Something is moving in sports-related sudden cardiac death ... is it time to change our minds?

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Leisure-time exercise was already encouraged by the European, Chinese, and Indian ancestries to remain fit, thus highlighting that an excellent physical condition has been central for subsistence during the large part of human history. In recent years, the advent of obesity and metabolic syndrome prompted a much stronger promotion of moderate to vigorous exercise to overcome the pernicious effects of sedentarism and struggle with cardiovascular disease pandemics. Such campaigns may have improved the guality of life and reduced cardiovascular risk factor burden but have been paradoxically threatened by significant cardiovascular side effects. Current evidence supports that long-term strenuous endurance exercise increases the risk of cardiac arrhythmias¹ and, possibly, impairs vascular function.² Foremost, strenuous bouts of endurance exercise have been associated with an increased risk of sudden death.³ The haemodynamic and metabolic stress characterizing intense bouts of exercise may elicit cardiac instability, trigger ventricular arrhythmias, and eventually result in sudden death, particularly in those individuals with pre-existing cardiac conditions. From a numerical and relative point of view, sudden cardiac death (SCD) events in athletes are extremely infrequent, but they have a terrible individual and societal impact, substantiating the need for research in the field, along with the implementation of preventative measures such as pre-participation screening. Whether such efforts have sufficed to modify the epidemiology of SCD warrants continuous monitoring.

In this issue of *Europace*, a German–French collaboration led by Philipp Bohm, Xavier Jouven, and Eloi Marijon updates the landscape of sudden cardiac arrest (SCA) in exercising individuals.⁴ Sudden cardiac deaths and aborted cardiac arrests in young individuals (18–35 years) occurring during moderate or vigorous exercise were prospectively collected from Germany and the Paris area between 2012 and 2019. Cases were recorded through a variety of registries, media reviews, and collaboration with hospitals and forensic departments, and only those of a 'presumably cardiac origin', as determined by central adjudication, were included. Overall, 147 cases of SCA were identified, mostly in male recreational sports participants and occurring during exercise of a vigorous intensity. Incidence could only be calculated in the French cohort by indexing to the registered 18- to 35-year-old population of the Paris area, yielding an estimate incidence of 4.77 cases per million young inhabitants per year. The most frequent cause of SCA was coronary artery disease (CAD; more than one-fourth of cases), followed by idiopathic ventricular fibrillation and myocarditis. Hypertrophic cardiomyopathy and arrhythmogenic cardiomyopathy accounted for <8% of cardiac arrests each.

Monitoring sports-related sudden cardiac death over time: is its incidence decreasing?

Sports-related SCD is a rare event, for which precise incidence estimates are difficult to ascertain. To calculate its incidence rate, accurate and standardized definitions of both the numerator (i.e. number of SCDs or cardiac arrests) and the denominator (i.e. individuals at risk in a certain period) are critical. Unfortunately, a number of logistic factors and decisions from researchers impinge the interpretation of these estimates and jeopardize comparability with previous reports (Table 1). The operationalization of a widely accepted definition of SCD (e.g., "death of a primarily cardiac etiology occurring within 1 hour of symptom onset or within 24 hours of having been observed asymptomatic") has been recently challenged. Indeed, time-based systems to classify "sudden" death, along with the subjectiveness of the "presumed" cardiac origin have been highlighted as major sources of heterogenity between studies.⁵ Moreover, because events are infrequent, large national or multinational studies are needed to collect sufficient SCD / SCA events and yield reliable conclusions. Very large studies require complex logistics, which quite often result in a substantial heterogeneity of data collection and clinical management of patients. Finally, the overall figures should be interpreted in the context of a specific population with a specific genetic background and sport practising habits. Exemplifying these issues, the number of identified events seems to be relatively lower in Germany (n = 86 in the whole country) than in Paris (n = 61 in the Paris area). In summary, while the exercise-related SCA estimate from Bohm et al. seems reassuringly low, direct comparisons with previous reports should be taken with extreme caution.

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 Table 1
 Sources of variability in the quantification of SCD in sport

Number of events	Population at risk
Inclusion or not of aborted cardiac arrest	 Definition of the population at risk All registered individuals Only athletes The whole population Individuals participating in a certain sporting event (e.g. a race).
Data comprehensiveness (i.e. collection of all cases)	
Changes in the definition of events (only events during exercise in athletes, inclusion of all events in athletes, all exercise-related events independent of athletic status) Changing definition of SCD Heterogeneity in the case studies	

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Individuals dying suddenly while exercising are likely to be carriers of previously undetected cardiac conditions. Classical studies pointed to hypertrophic cardiomyopathy in the USA and arrhythmogenic cardiomyopathy in Italy and some other European countries as the most frequent cardiomyopathies in athletes with SCD.³ These findings led to the promotion and instauration of pre-participation screening programmes aimed at detecting asymptomatic cardiomyopathies and other cardiac diseases. The Italian experience suggests that electrocardiogram-based screening may decrease SCD rates in athletes.⁶ However, even after screening instauration, SCD has not been eradicated, and unfortunately some cases still occur. Some may be due to the late development of an overt phenotypic cardiomyopathy (i.e. occurring a long time after screening), urging for repeated screening as long as regular sport participation continues.⁷ But what about those young individuals dying suddenly after repeated screening?

Bohm et al. work may help to address this relevant knowledge gap. In France, medical pre-participation evaluation and approval is required to participate in most licensed competitions; while screening is not mandatory in Germany, it is highly recommended. In this scenario, CAD, idiopathic ventricular fibrillation, and myocarditis were the most common causes of death while exercising. Hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy were infrequent,⁴ in contrast to classical studies.³ It is tempting to speculate that a progressive implementation of pre-participation screening programmes might have, at least partially, driven this change. In spite of the low sample size and large uncertainty intervals, previous French work showed that hypertrophic cardiomyopathy was still the most frequent cause of death in young athletes during the 2005-10 period.⁸ Exclusion of patients with structural heart disease during preparticipation screening may have relatively enriched the present cohort with those athletes with CAD. Screening programmes have for long time focused on ruling out structural heart disease and, particularly, cardiomyopathies,³ while failing to provide reasonable predictive performance for asymptomatic CAD. Exercise testing has a very low sensitivity and positive predictive value in young asymptomatic individuals, ruling out its use in systematic screening.³ Sensitive tools such as non-invasive coronary angiography are precluded in young individuals owing to high radiation exposure. On the other hand, screening for idiopathic ventricular fibrillation might not be currently feasible, while myocarditisrelated events may be transient in nature.

Overall, these results suggest, but do not confirm, that sudden death awareness and the instauration of (regulated or non-regulated) preparticipation screening programmes might have changed the aetiology of sports-related SCD. In this article, cardiac conditions less amenable to detection during pre-participation screening are the leading causes of SCD. Are there any chances of keeping fighting against SCD in sports?

... time to change our minds?

Sudden cardiac death results from the catastrophic sequence of two facts: a cardiac arrest followed by an inability to restore spontaneous circulation. While pre-participation screening targets a reduction in the cardiac arrest incidence by identifying individuals at the highest risk, the impact of sports-related SCD may also be reduced by improving the management of cardiac arrest. As shown by Bohm et al., further reduction with current screening tools is, at best, challenging and, to date, likely not cost-effective. In contrast, their results emphasize a remarkable benefit of improving logistics for cardiac resuscitation: overall survival aftar a cardiac arrest is as low as 38%, but gets close to 90% when cardiopulmonary resuscitation was initiated immediately by bystanders and an external defibrillator (AED) was used. Similar to this French-German study, Italian observational data showed that sports centres with AEDs had a 93% survival rate compared with a 9% rate in those without AEDs.⁹ A faster and better approach to cardiac arrest seems to be the main driver of improved outcomes of sports-related SCD events over time.¹⁰ The need to focus efforts on improving survival through a better approach to cardiac arrest events has been emphasized in recent position papers that advocated for mandatory action plans for sports centres and organizations.¹¹ Definitely, it is time for resuscitation training and improving AED availability.

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Bohm *et al.* have provided an important piece to understand the current state of SCD during exercise, its causes, and potential actions that need to be strengthened to reduce its impact. By doing so, they highlight the importance of a continuous surveillance and monitoring on the consequences of taken actions (e.g. pre-participation screening) to further refine efforts towards reducing the impact of SCD.

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