










# Sports-related sudden cardiac arrest in young adults

Philipp Bohm <sup>1,2</sup>, Tim Meyer <sup>1</sup>, Kumar Narayanan<sup>3,4</sup>, Matthias Schindler<sup>2</sup>,  
Oriane Weizman <sup>3</sup>, Frankie Beganton <sup>3</sup>, Christian Schmied<sup>2</sup>,  
Wulfran Bougouin <sup>3,5</sup>, Sergio Barra <sup>3,6</sup>, Florence Dumas <sup>3,5,7</sup>,  
Olivier Varenne<sup>3,5,8</sup>, Alain Cariou<sup>3,5,9</sup>, Nicole Karam <sup>3,10,11</sup>, Xavier Jouven<sup>3,10,11</sup>,  
and Eloi Marijon <sup>3,10,11\*</sup>

<sup>1</sup>Institute of Sports and Preventive Medicine, Saarland University, 66123 Saarbrücken, Germany; <sup>2</sup>Department of Cardiology, University Heart Center Zurich, HerzZentrum Hirslanden Zurich Witellikerstrasse 36, CH-8008 Zurich, Switzerland; <sup>3</sup>Paris-Sudden Death Expertise Center, INSERM U970, Paris Cardiovascular Research Center (PARCC), 56 rue Leblanc, 75015 Paris, France; <sup>4</sup>Cardiology Department, Medicover Hospitals, Madhapur, Hyderabad, Telangana 500081, India; <sup>5</sup>Intensive Care Unit, Jacques cartier Hospital, 6 Av. du Noyer Lambert, 91300 Massy, France; <sup>6</sup>Cardiology Department, Hospital da Luz Arrábida, V. N. PCT de Henrique Moreira 150, 4400-346 Vila Nova de Gaia, Portugal; <sup>7</sup>Emergency Department, Cochin Hospital, 25 Rue du Faubourg Saint-Jacques, 75014 Paris, France; <sup>8</sup>Cardiology Department, Cochin Hospital, 25 Rue du Faubourg Saint-Jacques, 75014 Paris, France; <sup>9</sup>Intensive Care Unit, Cochin Hospital, 25 Rue du Faubourg Saint-Jacques, 75014 Paris, France; <sup>10</sup>University of Paris, 103, Boulevard Saint-Michel, Paris, France; and <sup>11</sup>Cardiology Department, European Georges Pompidou Hospital, 20 rue Leblanc, 75015 Paris, France

Received 11 April 2022; accepted after revision 8 August 2022; online publish-ahead-of-print 18 October 2022

## Aims

Data on sports-related sudden cardiac arrest (SrSCA) among young adults in the general population are scarce. We aimed to determine the overall SrSCA incidence, characteristics, and outcomes in young adults.

## Methods and results

Prospective cohort study of all cases of SrSCA between 2012 and 2019 in Germany and Paris area, France, involving subjects aged 18–35 years. Detection of SrSCA was achieved via multiple sources, including emergency medical services (EMS) reporting and web-based screening of media releases. Cases and aetiologies were centrally adjudicated. Overall, a total of 147 SrSCA (mean age  $28.1 \pm 4.8$  years, 95.2% males) occurred, with an overall burden of 4.77 [95% confidence interval (CI) 2.85–6.68] cases per million-year, including 12 (8.2%) cases in young competitive athletes. While bystander cardiopulmonary resuscitation (CPR) was initiated in 114 (82.6%), automated external defibrillator (AED) use by bystanders occurred only in a minority (7.5%). Public AED use prior to EMS arrival (odds ratio 6.25, 95% CI 1.48–43.20,  $P = 0.02$ ) was the strongest independent predictor of survival at hospital discharge (38.1%). Among cases that benefited from both immediate bystander CPR and AED use, survival rate was 90.9%. Coronary artery disease was the most frequent aetiology (25.8%), mainly through acute coronary syndrome (86.9%).

## Conclusion

Sports-related sudden cardiac arrest in the young occurs mainly in recreational male sports participants. Public AED use remains disappointingly low, although survival may reach 90% among those who benefit from both bystander CPR and early defibrillation. Coronary artery disease is the most prevalent cause of SrSCA in young adults.

## Keywords

Sports activity • Young • Cardiopulmonary resuscitation • Defibrillation • Autopsy • Coronary artery disease

\* Corresponding author. Tel: +33 6 6283 3848; fax: +33 1 5609 3047. E-mail address: eloi\_marijon@yahoo.fr

© The Author(s) 2022. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

## What's new?

- This is the first prospective population-based study investigating sports-related sudden cardiac arrest (SrSCA) cases in individuals aged 18–35 years in the general population in two different countries, including survived cases.
- We report a low public automated external defibrillator use despite frequent witness, although survival at discharge may reach 90% among those who benefit from both bystander cardiopulmonary resuscitation and early defibrillation.
- Coronary artery disease is the most prevalent cause of SrSCA, underlining the need for targeted cardiovascular risk evaluation/prevention in the young.
- The study highlights the importance of establishing a definite diagnosis for SrSCA, including through autopsy and genetic testing in survivors.

## Introduction

Regular physical activity is associated with a decreased risk of cardiovascular disease and death.<sup>1</sup> However, the risk of an acute cardiac event is transiently raised during and immediately after vigorous exercise, creating the so-called *exercise paradox*.<sup>2</sup>

Sports-related sudden cardiac arrest (SrSCA) in young competitive athletes (under 35 years old involved in competitive sports) has always received considerable media and community attention.<sup>3</sup> However, recent reports have suggested that the majority of SrSCA occur in a recreational, rather than competitive setting.<sup>4,5</sup> Although the epidemiology of overall SCA (not only related to sports) among children and young adults in the community has been described,<sup>6</sup> to the best of our knowledge, no study has focused on SrSCA (including survived cases) in young adults. While inherited cardiomyopathies or channelopathies may represent the majority of causes in young competitive athletes, aetiologies among young victims from the general population (participating to recreational sports activities) could be different, especially considering that the proportion of ST-elevation myocardial infarction in young adults has increased considerably over recent years.<sup>7</sup> In addition, identifying current lacunae in the management of young SrSCA can help to develop and refine a strategy to improve survival.

In the present paper, we report the findings of a prospective, population-based study carried out in two countries aiming to determine the overall SrSCA burden in young adults, to characterize the circumstances, features, and causes of SrSCA, and to identify major influencing factors for survival.

## Methods

### Study design

This observational prospective cohort study enrolled all cases of SrSCA occurring in the general population aged 18–35 years, in Germany and the Great Paris area, France, during a 7-year period (May 2012 to May 2019). This study was approved by the ethical review committee, the independent Data Protection Centre Saarland, Germany, as well as the French data protection committee (CNIL-DR-2012-445 authorization n°912309).

### Definitions

Sports-related sudden cardiac arrest was defined as out-of-hospital cardiac arrest of presumably cardiac origin, occurring during competitive or recreational sports activities or within 1 h of sports cessation.<sup>7,8</sup> Apart from commotio cordis, cases related to trauma and other obvious non-cardiac causes such as drowning or drug overdose were excluded. Sports-related sudden cardiac death (SrSCD) was defined as a sudden death of presumably cardiac cause occurring during or within 1 h of cessation of competitive or recreational sports activities. A 'young competitive athlete' was defined as any

person, aged 18–35 years, who participated in an organized sports program (team or individual sport) requiring regular competition and training (individuals participating in college-sponsored intramural sports were not considered as young competitive athletes). Sudden deaths occurring in competitive or recreational athletes outside the context of sports activity (at night, at rest or during daily routine physical activities) were not included. Cases were centrally adjudicated.

## Detection of sports-related sudden cardiac arrest

Cases of SrSCA in Germany were detected via multiple sources including a confidential web-based data platform to record all SrSCA cases in competitive and recreational athletes within Germany ([www.scd-deutschland.de](http://www.scd-deutschland.de)), the German Resuscitation Registry, a systematic web-based weekly media monitoring and a collaboration with all medical examiners of the area.<sup>8</sup>

In Paris, data collection was accomplished via the Paris-Sudden Death Expertise Center (SDEC) registry,<sup>9</sup> encompassing a residential population of 6.7 million covering an area of 762 km<sup>2</sup>. Owing to a close collaboration between the two existing pre-hospital emergency medical services (EMS), all 48 hospitals and forensic units of the area, every case of OHCA aged ≥18 years occurring in the area has been systematically enrolled since May 2011, including all cases occurring during any sports activities.

Files were prospectively and regularly reviewed (every 6 months) by an independent events committee, to ensure the reliability of the data.

## Variables assessed

Case report forms used by the emergency teams included demographic characteristics (age, sex, history of known cardiovascular risk factors, or heart disease), location of SCA (residential or public place), SCA circumstances, type of sports and regular training regimen (recreational or competitive), the actual sporting activity at the time of the event, level of exercise at the time of SrSCA as assessed by the ambulance officers using a defined scale of 1–8 metabolic equivalents (MET), classified as light (<4 MET), moderate (4–6 MET), or vigorous (>6 MET), location type (sports facility or other area), presence of witnesses, bystander cardiopulmonary resuscitation (CPR) or automated external defibrillator (AED) use, and survival status to hospital admission.

In addition, available hospital and outpatient medical records for all subjects were systematically analyzed. Medical records for each SrSCA were reviewed by two cardiologists (and a third one in case of disagreement) to identify underlying mechanisms and ascertain aetiologies. In survivors without a definite diagnosis after the initial work-up performed in intensive care units, aetiological investigations were carried out in cardiology units, including cardiac magnetic resonance imaging, pharmacological tests, electrophysiology study, Holter-electrocardiogram recording, exercise stress test as well as genetic screening in some survivors. The diagnosis of idiopathic ventricular fibrillation (VF) was made among survivors when no specific phenotype was identified despite investigations.

Cause of death data in individuals who died in the field could only be obtained in cases where autopsy was performed or clinical features at the time of death allowed a reliable diagnosis. The study lead authors decided only after availability of all clinical data, including autopsy results, whether sudden death was of a 'presumably cardiac origin'. In Germany and France, the performance of autopsy is at the discretion of the physician certifying the death and is only mandated where the death is regarded as potentially 'suspicious'. The underlying aetiology was centrally adjudicated.

## Statistical analyses

This report was prepared in compliance with the STrengthening the Reporting of OBservational studies in Epidemiology checklist for observational studies. The overall incidence of SrSCA and its confidence interval (CI) were calculated in each participating district by dividing the average number of SrSCA reported per year by the locally registered 18–35-year-old population. To avoid any underestimate, incidence was calculated from the Paris Area dataset, where completeness of all SrSCA has been verified annually since 2012. Continuous variables were reported as means and corresponding 95% CIs and compared using unpaired t-tests in case of normal distribution or Mann–Whitney tests in case of non-normally distributed data. Categorical variables were reported as counts

and percentages and compared using  $\chi^2$  tests or Fisher's exact tests (in cases where any category contained less than five observations). Furthermore, various predictors were tested for their association with survival to hospital discharge by calculating their odds ratio (OR) and corresponding 95% CIs using multivariable logistic regression models. All analyses were performed using R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria).

## Results

### Sports-related sudden cardiac arrest burden and subjects' characteristics

A total of 147 SrSCAs ( $n=86$  in Germany,  $n=61$  in the Great Paris area) were recorded over the study period of 7 years (mean age  $28.1 \pm 4.8$  years), giving an overall burden of 4.77 (95% CI 2.85–6.68) cases per million inhabitant per year. The majority of events (75%) occurred during vigorous exertion. Ninety-six (66.7%) were alive at hospital admission and 56 (38.1% of the total) at hospital discharge. We denoted no significant increase in survival rate over time. Baseline characteristics of the study population with stratification by survival status are described in *Table 1*. There was a marked sex disparity with 140 SCAs in males and only 7 in females (male/female ratio of 20:1). The majority of SrSCAs were observed during football (soccer) ( $n=68$ , 46.3%) and running ( $n=35$ , 23.8%), which may reflect the popularity of these sports in Germany and in the Great Paris area (*Figure 1*). Most of the SrSCAs (93.9%) took place in public sports facilities (such as a sports club) or during an organized running event, and only 6.1% at home. The majority of SrSCAs occurred in recreational sports participants ( $n=132$ , 91.7%), with only 12 (8.3%) occurring in elite competitive athletes (athlete's status in the remaining 3 cases was unclear). Cardiorespiratory symptoms preceding the event were reported by 32 subjects (21.8%), of whom 14 had lipothymia/syncope and 13 reported typical chest pain. Smoking was the most common cardiovascular risk factor ( $n=22$ ), followed by obesity ( $n=15$ ), positive family history ( $n=9$ ), and hypertension ( $n=6$ ). Drug abuse was reported in three individuals (cannabis in two cases and amphetamines in one).

### Cardiac arrest management and predictors of survival

A total of 132 cases (91.7%) were witnessed and bystander CPR was initiated in 114 (82.6% of the witnessed cases) (*Table 1*). Defibrillation with an AED was performed in 89 cases (92.5%), mainly by EMS personnel (78/89), with bystander AED use (prior to EMS arrival) observed in only a minority of cases (11/89; 7.5% of all SrSCA). Return of spontaneous circulation was achieved in 110 cases (77.5%). Of 96 cases (66.7%) admitted alive to hospital, 60 (62.5%) underwent immediate coronary angiography within 120 min. Five SrSCA who died in-hospital did not undergo immediate coronary angiography and were eventually found to have coronary artery disease (CAD). In two of them, the diagnosis was made via delayed coronary angiography, while in the three others, the diagnosis was made only post-mortem. After considering potential confounders, only public AED use prior to EMS arrival was associated with significantly higher survival after SrSCA (OR 6.25, 95% CI 1.48–43.20,  $P=0.02$ ). Among cases that benefited from both immediate bystander CPR and AED use, 10 of 11 survived, leading to a survival rate at hospital discharge of 90.9% in this subgroup.

### Causes of sports-related sudden cardiac arrest

Among cases in which the cause of SCA could be ascertained with a high degree of certainty ( $n=89$ , 60.5% of all cases), all but three

were of cardiac origin (these three cases included exercise-associated hyponatremia, severe asthmatic attack, and intracerebral haemorrhage) (*Figure 2*). Coronary artery disease was the most common underlying aetiology of SrSCA ( $n=23$ , 25.8%); 20 individuals were diagnosed with an acute myocardial infarction (MI), of which 15 had single-vessel disease with a clear culprit lesion, most often involving the left anterior descending (LAD) artery, while the remaining 5 had multivessel CAD. Three individuals had chronic obstructive CAD with fixed coronary stenosis (defined as >50% stenotic narrowing in at least one coronary artery), of which one subject showed single-vessel disease. Sixteen of the CAD subjects had at least one cardiovascular risk factor, with smoking predominating. Cardiac symptoms were reported in 13 CAD subjects (56.5%), with typical chest pain being the leading symptom (76.9%).

Cardiomyopathies represented the second most common cause of SrSCA ( $n=19$ , 21.3%); seven cases were diagnosed with hypertrophic cardiomyopathy (HCM) and five cases with arrhythmogenic cardiomyopathy (AC) and dilated cardiomyopathy, respectively (*Figure 2*). Acute myocarditis was diagnosed in 10 subjects with a confirmed diagnosis via autopsy in 4 subjects.

Twelve survivors at hospital discharge were assigned to a diagnosis of idiopathic VF since no identifiable structural or electrical VF aetiology was eventually found after extensive investigations. However, genetic testing was only performed in four cases (33.3%). Sudden arrhythmic death syndrome, defined as sudden death in the context of a structurally normal heart with no evident abnormality on macroscopic and histological evaluation at post-mortem, was found in six cases. Five subjects had anomalous coronary artery origin (*Figure 2*).

Considering only elite competitive athletes, causes of SrSCA comprised AC ( $n=3$ ), followed by CAD ( $n=2$ ) and myocarditis ( $n=2$ ).

Overall, only 25 of the 91 deceased (27.5%) were autopsied. A morphologically normal heart was evidenced in six cases, while five presented CAD and four presented signs of myocarditis (*Table 2*). Genetic testing was performed in 11 SrSCA survivors, of whom 4 presented with idiopathic VF and AC, respectively.

In 58 cases, there was insufficient information to ascertain the cause of death, as they either died in the field or adequate investigations (including an autopsy) could not be performed.

## Discussion

This first comprehensive assessment of SrSCA in the general young adult population 18–35 years of age revealed a more frequent occurrence in recreational sports participants rather than among elite athletes, with a striking male predominance. Although almost always witnessed, the percentage of bystander AED use was disappointingly low. This is important, as AED use clearly improved survival, particularly when associated with bystander CPR. Coronary artery disease was found to be the most common underlying cause of young SrSCA despite the young age of the participants, underlining the need for targeted cardiovascular risk evaluation/prevention in the young. Lastly, the very low autopsy rates as well as the low rate of genetic testing in SrSCA survivors with a structurally normal heart, combined with the significant number of undiagnosed cases, represent an important missed opportunity to establish aetiology and prevention for first degree relatives.

Most cases of SrSCA occur in recreational sports participants rather than in competitive athletes, contrary to what may be perceived by the general public based on the striking media attention given to SCA in athletes. This was previously observed in all-comers SrSCA where the mean age was higher.<sup>4</sup> However, this does not necessarily mean that the risk of SrSCA is lower in elite athletes, rather that the number of recreational sports participants is much higher. Regarding sex ratio, our finding of an overwhelming male predominance in SrSCA is in line with most studies.<sup>10,11</sup> The increased overall risk of SCD in men

**Table 1** Baseline characteristics of the study population with stratification by survival status

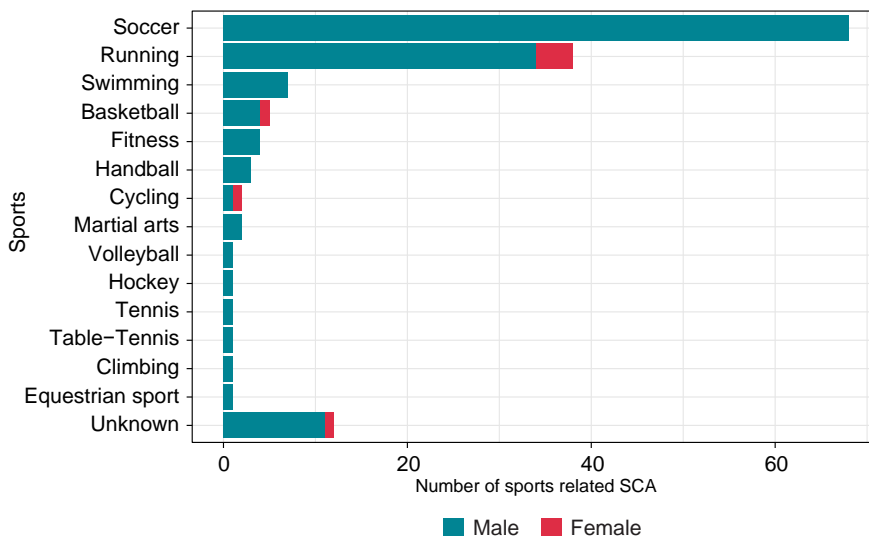
	Total (N = 147)	Survived (N = 56)	Deceased (N = 91)	P value
Age, years, mean (95% CI)	28.1 (27.3–28.9)	27.9 (26.5–29.3)	28.2 (27.2–29.2)	0.72
Male (n, %)	140 (95.2)	51 (91.1)	89 (97.8)	0.06
Time of occurrence				0.87
During the week (n, %)	72 (52.9)	26 (52.0)	46 (53.5)	
At the weekend (n, %)	64 (47.1)	24 (48.0)	40 (46.5)	
Missing	11	6	5	
Site of incidence				0.31
Domicile (n, %)	9 (6.1)	2 (3.6)	7 (7.7)	
Public place (n, %)	138 (93.9)	54 (96.4)	84 (92.3)	
Witnessed status				0.02
No (n, %)	12 (8.3)	1 (1.8)	11 (12.4)	
Yes (n, %)	132 (91.7)	54 (98.2)	78 (87.6)	
Missing	3	1	2	
Bystander CPR				< 0.001
No (n, %)	24 (17.4)	2 (3.8)	22 (25.9)	
Yes (n, %)	114 (82.6)	51 (96.2)	63 (74.1)	
Missing	9	3	6	
ROSC				< 0.001
No (n, %)	32 (22.5)	0 (0.0)	32 (37.2)	
Yes (n, %)	110 (77.5)	56 (100.0)	54 (62.8)	
Missing	5	—	5	
Initial rhythm				0.32
VF (n, %)	89 (89.0)	45 (91.8)	44 (86.3)	
Asystole (n, %)	10 (10.0)	3 (6.1)	7 (13.7)	
PEA (n, %)	1 (1.0)	1 (2.0)	0 (0.0)	
Missing	47	7	40	
Defibrillation				0.01
Lay bystanders (n, %)	11 (7.5)	10 (17.9)	1 (1.1)	
Medical service (n, %)	78 (53.1)	35 (62.5)	43 (47.3)	
Not indicated (n, %)	11 (7.5)	4 (7.1)	7 (7.7)	
Undetermined (n, %)	47 (32.0)	7 (12.5)	40 (44.0)	
Survival at hospital admission				—
Yes (n, %)	96 (66.7)	56 (100.0)	40 (45.5)	
No (n, %)	48 (33.3%)	0 (0.0%)	48 (54.5%)	
Missing	3	—	3	
Survival at hospital discharge				—
No (n, %)	91 (61.9%)	0 (0.0%)	91 (100.0%)	
Yes (n, %)	56 (38.1%)	56 (100.0%)	0 (0.0%)	

Values are given as median (IQR) or numbers (percentages).

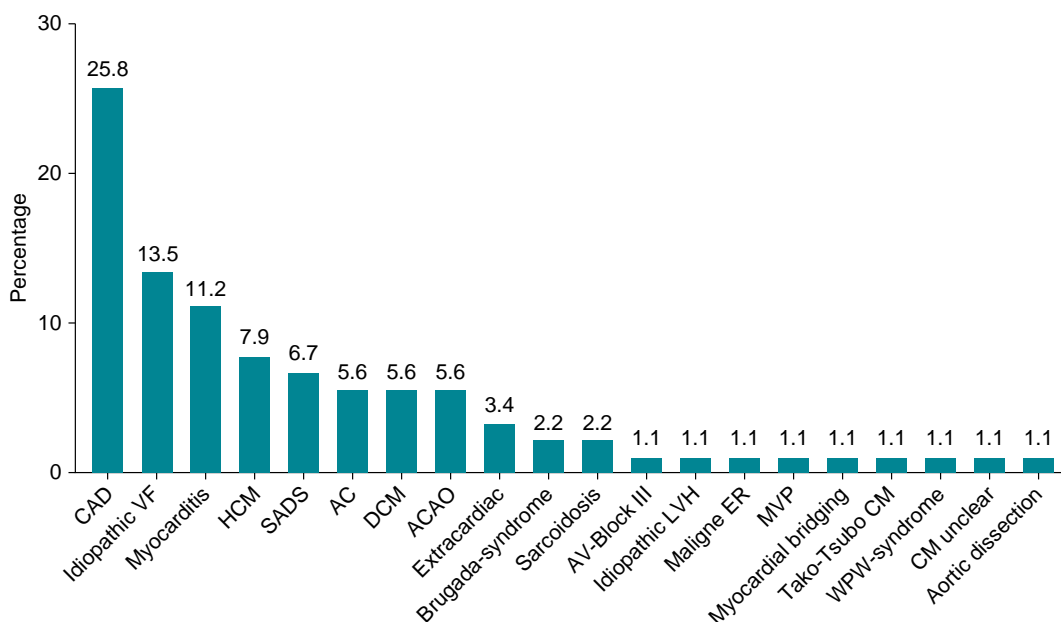
CI, confidence interval; CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation.

in the general population or in specific sub-groups such as those with heart failure or CAD is well-recognized, but the difference may be especially striking in the setting of sports, despite comparable sports participation by women.<sup>12</sup> The reasons for this are not well understood and could include several factors, such as (i) gender differences in the vulnerability to arrhythmic substrates, (ii) the increased prevalence of CAD and myocardial ischaemia among men (CAD was not

encountered among women victims in this study), (iii) the more frequent exposure to the triggering effect of high-intensity exercise (men have a cumulative greater exposure to vigorous sports, and the increased SCA risk during an episode of vigorous exertion is much less pronounced among women), (iv) the fact that the relative risk of exercise-induced SCA is reduced in a dose-dependent fashion by habitual exercise less markedly among men compared with women,



**Figure 1** Sports engaged in at the time of SrSCA. Shaded proportions of the bars represent the female ratio.



**Figure 2** Bar chart showing the causes of the 89 SrSCAs with definitive diagnosis in the general population 18–35 years. AC, arrhythmogenic cardiomyopathy; ACAO, anomalous coronary artery origin; CAD, coronary artery disease; CM, cardiomyopathy; DCM, dilated cardiomyopathy; ER, early repolarization; HCM, hypertrophic cardiomyopathy; LVH, left ventricular hypertrophy; MVP, mitral valve prolapse; SADS, sudden arrhythmic death syndrome; SrSCA, sports-related sudden cardiac arrests; VF, ventricular fibrillation; WPW, Wolff-Parkinson-White-Syndrome.

(v) differences in autonomic modulators, and even (vi) hormonal influences including that of circulating oestrogens.<sup>11,12</sup> Understanding the mechanisms behind the markedly reduced susceptibility of women to SrSCA could have important implications for SCA prevention overall and this area clearly warrants further research.

While there was a high proportion of bystander CPR, pre-EMS arrival, AED use by lay bystanders was only performed in a minority of

cases. This is extremely important, given that early AED use was the strongest determinant of survival, with  $\geq 90\%$  of survival at hospital discharge in the subgroup of subjects who benefited from both early CPR and defibrillation, in line with a previous report on SCA using mobile AED response system during road races marathon in Japan.<sup>13</sup> Very high survival in both young and older sports participants is possible in the setting of SrSCA when AED use and early CPR are provided,<sup>14–16</sup>

**Table 2** Autopsy results of SrSCA

Autopsy (macroscopic and microscopic)	Number (n = 25)
Morphologically normal heart	6
Coronary artery disease	5
Myocarditis	4
Hypertrophic cardiomyopathy	2
Dilated cardiomyopathy	1
Cardiomyopathy of unknown origin	1
Sarcoidosis	1
No results	5

SrSCA, sports-related sudden cardiac arrest.

with the higher survival of SrSCA compared with non-SrSCA, and of SrSCA occurring in sports facilities compared with those occurred outside, mostly explained by increased rates of AED use and early CPR.<sup>17,18</sup> Thus, understanding the reasons for low AED use by lay responders is crucial. These reasons are likely multifactorial, with various issues playing a role such as the unavailability of AEDs at the time of SCA, unfamiliarity with equipment, fear related to delivering a shock and regional legislation related to AED use by public. Modern public access AED programs have yielded higher survival rates and our data confirms this fact in the setting of SrSCA as well.<sup>19</sup> Public access defibrillation programs should be more widely deployed to improve outcomes in SCA overall, and SrSCA in particular.

Our data also highlight that CAD was the most important aetiology seen in this young group, predominantly as single-vessel disease involving the LAD. Acute coronary syndrome with a clearly identifiable culprit lesion was the main mechanism, indicating that shear forces induced by physical activity might have induced plaque disruption through increased vascular wall stress.<sup>20</sup> A previous study had already suggested that culprit lesions in the LAD in the context of single-vessel disease was the mostly likely CAD-related SrSCA mechanism.<sup>21</sup> Coronary artery disease-associated SrSCA also occurred in the setting of stable multivessel CAD, wherein exercise-related ischaemia may have triggered lethal ventricular arrhythmias. Previous investigators have reported less extensive CAD in young MI patients compared with older subjects, and single vessel disease involving LAD was most frequent.<sup>22</sup> The fact that young CAD subjects were unaware of the underlying condition and usually maintained physical activity despite having chest pain (showing a lack of symptom awareness) could help explain why SCA may often present as the first manifestation of CAD in young individuals participating in recreational or competitive sports. A recent retrospective nationwide Australian study confirmed our results with CAD prevailing in a cohort  $\leq 35$  years old and with a median age very similar to that reported in our study.<sup>23</sup> This apparent shift in causes of SrSCA in young individuals  $< 35$  years old might partly be related to insufficient screening strategies for the detection of premature CAD, as preparticipation screening with current techniques is mainly associated with the identification of structural heart diseases such as cardiomyopathies, while CAD may be less often diagnosed when it is present. Also, the increasing incidence of CAD as a cause of SrSCA might be associated with a specific risk factor pattern in affected young CAD individuals. In our study, smoking and obesity prevailed as modifiable cardiovascular risk factors, and substance abuse (including cannabis or amphetamines) was seen in three subjects with SCA. Our results suggest that CAD epidemiology in the young may be changing with the need for enhanced primary prevention. This includes a better identification of modifiable cardiovascular risk factors such as smoking/obesity

and awareness of negative effects of illicit drugs, as well as targeted screening with exercise testing and echocardiographic detection of atherosclerotic plaques in the aorta to identify those individuals at high risk of cardiac events. Overall, there is a need to reconsider the traditional age cut-off of 35 years as a threshold to distinguish younger individuals in whom CAD is considered less prevalent, and referral for early coronary angiography should be considered in the absence of an obvious alternative cause.

Inherited cardiomyopathies were the next most common underlying cause of SrSCA after CAD. Genetic differences among populations in different geographic regions may result in a variable contribution of cardiomyopathies to SrSCA, such as the relatively higher prevalence observed in the Paris area. HCM was the leading cardiomyopathy, but its overall prevalence was still low, in line with recent studies showing a low prevalence of HCM, ascribable to more stringent autopsy criteria in addition to genetic heterogeneities among populations.<sup>24,25</sup> Primary electrical disorders without any underlying structural heart disease have a smaller but important role to play in this young population. This is confirmed by autopsy-based studies from different parts of the world.<sup>6,26</sup> In our study, 11 patients had genetic testing, but none had evidence of known causative mutations for primary electrical disease. Myocarditis was the third most common acquired cardiac disorder causing SrSCA.

The very low autopsy rates in young victims of SrSCA noted in this study represent an important missed opportunity to establish aetiology. This reflects the present legal situation in both Germany and France, where autopsies are mandated only if the death is considered 'suspicious'. For the rest, it is purely at the discretion of the certifying doctor and is clearly underutilized for a variety of reasons such as the lack of sensitization to the importance of obtaining a definitive diagnosis and the hesitancy to discuss the topic with the family. There is an urgent need to evolve a standardized approach to sudden death, including a thorough post-mortem examination, preferably performed by an expert cardiac pathologist. Autopsy with the use of molecular techniques is a crucial step in establishing the cause of death with significant implications for the clinical and genetic evaluation of surviving family members, potentially preventing avoidable loss of life. In our study, while no diagnosis could be established in 61 cases, none were autopsied, making targeted intervention for first degree relatives difficult. In addition, the low rate of genetic testing in SrSCA survivors without a clear diagnosis most likely has made some missed cases of diagnosis, both in probands as well as relatives, underlining the need to focus more thoroughly on the survivors.

## Study limitations

This is the first study investigating SrSCA cases in individuals aged 18–35 years in the general population in two different countries, with the advantage of having an extensive cardiac-work-up in most of the survivors. However, some limitations need to be acknowledged. While this was a prospective registry, the cause of death could not always be determined with certainty in all cases. This is a universal limitation in SCD studies, particularly when individuals succumb in the field or immediately after hospital admission precluding further diagnostic investigation. Autopsies as well as genetic testing were rarely performed. Slightly different criteria amongst centres may have led to misdiagnoses in a small number of cases. Furthermore, autopsies were not performed in a single reference centre due to the legal situation in Germany and France.

Incidence calculation was only performed for the Great Paris area to ensure a most precise numerator/denominator. However, the estimated incidence of SrSCD in young adults is likely an underestimation given the consideration of the entire locally registered 18–35-year-old population (the denominator) as being potentially at risk of SrSCD, rather than estimating the proportion who were participating in sports

(there are no reliable data to estimate actual recreational sports participation).

## Conclusions

Among young adults in the general population, SrSCA occurred mainly in recreational sports participants rather than competitive athletes, with a marked male predominance. Although survival at discharge may reach 90% among those who benefit from both bystander CPR and early defibrillation, the use of publicly available AEDs was very low despite frequent witness presence. Coronary artery disease is the most prevalent cause of SrSCA, underlining the need for targeted cardiovascular risk evaluation/prevention in the young. The low autopsy rates as well as the low rate of genetic testing in SrSCA survivors without clear diagnosis represent an important missed opportunity. The study highlights the need for a better education of sports participants on warning symptoms, the population on basic life support, and the medical society on the importance of establishing a definite diagnosis for SrSCA.

## Acknowledgements

The authors of the German Resuscitation Registry would like to thank the German Society of Cardiology for their patronage as well as the German Heart Foundation for their funding. We also appreciate very much the efforts of all our colleagues and other involved persons and would like to thank them. We thank the Paris-SDEC for providing the logistical support, and the Paris-SDEC collaborators for their multidisciplinary expertise that allows an optimal approach in the fight against sudden cardiac death through this collaborative network since 2011.

## Funding

This work was supported by the German Heart Foundation. The Paris-SDEC activities are supported by the Institut National de la Santé et de la Recherche Médicale, University of Paris, Assistance Publique-Hôpitaux de Paris, Fondation Coeur et Artères, Global Heart Watch, Fédération Française de Cardiologie, Société Française de Cardiologie, Fondation Recherche Médicale, as well as unrestricted grants from industrial partners (Abbott, Biotronik, Boston Scientific, Medtronic, MicroPort and Zoll). Sudden Death Expertise Center Executive Committee is part of the ESCAPE-NET project (Horizon2020 programme).

**Conflict of interest:** None declared.

## Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

## References

- Paffenbarger RS Jr, Hyde RT, Wing AL, Lee IM, Jung DL, Kampert JB. The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. *N Engl J Med* 1993;**328**:538–45.
- Albert CM, Mittleman MA, Chae CU, Lee IM, Hennekens CH, Manson JE. Triggering of sudden death from cardiac causes by vigorous exertion. *N Engl J Med* 2000;**343**:1355–61.
- Harmon KG, Asif IM, Maleszewski JJ, Owens DS, Prutkin JM, Salerno JC *et al*. Incidence, cause, and comparative frequency of sudden cardiac death in national collegiate athletic association athletes: a decade in review. *Circulation* 2015;**132**:10–9.
- Marijon E, Tafflet M, Celermajer DS, Dumas F, Perier MC, Mustafic H *et al*. Sports-related sudden death in the general population. *Circulation* 2011;**124**:672–81.
- Bohm P, Scharhag J, Meyer T. Data from a nationwide registry on sports-related sudden cardiac deaths in Germany. *Eur J Prev Cardiol* 2016;**23**:649–56.
- Bagnall RD, Weintraub RG, Ingles J, Dufloy J, Yeates L, Lam L *et al*. A prospective study of sudden cardiac death among children and young adults. *N Engl J Med* 2016;**374**:2441–52.
- Arora S, Stouffer GA, Kucharska-Newton AM, Qamar A, Vaduganathan M, Pandey A *et al*. Twenty year trends and sex differences in young adults hospitalized with acute myocardial infarction. *Circulation* 2019;**139**:1047–56.
- Bohm P, Scharhag J, Egger F, Tischer KH, Niederseer D, Schmied C *et al*. Sports-related sudden cardiac arrest in Germany. *Can J Cardiol* 2021;**37**:105–12.
- Waldmann V, Bougouin W, Karam N, Dumas F, Sharifzadehgan A, Gandjbakhch E *et al*. Characteristics and clinical assessment of unexplained sudden cardiac arrest in the real-world setting: focus on idiopathic ventricular fibrillation. *Eur Heart J* 2018;**39**:1981–7.
- Marijon E, Bougouin W, Périer MC, Celermajer DS, Jouven X. Incidence of sports-related sudden death in France by specific sports and sex. *JAMA* 2013;**310**:642–3.
- Rajan D, Garcia R, Svane J, Tfelt-Hansen J. Risk of sports-related sudden cardiac death in women. *Eur Heart J* 2022;**43**:1198–206.
- Marijon E, Bougouin W, Celermajer DS, Périer MC, Dumas F, Benameur N *et al*. Characteristics and outcomes of sudden cardiac arrest during sports in women. *Circ Arrhythm Electrophysiol* 2013;**6**:1185–91.
- Kinoshita T, Tanaka S, Sagisaka R, Hara T, Shirakawa T, Sone E *et al*. Mobile automated external defibrillator response system during road races. *N Engl J Med* 2018;**379**:488–9.
- Marijon E, Bougouin W, Celermajer DS, Perier MC, Benameur N, Lamhaut L *et al*. Major regional disparities in outcomes after sudden cardiac arrest during sports. *Eur Heart J* 2013;**47**:3632–40.
- Karam N, Pechmajou L, Narayanan K, Bougouin W, Sharifzadehgan A, Anys S *et al*. Evolution of incidence, management, and outcomes over time in sports-related sudden cardiac arrest. *J Am Coll Cardiol* 2022;**25**:238–46.
- Marijon E, Uy-Evanado A, Reinier K, Teodorescu C, Narayanan K, Jouven X *et al*. Sudden cardiac arrest during sports activity in middle age. *Circulation* 2015;**21**:1384–91.
- Marijon E, Bougouin W, Karam N, Beganton F, Lamhaut L, Perier MC *et al*. Survival from sports-related sudden cardiac arrest: in sports facilities versus outside of sports facilities. *Am Heart J* 2015;**170**:339–45.
- Pechmajou L, Sharifzadehgan A, Bougouin W, Dumas F, Beganton F, Jost D *et al*. Does occurrence during sports affect sudden cardiac arrest survival? *Resuscitation* 2019;**141**:121–7.
- Baekgaard JS, Viereck S, Moller TP, Erbsoll AK, Lippert F, Folke F. The effects of public access defibrillation on survival after out-of-hospital cardiac arrest: a systematic review of observational studies. *Circulation* 2017;**136**:954–65.
- Burke AP, Farb A, Malcom GT, Liang Y, Smialek JE, Virmani R. Plaque rupture and sudden death related to exertion in men with coronary artery disease. *JAMA* 1999;**281**:921–6.
- Karam N, Pechmajou L, Dumas F, Bougouin W, Sharifzadehgan A, Beganton F *et al*. Comprehensive assessment of coronary artery disease in sports-related sudden cardiac arrest. *Circulation* 2018;**138**:429–31.
- Zimmerman FH, Cameron A, Fisher LD, Grace NG. Myocardial infarction in young adults: angiographic characterization, risk factors and prognosis (coronary artery surgery study registry). *J Am Coll Cardiol* 1995;**26**:654–61.
- Ha FJ, Han HC, Sanders P, La Gerche A, Teh AW, Farouque O *et al*. Sudden cardiac death related to physical exercise in the young: a nationwide cohort study of Australia. *Int Med J* 2021. <https://doi.org/10.1111/imj.15606>.
- Landry CH, Allan KS, Connelly KA, Cunningham K, Morrison LJ, Dorian P. Sudden cardiac arrest during participation in competitive sports. *N Engl J Med* 2017;**377**:1943–53.
- Finocchiaro G, Papadakis M, Robertus JL, Dhutia H, Steriotis AK, Tome M *et al*. Etiology of sudden death in sports: insights from a United Kingdom regional registry. *J Am Coll Cardiol* 2016;**67**:2108–15.
- Eckart RE, Shry EA, Burke AP, McNear JA, Appel DA, Castillo-Rojas LM *et al*. Sudden death in young adults: an autopsy-based series of a population undergoing active surveillance. *J Am Coll Cardiol* 2011;**58**:1254–61.