCD [22]. For various reasons (including different cost structures of individual countries as well as regionally different distribution pattern of cardiac diseases), there is currently no international consensus regarding a standardised medical screening procedure between the various professional medical associations. In Italy, a nationwide programme including a systematic evaluation of competitive athletes prior to participation, was introduced in 1982. This programme was based on personal/family history, physical examination and a 12-lead ECG [22]. This subsequently led to a significant reduction in sudden death of young athletes, in particular through the prevention of SCD on the basis of a cardiomyopathy [22]. The current recommendations of the European Society of Cardiology (ESC) and the International Olympic Committee include a 12-lead ECG in addition to a personal/family history, physical examination and a 12-lead ECG [22]. This subsequently led to a significant reduction in sudden death of young athletes, in particular through the prevention of SCD on the basis of a cardiomyopathy [22]. The current recommendations of the European Society of Cardiology (ESC) and the International Olympic Committee include a 12-lead ECG in addition to a personal/family history and a physical examination [29, 30] (fig. 1). In contrast, the American Heart Association (AHA) advocates only personal/family history and physical examination [31]. This is attributed to impracticality and a lack of funding guarantees in the US, and the cost-benefit ratio (also with reference to the expensive additional diagnostic of “false positive” ECGs) appears unfavourable.

In general, the resting ECG remains the gold standard for detection of electrical abnormalities such as Wolff-Parkinson-White syndrome and ion channelopathies. In addition, it is very effective in identifying cardiomyopathies. For example, ECG findings are abnormal in >90% of individuals with hypertrophic cardiomyopathy and >75% of individuals with ARVC [32, 33]. However, underlying cardiac disorders such as CAA or CAD usually escape the resting ECG and early stage cardiomyopathies may not be detected either.

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**Figure 1:** Screening recommendations for competitive athletes aged <35 years.
Concerns regarding ECG screening in young athletes are mainly due to the potential number of false-positive tests resulting in unnecessary investigations or even the false disqualification of athletes [24, 31]. The overlap between physiological ECG changes as a result of cardiac adaptation to sustained physical exercise (athlete’s heart) and similar changes seen in pathological states is important to consider, and evaluation should be performed by experts in the field of sports cardiology and inherited cardiac diseases [34, 35]. Physiological ECG findings in athletes include sinus bradycardia, sinus arrhythmia, atrioventricular block I (and possibly IIa), as well as isolated voltage criteria for left ventricular hypertrophy and repolarisation changes which all may be classified as abnormal in a nonathlete population [36]. These normal ECG findings may be seen in ~90% and do not require additional diagnostic work-up. Only 5%–10% of ECG findings in athletes are regarded as an expression of possible underlying cardiac diseases, notably cardiomyopathies and ion channelopathies [36, 37]. In recent years, there have been major advances in the interpretation of the ECG in athletes with the aim to improve specificity, culminating in the Seattle criteria [37, 38]. Recent data based on a large cohort of black athletes further increased specificity without compromising the sensitivity in detecting pathology [39]. This was mainly a result of several ECG patterns such as atrial enlargement, axis deviation and right ventricular hypertrophy in isolation which had been found to have a low diagnostic yield for cardiac disease [39, 40]. Applying these ‘refined criteria’ in a cohort of Arabic, black and Caucasian athletes revealed a further increase in specificity across all ethnicities compared with the Seattle criteria and the ESC recommendations [41]. Thus, these “refined ECG criteria” may be incorporated into the current ECG interpretational guidelines in the near future (fig. 2).

Screening of recreational athletes aged >35 years is somewhat different from that of younger athletes since the risk of sports-related acute cardiovascular events is almost exclusively related to the development and progression of atherosclerotic CAD [8, 18, 24]. Therefore, the main objective of cardiovascular screening of the older athlete is ruling out significant occult CAD. The increasing number of older individuals engaged in recreational or competitive sports activity makes the preparticipation screening of this population an emerging task. The ESC and the European Asso-

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**Figure 2:** Refined ECG criteria in the athlete (modified from: Sheikh N, Papadakis M, Ghani S, Zaidi A, Gati S, Adami PE, et al. Comparison of electrocardiographic criteria for the detection of cardiac abnormalities in elite black and white athletes. Circulation. 2014;129(16):1637–49). AV = atrioventricular; BA = black athlete; LBBB = left bundle branch block; LVH = left ventricular hypertrophy; PVC = premature ventricular contraction; RBBB = right bundle branch block; WA = white athlete.
Association for Cardiovascular Prevention and Rehabilitation (EACPR) guidelines, as well as the AHA guidelines, recommend at least some degree of cardiovascular screening in older athletes. The EACPR recommends as first line evaluation a self-assessment of the habitual physical activity level and the risk factors by use of validated questionnaires [42]. If indicated, further evaluation is performed by a qualified physician using the ESC Systematic Coronary Risk Evaluation (SCORE) [43]. Individuals with an increased risk for coronary events should undergo maximal exercise testing (and possibly further cardiological evaluations) [42] (fig. 3). The AHA recommends maximal exercise testing for all competitive athletes aged > 40 years (men) or 50 years (women) with one additional risk factor [44]. It is known that the test performance of exercise testing increases with a greater pretest probability of CAD [24, 44]. However, a negative exercise ECG test does not rule out the presence of CAD. Plaque rupture, which is regarded as an important mechanism of SCD in older athletes, can occur in coronary lesions with mild to moderate coronary stenoses [8]. Thus, imaging of coronary plaque to identify lesions vulnerable to rupture (coronary computed tomography) might be incorporated more often in the future although it is not so far cost-effective [45]. It remains to be determined what constitutes the best methods for screening recreational/competitive athletes >35 years. However, this important issue will be of relevance for public health in general, given the high participation rates of athletes >35 years in competitive events.

On-site prevention of sports-related sudden cardiac death

Cardiovascular screening will never be able to detect all individuals at risk, regardless of the screening strategy applied. Thus, it is of utmost importance that in the case of a serious adverse event such as SCA, immediate cardiopulmonary resuscitation (CPR), defibrillation (if needed) and advanced cardiac life support are performed [46]. Data from Marijon et al. showed that although most SrSCD cases were witnessed (93%), bystander CPR was commenced in only 30.7% of cases [18]. The initial cardiac rhythm in their study was ventricular fibrillation or pulseless fast ventricular tachycardia in 46.1%. Bystander CPR and initial use of cardiac defibrillation were the strongest independent predictors for survival to hospital discharge [18]. These data emphasise that access to early defibrillation through on-

site automated external defibrillators (AEDs) and qualified persons are crucial to improve survival [47]. Sporting bodies such as the European Football Union UEFA have introduced a training course for doctors from all member countries in acute emergency care on the playing field. Furthermore, the International Federation of Football Associations FIFA has released “11 steps to prevent SCD” as part of a preventive programme and equipped all football associations with a “medical emergency bag” which includes an AED [48]. However, awareness of SrSCD as an important public health issue still has to be broadened in the society. For example, we do not have much information about the current status regarding emergency preparedness at sports clubs or fitness centres. This is of particular importance since many recreational athletes who may not have been screened at all, exercise at those facilities. Furthermore, education about CPR and the use of AEDs should be offered more extensively.

Conclusions

SCD is the leading medical cause of death in athletes. However, the exact incidence remains unclear owing to differences in methodology. In the future, the overall incidence of athletes is expected to rise as more older and possibly less fit individuals participate in recreational/competitive sports activity. Prescription of individually tailored exercise regimens with a safe upper limit may become of increasing importance, especially in individuals with high risk. PPS may detect many potential causes of SCD and should therefore not only be confined to elite athletes. Importantly, the content of cardiovascular screening will be different with regard to age as younger athletes are most commonly affected by underlying inherited/congenital cardiac disease, whereas in older athletes CAD predominates by far. Taking into account the ethnic diversity of the populations, the different regional distribution patterns of cardiac diseases may also have an impact on the appropriate choice of screening procedures. Therefore, national registries are warranted to investigate regional distribution patterns of cardiovascular causes of sudden death (under consideration of genetic and environmental factors). Regarding secondary prevention, educational efforts should be made to optimise safety measures at sporting facilities and to improve the ‘chain of survival’.

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The full list of references is included in the online version of the article at www.cardiovascmed.ch.
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