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Does Occurrence during Sports affect Sudden Cardiac Arrest Survival?
Short Title: Survival in Sports-Related Sudden Cardiac Arrest

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ABSTRACT (Word count 249)

Objectives: A higher survival rate was observed in Sudden Cardiac Arrest (SCA) occurring during sports activities, although the underlying mechanisms remain unclear. We tested the hypothesis that better initial management, rather than sports *per se*, may account for the observed better outcomes during sports activities.

Methods: Data was taken between May 2011 and March 2016 from a prospective ongoing registry that includes all SCA in Paris and suburbs (6.7 million inhabitants). Sports-related SCA (i.e. SCA occurring during sport activities or within one hour of cessation of the activity) were identified.

Results: Over the study period, 13,400 SCA occurred, of which 154 were sports-related (median age: 51.2 years, 96.1% males). At discharge, sports activity was associated with an 8-times higher survival rate (39.7% vs. 5.1%, $P<0.001$). Logistic regression showed that after considering potential confounders, including age, gender, SCA location, witness presence, time to response, and initial shockable rhythm, occurrence of SCA during sports was associated with a higher survival rate (OR 1.77, 95% CI 1.14-2.74, $P=0.01$). However, after further adjustment for initial basic life support, i.e. bystander CPR and AED use, there was no association between sports setting and survival at hospital discharge (OR 1.43, 95% CI 0.91-2.23, $P=0.12$).

Conclusion: Sports-related SCA is a rare event, with an 8-times higher survival rate compared to non-sports-related SCA. Better initial management, including bystander CPR and AED use, rather than sports *per se*, mainly accounts this difference. This highlights the major importance of population education to basic life support in improving SCA outcome.

Keywords: Sudden death; Exercise; Screening; Prevention; Education

79 **Abbreviations list**
80 SCA: Sudden Cardiac Arrest
81 SDEC: Sudden Death Expertise Centre
82 CCPPRB: Committee for the Protection of Human Subjects in Biomedical Research
83 CNIL: Commission Nationale Informatique et Liberté
84 EMS: Emergency Medical Service
85 AED: Automated External Defibrillation
86 ECG: electrocardiogram
87 ROSC: return of spontaneous circulation
88 ECMO: Extra-Corporeal Membrane Oxygenation
89 CPC: Cerebral Performance Category
90 STROBE: Strengthening the Reporting of Observational Studies in Epidemiology
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INTRODUCTION

Despite the well-documented benefits of regular sport activity on the reduction of cardiovascular events,[1] the risk of Sudden Cardiac Arrest (SCA) is transiently increased during or shortly after exercise, a concept that is known as the exercise paradox.[2–4] Sports-related SCA have traditionally been associated with young competitive athletes due to the high media coverage and emotional impact of SCA occurring during competition, in a population that is commonly considered as healthy and fit.[5,6] However, more recent studies have shown that sports-related SCA occur more frequently among recreational athletes, especially among middle age participants, with an estimated number of 8000-10000 cases each year in Europe and approximately half this number in the United States.[7–10]

Beyond the issue of incidence in different subgroups of sport participants, the impact of occurrence during sports on SCA prognosis has not been well investigated. Several studies have shown a higher crude survival rate of sports-related SCA compared to non-sports related SCA.[8,11,12] In which extent this better outcome is related to participants' characteristics and to exercise *per se*, rather than to external factors associated to the specific setting of sports practice has not been fully evaluated.

Using data from a large prospective community-based study in the Paris area, carried out in the general population, we tested the hypotheses that a better initial management, rather than sports *per se*, may account for the observed better outcomes during sports activities.

METHODS

Study Population and Setting

The Paris-Sudden Death Expertise Centre (SDEC) registry was initiated in May 15, 2011.[13–15] It includes all SCA occurring in Paris and its suburbs, which accounts for a residential population of approximately 6.7 million (10% of the overall French population). This prospective study is conducted according to the Declaration of Helsinki, with the approval of the Committee for the Protection of Human Subjects in Biomedical Research (CCPPRB) and the French data protection committee (Commission Nationale Informatique et Liberté, CNIL).

In the Paris area, the Emergency Medical Service (EMS) is a two-tiered response system: a Basic Life Support tier served by fire-fighters of the Brigade de Sapeurs Pompiers de Paris, who can apply Automated External Defibrillation (AED), and an advanced cardiac life support tier served by ambulance teams with an emergency physician, a nurse, and/or a paramedic (Service d'Aide Médicale Urgente). For every SCA assessed by EMS, each of the EMS tiers sends a nominative report form to the SDEC (source 1). To ensure completeness, an electronic query algorithm is also performed in the advanced cardiac life support computer system to identify every case of SCA (source 2). Finally, regular controls based on diagnostic codes are conducted in selected intensive care units (control). With this meticulous data collection and verification, the exhaustiveness of the database was estimated to be 98.6%.[16]

Sports-related SCA was defined as SCA occurring during sport activities or within one hour of cessation of the activity. Sports-related sudden deaths related to trauma (for example, runner or cyclist hit by a car) were excluded. [17][18] Sports facilities were defined as activities practiced (i) in places specially designed, regardless of their size (including stadium, tennis facilities, etc), or (ii) in the context of competition. By contrast, setting was defined as outside of sports facilities for others—individuals who performed sports activities without any structure or organized competition.[19]

Collected Utstein Data

Data are collected according to the Utstein recommendations.[20] Exclusion criteria were patient's age of less than 18 years, SCA occurring outside the area of interest, prior terminal condition (such as metastatic malignancy), or obvious non-medical cause according to Utstein templates (traumatic, drug overdose, drowning, asphyxia...). Collected data include general information regarding demographic characteristics, past medical history, basic life

support (cardiopulmonary resuscitation (CPR) and AED use), initial cardiac rhythm, electrocardiogram (ECG) characteristics when return of spontaneous circulation (ROSC) is obtained, use of Extra-Corporeal Membrane Oxygenation (ECMO), targeted temperature control, coronary angiography and angioplasty. Survival and neurological status (according to Cerebral Performance Category (CPC) score, considering a CPC score of 1 or 2 as a favorable outcome) at hospital admission and discharge are also recorded. At least two independent reviewers determine the causes of SCA after analyzing each file. They also systematically review each record in order to guarantee data completion and validity.

Statistical Analysis

This report was prepared in compliance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist for observational studies.[21] Variables were reported as mean, SD, proportion, median and interquartile range, as appropriate. Comparisons between groups (sports versus non-sports-related) were performed using the χ^2 test or the Fisher exact test for categorical variables, and the Student t test or Mann-Whitney test for continuous variables, as appropriate. Logistic regression models were used to estimate the odds ratios (OR) and their 95% confidence interval (95% CI) for the association between the time of SCA occurrence and the odds of being alive at hospital discharge. A univariate analysis was first performed with all the descriptive variables, and the association between these variables and the survival rate was tested using the Wald test. Multivariate analysis was performed with adjustment for all the variables that were significant in the univariate analysis. All tests were two-tailed, and *P* values of less than 0.05 were considered to indicate statistical significance. All data were analyzed at the Sudden Death Expertise Centre, INSERM, Unit 970, Paris, using R software, version 3.3.1. The authors had full access to data and designed the statistical analysis, had final responsibility for the decision to submit the manuscript for publication, and vouch for the accuracy and completeness of the data and the analyses.

RESULTS

Characteristics of SCA occurring during sport activities

Between May 2011 and March 2016, 18,306 out-of-hospital cardiac arrests were recorded. Of those, 2,655 patients had obvious non-medical causes and 435 patients had a prior terminal condition. Therefore, 15,216 SCA were identified. After excluding 1,816 patients aged over 90, 13,400 patients were included in the study; 154 occurred during sports activities (Figure 1).

Baseline characteristics of SCA, according to the occurrence during sports activities, are described in Table 1. Sports-related SCA victims were younger (median age: 51.2 [40.8-60.7] vs. 69.8 [57.0-81.4] years in the non-sports population, $P<0.001$), with a higher proportion of males (96.1% vs. 64.1%, $P<0.001$). Sports-related SCA occurred mainly during running (59 cases, 38.3%), cycling (21 cases, 13.6%), football (15 cases, 9.7%) and fitness activities (13 cases, 8.4%; Supplementary Figure), with 43.8% (49 cases) occurring in public sports facilities.

Initial management and Basic Life Support

Compared to non-sports related SCA, sports-related SCA occurred more frequently in a public location (90.9% vs. 20.3%, $P<0.001$). Witnesses were more often present (95.4% vs. 70.7%, $P<0.001$), and were more likely to initiate CPR (82.9% vs. 54.5%, $P<0.001$), and to use AEDs prior to EMS arrival (15.3% vs. 2.3%, $P<0.001$), compared to non-sports related SCA. Bystander CPR was performed in 121 cases (79.1%) in the sports-related SCA group vs. 4,639 cases (38.6%) in the non-sports related SCA group ($P<0.001$), with an AED used in 21 cases (14.7%) of sports-related SCA vs. 130 cases (1.4%) of non-sports related SCA ($P<0.001$).

In the particular case of SCA occurring in sports complex, 47 cases (95.9%) were witnessed. Bystander CPR was performed in 43 cases (87.8%), with an AED used in 12 cases (25.5%). Outside sports complexes, when comparing all SCA occurring in public areas, the rate of bystander CPR (83.6% vs. 64.3%, $P<0.001$), and AED use (15.6% vs. 6.5%, $P<0.001$) were still higher during sports activities.

Advanced medical resuscitation

The proportion of EMS-witnessed SCA (10.8% vs. 11.5%, $P=0.89$) and of time delay < 9 min between the call-to-EMS and EMS arrival did not differ between the two groups (39.6% vs. 41.9%, $P=0.63$). The rate of shockable

initial rhythm was higher during sports activities (77.8% vs. 20.2%, $P<0.001$), and ECMO was more frequently used (14.9% vs. 2.6%, $P<0.001$).

ROSC was more frequently obtained in sports-related SCA (62.9% vs. 29.4%, $P<0.001$), and the survival rate at hospital admission was higher (79.7% vs. 23.3%, $P<0.001$). Among survivors to hospital admission, there was no significant difference in the rates of targeted temperature control (53.6% vs. 53.3%, $P=0.77$) and coronary angiography (70.9% vs. 61.0%, $P=0.20$) (Table 1).

Presumed cause of SCA and past medical history

Sports-related SCA patients were less likely to have a prior history of heart disease (16.5% vs. 33.9%, $P=0.014$) and coronary artery disease (7.0% vs. 18.9%, $P=0.015$). In terms of cardiovascular risk factors, sports-related SCA were less frequently active smokers (19.6% vs. 34.2%, $P<0.001$) and diabetics (5.6% vs. 21.0%, $P=0.006$). There was no difference in the rates of dyslipidemia and hypertension between the 2 groups.

Among patients who survived at hospital admission, the cause of SCA could be identified in 89 (75.4%) sports-related SCA and 1,949 (72.1%) non-sports-related SCA ($P=0.49$). When the SCA etiology was found, a cardiac cause was more frequently identified in the sports-related SCA group (94.4 vs. 63.7, $P<0.001$). CAD was the most frequent cause of SCA in the global SCA population, with a higher prevalence in sports compared to non-sports related SCA (66.3% vs. 50.4%, $P=0.003$) (Figure 2).

Survival influencing factors

Sports-related SCA had a better survival rate at hospital discharge (39.7% vs. 5.1%, $P<0.001$) with a similar rate of CPC score 1 or 2 at discharge among survivors (94.2% vs. 94.8%, $P=0.986$), compared to non-sports related SCA.

On univariate analysis, shockable initial rhythm was the strongest survival predictor (OR 29.43, 95% CI 23.82-36.72, $P<0.001$), followed by bystander CPR (OR 16.48, 95% CI 11.54-24.55, $P<0.001$) and occurrence during sports (OR 12.22, 95% CI 8.66-17.13, $P<0.001$) (Table 2).

After adjustment for age, gender, SCA location, call to EMS arrival < 9 min, and initial shockable rhythm, occurrence during sports was associated with a higher survival rate (1.66 95% CI 1.08-2.54, $P=0.025$). However, after adjustment for witnessed status, i.e. bystander CPR and witness presence, there was no association between occurrence of SCA during sports activity and survival at hospital discharge (OR 1.41, 95% CI 0.91-2.17,

211 $P=0.122$) (Table 3). Occurrence during was not associated neither with survival with a better neurological outcome
212 (OR 1.40, 95% CI 0.89-2.19, $P=0.14$).
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DISCUSSION

In this prospective and extensive collection of all cases of SCA occurring in Paris and its suburbs over a five-year period, sports-related SCA occurred mainly in middle-aged men. Survival rate at hospital discharge was 7 to 8 times higher in sports-related SCA, despite a very similar in-hospital medical management. Higher rates of bystander' CPR and AED use in sports-related SCA appear to account for this higher survival rate, whereas sports activity *per se* was not associated to a better outcome, illustrating the major yield of bystanders in improving SCA prognosis.

There is conflicting evidence regarding the impact of sport occurrence on the survival after SCA. Whereas most studies in the general population have reported a higher survival rate in sports-related SCA, the exact role occurrence during sports in this better prognosis remains unclear.[11,22] Several hypotheses have been made, linking the better outcome to a cardioprotective role of sports on the endothelium and vascular function, as well as to the higher activation of the sympathetic system during sports.[11] Other hypotheses focused on the better management of sports-related SCA that could also be playing a role in this better survival rate.[19]

Although we observed a dramatically higher rate of survival when SCA occurs during sports, after adjustment for the main known prognostic factors, exercise *per se* was not associated to a better survival rate. EMS arrival delays and in-hospital management could not account for this improved survival neither since they did not differ according to whether SCA occurred during sports or not. Besides, we previously demonstrated that differences in the characteristics of accepting hospital did not influence SCA outcome in Paris and its suburbs.[23] Conversely, we observed differences in bystanders' response to SCA, with a higher rate of bystander CPR and AED use in sports-related SCA, even when considered only witnessed SCA occurring in public areas.

Our results illustrate the major impact of the early phase of SCA management, and the paramount role of bystanders in improving SCA prognosis. This finding has been previously demonstrated in the context of sports-related SCA through a French national study, where major heterogeneities have been observed among districts in terms of survival after sports-related SCA, mainly due to differences in the rate of bystander-initiated CPR.[24] Efforts should be made to improve bystanders CPR and AED use rate in all-comers SCA where the rate of CPR and AED remains low, leading to a much lower survival rate than in the sports setting.[25]

Efforts for reducing sports-related SCA burden have focused on the identification of athlete who are at risk of SCA. Most studies on sports-related SCA have focused on young competitive athletes and the priority has been given to pre-participation screening in competitive sport. [5,26–28] However, in our study, most sports-related SCA cases occurred in middle-aged leisure athletes, among whom the identification of participants at risk of SCA is more difficult. European Guidelines recommended a clinical evaluation, including exercise testing may be considered for sedentary people with cardio-vascular risk factors who intend to engage in vigorous physical activity.[29] The efficiency of this strategy in reducing the incidence of sports-related SCA has not been demonstrated, and SCA-risk assessment among athletes have been challenging. Given the difficulty in reducing the incidence of sports-related SCA, more efforts should focus on implementing measures to improve SCA survival rate once it occurred, mainly by population education to basic life support. Besides bystanders' education, education of sports participants could possibly reduce the incidence of SCA. In a previous study, we observed that most patients with sports-related SCAs presented warning symptoms before SCA, but maintained their physical activity anyway.[14] Educating the participants to recognize warning symptoms and seek medical advice before SCA could help avoiding several cases of SCA.

Several limitations have to be acknowledged, first, due to the very low rate of systematic autopsy in France, the cause of OHCA could not be established in all cases. Second, information regarding the degree of physical activity on a daily basis was not available in the database and causality between SCA and sports activity could be debated in cases where the level of physical exercise was low. Finally, this study was conducted in Paris and its suburbs. The extent to which similar results could be obtained in countries with a different health care system needs further evaluations.

In conclusion, sports-related SCA is a rare event with a much better prognosis than SCA during at rest or during other activities. Better initial management, including higher rates of bystander CPR and AED use, rather than sports *per se*, account for this difference. This observation highlights the major impact of bystanders' basic life support in improving SCA survival, and the need to extend population education to basic life support.

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332 Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart
333 Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the
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373 **Appendix – Paris-SDEC 2019 Investigators Listing (Supplementary File)**

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386

387 **Figure legends**

388 **Figure 1: Study Flowchart between May 2011 and March 2016**

389 Between May 2011 and March 2016, 18,306 out-of-hospital cardiac arrests, of which 15,216 fulfilled the
390 definition of SCA. Among them, 154 were sports-related.

391 *SCA: Sudden Cardiac Arrest*

392 **Figure 2: Presumed Causes of Sudden Cardiac Arrest According to Occurrence During Sports**

393 Coronary artery disease was the most frequent cause of SCA, with a higher prevalence in sports-related compared
394 to non-sports related SCA. Non-cardiac causes were more frequent in non-sports related SCA.

395 *VF: ventricular fibrillation*

396 **Supplementary Figure: Types of Sports Practiced at the time of Sudden Cardiac Arrest**

397 Sports-related SCA occurred mainly during running (59 cases, 38.3%), cycling (21 cases, 13.6%), football (15
398 cases, 9.7%) and fitness activities (13 cases, 8.4%)

Table 1: Characteristics and Management of the Sudden Cardiac Arrest According to Occurrence During Sports

	N	Non-sports related SCA N=13,246	Sports related SCA N=154	P value
Demographic data				
Age, years	13,400	69.8 [57.0-81.4]	51.2 [40.8-60.7]	<0.001
≤ 40 years		763 (5.7)	39 (25.3)	<0.001
40-60 years		3284 (24.8)	73 (47.4)	<0.001
≥ 60 years		9199 (69.4)	42 (27.3)	<0.001
Male gender	13,351	8455 (64.1)	148 (96.1)	<0.001
Risk factors[†]				
Hypertension	2,850	1111 (40.5)	28 (25.9)	0.751*
Dyslipidemia	2,828	626 (23.0)	24 (22.2)	0.368*
Current smoker	2,812	926 (34.2)	21 (19.6)	<0.001*
Diabetes mellitus	2,846	575 (21.0)	6 (5.6)	0.006*
Medical history[†]				
Known heart disease	2,865	932 (33.9)	19 (16.5)	0.014*
Know coronary artery disease	2,820	512 (18.9)	8 (7.0)	0.015*
Characteristics of cardiac arrest				
Public location	13,298	2664 (20.3)	140 (90.9)	<0.001*
Witnessed status	12,184			<0.001*
Non-witnessed		3520 (29.3)	7 (4.6)	
Witnessed without CPR		3872 (32.2)	25 (16.3)	
Witnessed with CPR		4639 (38.6)	121 (79.1)	
AED use	9,202	130 (1.4)	21 (14.7)	<0.001*
EMS witnessed	12,080	1369 (11.5)	16 (10.8)	0.887*
Call to EMS arrival <9min	12,809	5313 (41.9)	53 (39.6)	0.632*
Initial shockable rhythm	11,354	2265 (20.2)	112 (77.8)	<0.001*
ECMO	12,397	346 (2.6)	23 (14.9)	<0.001*
In hospital management[†]				
Coronary angiography	2,858	1673 (61.0)	83 (70.9)	0.199*
Targeted temperature control	2,773	1419 (53.3)	59 (53.6)	0.771*
Outcome				
ROSC	11,192	3242 (29.4)	95 (62.9)	<0.001*
Survival at hospital admission	13,396	3084 (23.3)	122 (79.7)	<0.001*
Survival at hospital discharge	13,003	658 (5.1)	58 (39.7)	<0.001*
Survival with CPC 1 or 2	12,974	600 (4.7)	49 (35.3)	<0.001*

Values are median [25-75th percentile] or n patients (%). Percentages were calculated on the basis of the total number of known events. SCA: Sudden Cardiac Arrest; CPR: CardioPulmonary Resuscitation; AED: Automated External Defibrillator; EMS: Emergency Medical Service; ECMO: ExtraCorporeal Membrane Oxygenation; ROSC: Return of Spontaneous Circulation; CPC: Cerebral Performance Category.

[†]Among survivors to hospital admission (N= 3084, including 122 sport-related SCA).

*Adjusted for age and gender

Table 2. Factors Associated with Survival at Hospital Discharge for Sudden Cardiac Arrest

	Univariate analysis		Multivariate Model	
	OR (95% CI)	P value	OR (95% CI)	P value
Sports activity	12.22 (8.66-17.13)	<0.001	1.41 (0.91-2.17)	0.122
Age, y				
≤ 40	4.20 (3.27-5.34)	<0.001	2.88 (2.09-3.94)	<0.001
41-59	3.37 (2.86-3.97)	<0.001	1.98 (1.62-2.43)	<0.001
≥ 60	1.00		1.00	
Male gender	2.00 (1.68-2.41)	<0.001	0.90 (0.71-1.14)	0.3739
Public location	7.00 (5.99-8.20)	<0.001	2.60 (2.14-3.17)	<0.001
Witnessed status				
Non witnessed	1.00		1.00	
Witness without CPR	4.13 (2.80-6.31)	<0.001	1.98 (1.27-3.22)	0.004
Witness with CPR	16.48 (11.54-24.55)	<0.001	5.12 (3.38-8.11)	<0.001
AED use	6.36 (4.42-9.02)	<0.001		
EMS witnessed	2.16 (1.78-2.62)	<0.001		
Call to EMS arrival < 9 min	1.34 (1.14-1.57)	<0.001	1.33 (1.10-1.61)	0.003
Initial shockable rhythm	29.43 (23.82-36.72)	<0.001	16.13 (12.71-20.68)	<0.001

CPR: CardioPulmonary Resuscitation. AED: Automated External Defibrillation. EMS: Emergency Medical Service. ECMO: ExtraCorporeal Membrane Oxygenation.
394 patients had unknown survival at discharge status (including 8 sports related SCA).

Table 3. Multivariate survival analysis

	Non-sports	Sports	
	N=12860	N=143	P
Survival, n (%)	658 (5.1)	58 (39.7)	<0.001
OR, Model 0	1	12.22 (8.66-17.13)	<0.001
OR, Model 1	1	7.19 (5.02-10.22)	<0.001
OR, Model 2	1	6.91 (4.68-10.11)	<0.001
OR, Model 3	1	3.23 (2.17-4.75)	<0.001
OR, Model 4	1	1.66 (1.08-2.54)	0.021
OR, Model 5	1	1.41 (0.91-2.17)	0.122

Model 0: Sports

Model 1: Sports + Age + Gender

Model 2: Sports + Age + Gender + Call to EMS arrival < 9 min

Model 3: Sports + Age + Gender + Call to EMS arrival < 9 min + Home location

Model 4: Sports + Age + Gender + Call to EMS arrival < 9 min + Home location + Initial shockable rhythm

Model 5: Sports + Age + Gender + Call to EMS arrival < 9 min + Home location + Initial shockable rhythm + Bystander initiated CPR

Out-of-Hospital Cardiac Arrests
N = 18,306

435 Prior terminal conditions
2,655 Obvious non-cardiac causes

Sudden Cardiac Arrest (SCA)
N = 15,216

1,816 Patients ≥ 90 years

SCA (18-89 years)
N = 13,400

Non sports-related SCA
N = 13,246

Sports-related SCA
N = 154

Sports-Related Sudden Cardiac Arrest

**8-fold higher
survival rate**

**Better initial
management**

**BLS explains the
better survival**

SCA

39.7%

5.1%

X2

X10

**Sports activity
OR 1.43, P=0.121**

(survival rate at discharge)

(rates, versus non-SRSD)

(multivariate survival analysis)