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Incidence, Survival and Bystander Response

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Published in:
Surgical Endoscopy

DOI (link to publication from Publisher):
10.1016/j.resuscitation.2022.01.021

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

RESUSCITATION 172 (2022) 84–91

Available online at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Out-of-hospital cardiac arrest related to exercise in the general population: Incidence, survival and bystander response

Signe Amalie Wolthers[a,b,*], *Theo Walther Jensen*[b,c], *Stig Nikolaj Blomberg*[c], *Mathias Geldermann Holgersen*[b,d], *Freddy Lippert*[c], *Søren Mikkelsen*[e], *Ole Mazur Hendriksen*[a], *Christian Torp-Pedersen*[f,g], *Helle Collatz Christensen*[a,b,h]

[a] *Prehospital Center Region Zealand, Næstved, Denmark*
[b] *Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*
[c] *Copenhagen Emergency Medical Services, The Capital Region of Denmark, Ballerup, Denmark*
[d] *Paediatric Pulmonary Service, Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital, Rigshospitalet, Denmark*
[e] *Prehospital Research Unit, Department of Anaesthesiology and Intensive Care, Odense University Hospital, Denmark*
[f] *Department of Cardiology, Nordsjaellands Hospital, Hillerød, Denmark*
[g] *Aalborg University Hospital, Aalborg, Denmark*
[h] *Danish Clinical Quality Program (RKKP), National Clinical Registries, Denmark*

Abstract

Background: Regular exercise is known to prevent cardiovascular disorders, but it may also trigger acute cardiac events. This study examined the incidence, prognosis, and outcomes of out-of-hospital cardiac arrest (OHCA) related to exercise in the general population of Denmark.

Methods: This retrospective cohort study examined all the OHCAs in the Danish Cardiac Arrest Registry from 2016 to 2019. OHCA related to exercise was identified in a nationwide electronic database and coupled to the patient register. Descriptive statistics were used in combination with a multivariate logistic regression model to assess predefined factors.

Results: A total of 20,470 OHCAs were identified, of which 459 (2.2%) were related to exercise. Most were male (75.3%), with a median age of 61 years. Further, 95% of exercise-related OHCA received bystander cardiopulmonary resuscitation, compared to 77.4% in non-exercise-related OHCA ($p < 0.001$), and 38.3% received defibrillation by bystanders versus 7.5% in the non-exercise group ($p < 0.001$). Exercise-related OHCAs had a 30-day survival rate of 57.7% compared to 12.6% in the non-exercise group, yielding an adjusted odds ratio of 5.56. The 30-day survival rate of exercise-related subjects aged 15–35 years was 80.0%, compared to 25.0% in the non-exercise group. When comparing sports categories, team sports were associated with the greatest chance of survival (odds ratio of 18.5 versus a non-exercise odds ratio of 0.09).

Conclusion: Exercise-related OHCA has a low incidence and is related to a significantly better prognosis when compared to non-exercise OHCA. Furthermore, many patients experiencing exercise-related OHCA received defibrillation and cardiopulmonary resuscitation by bystanders. These findings could help plan and execute campaigns and education.

Keywords: Out-of-hospital cardiac arrest, Bystander CPR, Defibrillation, Resuscitation, Exercise, Emergency Medical Service, Outcome after OHCA

Abbreviation: ROSC, Return of spontaneous circulation

* Corresponding author.
E-mail address: s.a.wolthers@gmail.com (S.A. Wolthers).

https://doi.org/10.1016/j.resuscitation.2022.01.021
Received 27 October 2021; Received in Revised form 15 January 2022; Accepted 19 January 2022

Introduction

Exercise has been shown to reduce the risk of cardiovascular disease. However, it can also be related to a transient increased risk of cardiac events, including sudden cardiac arrest.[1]

Previous studies have reported low annual incidences of out-of-hospital cardiac arrest (OHCA) related to exercise compared to other subgroups of OHCA with rates between 0.48 and 2.1 per 100.000 person-years[2–5] and 0.3–7% of all OHCAs.[3,6] No standardised definition of the timeframe concerning OHCA related to exercise is established; however, the onset of symptoms during or up to one hour after exercise is a typical definition.[3,4,7] Reported survival rates of exercise-related OHCA vary from 5.5% to 77%, with substantial differences regarding sample size and inconsistent outcome definitions.[3–5,8–10] This necessitates further investigation and cohesion to standardised reporting using the Utstein Reporting Template.[11] Despite conflicting survival rates, there is consensus that OHCA related to exercise has a better prognosis than that not related to exercise.[3–6,10,12] Another consistent finding is the younger age of the patients suffering from OHCA related to exercise compared to those with other OHCAs.[4,5,12]

The Danish Emergency Medical System introduced a nationwide registry of electronic medical reports in 2016.[13] This medical report system allows electronic searches and to identify the subgroups of OHCA. Hence, this novel reporting enables the investigation of the comprehensive characteristics of OHCA related to exercise.

Few prior studies have evaluated population-based outcomes and characteristics of OHCA related to exercise; despite the worldwide media attention, a significant part of this area remains unidentified. The importance of early actions performed by bystanders, such as cardiopulmonary resuscitation and defibrillation, is known to be associated with increased survival; however, data on the use of defibrillators remain limited. As such, an improved understanding of exercise-related OHCA is fundamental to both prophylactic and treatment strategies, and the findings of this study may lead to further improvement in patient safety and outcome. This study aims to report the national incidence of exercise-related OHCAs among cases attended by the Danish Emergency Medical Service (EMS) and assess survival, defined as the return of spontaneous circulation (ROSC), followed by a 30-day survival. Additionally, aspects associated with better outcomes are evaluated, including the following: observation of occurrence, bystander cardiopulmonary resuscitation (CPR), initial electrocardiographic (ECG) rhythm, use of an automated external defibrillator (AED) by bystanders and defibrillator/monitor by EMS personnel, type of exercise, and baseline demographics.

Methods

This was a registry-based nationwide cohort study with data from the Danish OHCA registry from 1 January 2016 to 31 December 2019, with OHCA during or up to one hour after exercise.

The Danish Cardiac Arrest Register includes all cases of OHCA where resuscitation was initiated in Denmark. Data have been collected in the electronic-based Danish EMS reporting system since 2016. Thus, the registry covers detailed data, including the EMS reports. The data are obtained from executive entries in conjunction with advanced text searches of prehospital charts, enabling the identification of all OHCAs where resuscitation was initiated in Denmark. All cases underwent an elaborate validation process in which all the identified events were manually scrutinised. This validation process was conducted by an external verification team to ensure high-quality data from approximately 5400 cases of annually occurring OHCAs in Denmark. In the verification process, supplementary sources of data were linked to each case of OHCA. Specific points of interest in the validation process were survival, initiation of CPR by the bystander, use of an AED, and actions of EMS personnel. The initial ECG rhythm was defined as the first ECG rhythm recorded by EMS personnel using a standardised monitor/defibrillator.

Three raters independently identified the presumed causes of OHCA related to exercise. Cases were assessed based on the Utstein model regarding aetiology, using the following subgroups of eliciting causes for OHCA: presumed cardiac origin, unknown cause, other medical cause, trauma, drug overdose, drowning, electrocution, or asphyxia (external). The cause of OHCA was supported by free-text description. Any discrepancy was resolved by the third-party members. Cases with a lack of relevant information concerning the cause and cases with several conflicting causalities were labelled as 'NA' and 'inconclusive', respectively. All cases identified as exercise-related OHCA were manually categorised by two individual researchers. The verified cases were assessed and coupled with relevant electronic prehospital medical records. Exercise-related cases were categorised and classified into six subgroups: team sports (soccer, handball, volleyball, tennis, and badminton); fitness (gymnastics, aerobics, cross-fit, weight lifting, strength training, dancing, yoga, pilates, athletics); running/jogging (marathon, ironman, triathlon, running, jogging, power walking, roller-skating); cycling (cycling, mountain biking, spinning); waters (swimming, sailing, surfing, kitesurfing, rowing, kayaking); miscellaneous (bowling, hunting, golf, equestrian sports). Furthermore, sports categories were subdivided into either moderate-intensity sports, defined as 3–6 Metabolic Equivalents (METs), or vigorous-intensity sports with >6 METs.[14] This division of sports categories was based on the 2018 Physical Activity Guidelines adapted from the Center for Disease Control and Prevention.[15]

Data were collected in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement (STROBE). Descriptive statistics included the abovementioned variables labelled with absolute numbers and percentages. Comparative analyses were performed using non-parametric testing to examine the subgroups. Further, continuous data were analysed using Student's t-test, and the remaining associations between the characteristics of arrest and 30-day survival were examined using Fisher's exact test. Moreover, logistic regression analysis was performed for adjusted multivariate analysis. Statistical significance was considered at a p-value of <0.05, and all statistical tests were performed using R version 1.3.1093.[16].

The General Data Protection Regulation (GDPR) was followed according to Danish law, and the study was registered and approved by the Danish Data Protection Agency (reference 2007–58-0015, GEH-2014–019, I-suite 02737). According to Danish legislation, register-based research does not require ethical committee approval or patient consent.

Results

Within four years, from January 2016 to December 2019, 20,470 cases of OHCA were attended by the Danish EMS. Through an

electronic database search, 1,429 cases were found to be related to sports or exercise. Further manual validation resulted in the exclusion of 916 cases, of which the major causes of exclusion were cases not related to exercise due to trauma or drowning. Finally, after evaluating missing data and excluding duplets, 459 cases were analysed (Fig. 1). This was equivalent to an incidence of 2.2% of all OHCAs in the four-year period, corresponding to an incidence in the general Danish population of 1.7 per 100,000 person-years. A revised STROBE diagram (Fig. 1) depicts the eligibility of the patients and respective included samples.

Patient characteristics and survival outcomes are reported in Table 1, comparing the OHCA related to exercise with the overall OHCA data. For OHCAs related to exercise, the median age was 61.0 IQR (52.0–72.0), and 75.3% were male. Exercise-related OHCA was more frequently witnessed by bystanders, more likely to have CPR by bystanders and more likely to be defibrillated with AED by bystanders compared to non-exercise-related OHCA ($p < 0.001$ for all comparisons). Further, non-shockable rhythms (pulseless electrical activity [PEA]/asystole), as the initial ECG rhythm, were less common in patients with exercise-related OHCA than in those with non-exercise-related OHCA, respectively 29.8% vs. 69.7%, ($p < 0.001$) (Table 1). The remaining 25% (n = 115) presented with an ECG indicative of return of reorganised rhythm with palpable pulse when assessed by the EMS personnel.

A comparison of survival outcomes is illustrated in Table 2. ROSC at any time before admission to the hospital was seen in 74.1% (n = 340) of exercise-related OHCAs and 30.3% (n = 6208) of the non-exercise-related OHCAs. The patient status at the time of hospital admission was evaluated by comparing cases with ROSC (both conscious and unconscious) at admission with the groups of ongoing CPR and those declared dead at the scene or before admission at the hospital. A substantial difference between exercise-related and non-exercise-related OHCAs was also seen in terms of status after admission to the hospital, with ROSC rates of 70.6% (n = 324) in the exercise group and 26.0% (n = 5282) in the non-exercise group ($p < 0.001$). The 30-day survival of OHCAs related to exercise was almost 60% compared to merely more than 10% in non-exercise-related OHCAs ($p < 0.001$).

Most exercise-related OHCAs were related to fitness (17.6%, n = 81), team sports (12.6%, n = 58), and water sports (7.0, n = 33%), while the least common sports categories were athletics (0.2%, n = 1), combat sports (0.2%, n = 1), and hiking (0.2%, n = 1).

In OHCA related to exercise, younger age was associated with a higher chance of survival, with a median age of 61 years (IQR 50.0–70.0) for the survival group, compared to 67.5 years (IQR 56.3–76.0) in the non-survival group ($p < 0.001$). Furthermore, a substantial difference between the groups regarding the initial ECG rhythm was observed. Non-shockable initial ECG rhythm was observed in 14.0% of patients in the survival group, compared to 59.0% in the non-survival group ($p < 0.001$). The use of AEDs by bystanders was also significantly different between the survival group and the non-survival group ($p < 0.001$) at 48.3% and 25.4%, respectively. Additionally, the frequency of bystanders who witnessed OHCAs were significantly higher in the survival group (83.0%) than in the non-surviving group (71.1%) ($p = 0.022$).

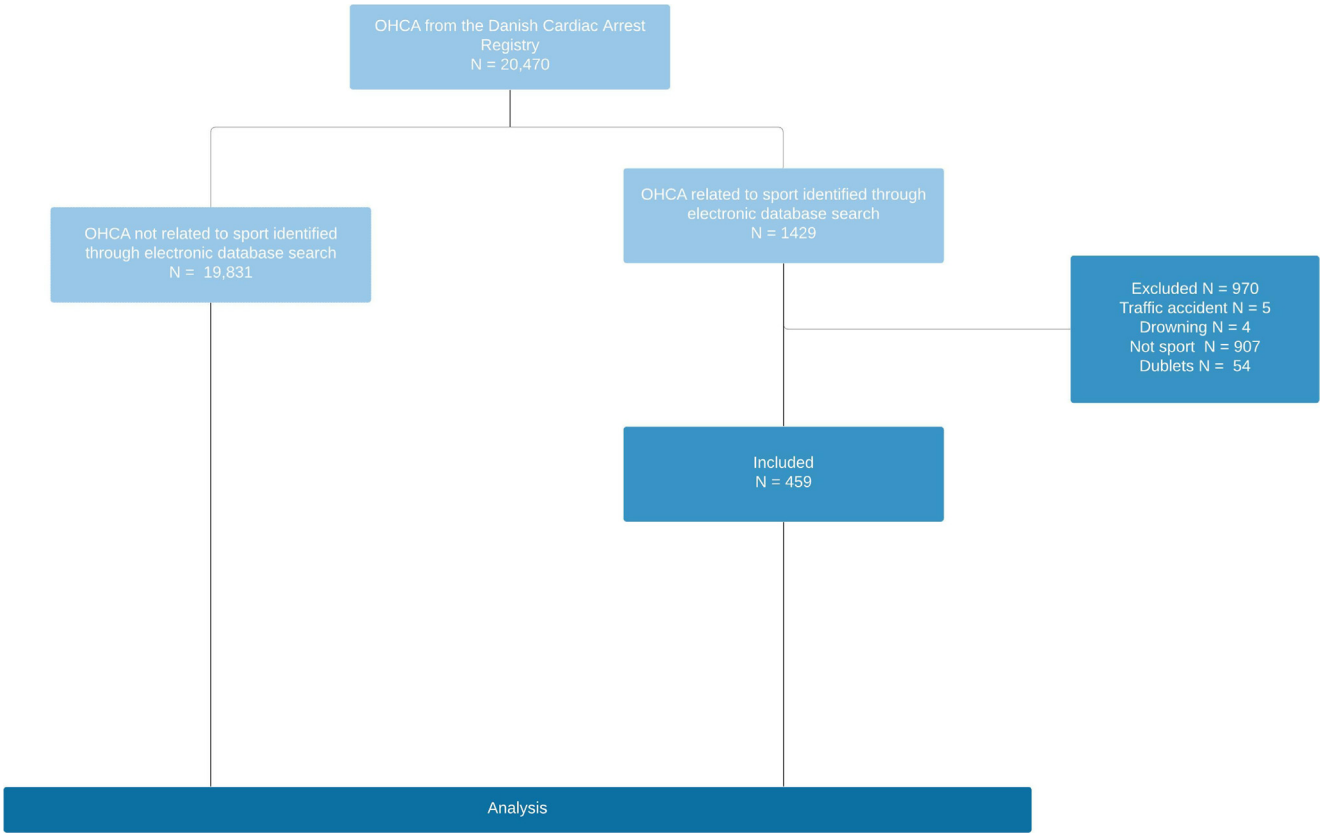


Fig. 1 – Strengthening the Reporting of Observational studies in Epidemiology Flow Chart of the Extraction, Validation and Screening of OHCAs Included in Present Study.

Table 1 – Descriptives of Exercise-related OHCA Compared to Non-Exercise Related OHCA.

	Exercise-related OHCA N = 459	Non-exercise related OHCA N = 20,470	p-value
Age, yr,median, IQR	61 (52.0 – 72.0)	73 (63.0 – 82.0)	<0.001
Missing	53 (10.4)	828 (3.9)	
Sex, male,%	347 (75.3)	12,253 (59.9)	<0.001
Missing	66(14.3)	1035(5.0)	
Witnessed			
By Bystander	354 (77.1)	8,803 (43.0)	<0.001
Missing	2 (0.4)	376(1.8)	
By EMS	33 (6.4)	2,202(10.4)	<0.001
Missing	1(0.2)	366 (1.8)	
CPR			
*By Bystander**	413 (95.0)	14,534 (77.4)	<0.001
Missing		22 (0.1)	
By EMS	364 (79.3)	18,778 (91.9)	<0.001
Missing	3(0.6)	369 (1.8)	
Time to first EMS Response (min, median)*	6.0(4 –10)	7.0 (5 – 10)	0.49
Missing	24(5.2)	2,472 (12.1)	
Initial Rhythm			
VT/VF	207 (45.0)	3,040 (14.9)	
PEA/Asystole	137 (29.8)	14,267 (69.7)	<0.001
Defibrillation			
By Bystander	176 (38.3)	1,527 (7.5)	<0.001
Missing	3 (0.6)	473 (2.3)	
By EMS	250 (54.5)	3,137 (14.9)	<0.001
Missing	1(0.2)	432 (2.1)	

Missing data are excluded from the denominator *Excludes EMS witnessed cases. Summary statistics are presented as numbers (%) or mean with standard deviation and Interquartile range. yr. years; IQR. Interquartile range; EMS. Emergency Medical Service; min. minutes; CPR. Cardio-pulmonal resuscitation; VT. Ventricular tachycardia; VF Ventricular Fibrillation; PEA. Pulseless Electrical Activity.

Table 2 – Survival Outcome of Exercise-related OHCA and Non-exercise related OHCA.

	Exercise related OHCA N = 459	Non-exercise related OHCA N = 20,298	p-value
ROSC at Any Time	340 (74.1)	6,208 (30.3)	<0.001
Missing	0(0.0)	378 (1.8)	
Status at Admission			
ROSC -Unconscious	146 (31.8)	3,523 (17.2)	
ROSC - Conscious	178 (38.7)	1,759 (8.6)	
Dead at Admission	73 (15.9)	13,227 (64.6)	
Ongoing CPR	57 (12.4)	1,810 (8.8)	<0.001
30-day Survival	265 (57.7)	2,577 (12.6)	<0.001

Missing data are excluded from the denominator. Summary statistics are presented as numbers (%). ROSC. Return of Spontaneous Circulation; CPR. Cardiopulmonary Resuscitation.

In patients aged 15–35 years, the distribution of age was similar between the exercise-related and non-exercise-related OHCA. Furthermore, in this age subgroup of OHCAs, male sex was overrepresented, accounting for approximately 70% of cases in both groups. Moreover, primary ECG rhythm was more likely to be shockable, defibrillation by bystanders was more frequent, and ROSC at any time and 30-day survival were more likely in patients suffering from OHCA related to exercise, as shown in Table 3.

Fig. 2 presents a multivariate analysis to evaluate the role of age, sex, presence of witnesses, the use of AED, initial ECG rhythm, and whether the OHCA was exercise-related in explaining survival. The model indicates that OHCA related to exercise is a strong predictor of survival with an OR of 5.56 (95% CI: 4.35–7.14). The OHCAs witnessed by the bystanders and their use of AEDs were found to be predictors of survival. Additionally, the male patients were found to have an OR for survival of 1.24 (95% CI: 1.12–1.37).

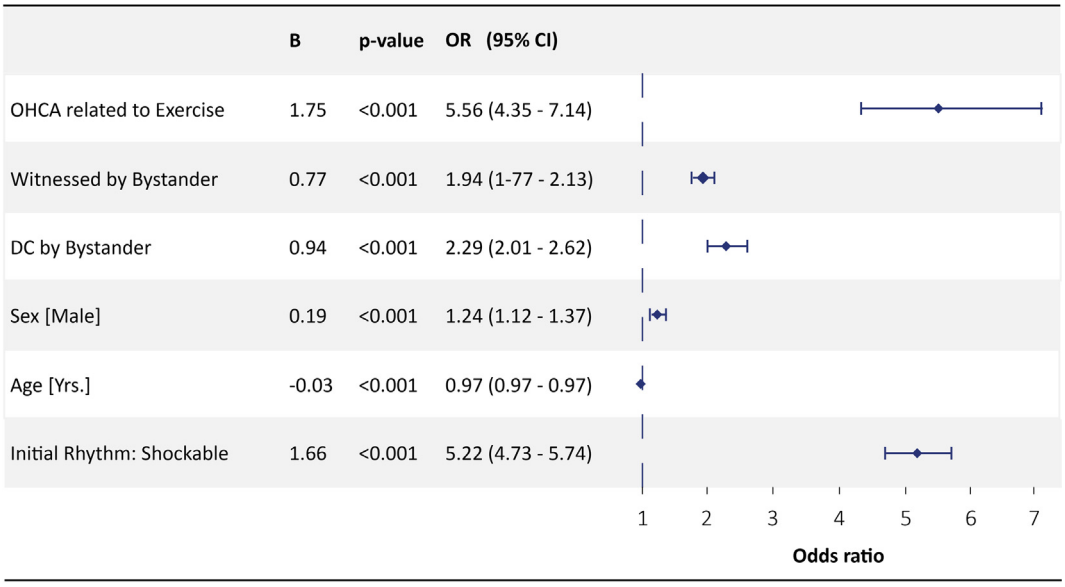
Subgroup analysis of different sport categories, with 30-day survival as the explanatory variable and non-exercise-related OHCAs as the reference group, adjusted for age and sex, is illustrated in Fig. 3. All categories of exercise-related OHCA showed significantly higher survival rates than those of non-exercise-related OHCA. Team sports were associated with the highest OR for survival at 18.5 (95% CI: 10.47–34.76, $p < 0.001$), while cycle sports had the smallest OR in the sports categories at 4.81 (95% CI: 3.17–7.32, $p < 0.001$).

The comparison of OHCA cases during moderate- and vigorous-intensity exercises did not show any significant difference, with a 30-day survival OR of 1.03 (95% CI: 0.58–1.87, $p = 0.9$).

Table 3 – Characteristics of Exercise Related OHCA among Subjects between 15 to 35 Years of Age.

	Exercise related OHCA *N = 39*	Non-exercise related OHCA *N = 769*	p-value
Age, yr, median (IQR)	16 (11.0 – 23.0)	24 (17.0 – 30.0)	0.01
Sex, male	28 (62.2)	528 (68.7)	0.41
Initial Rhythm			
VT/VF	15 (33.3)	81 (10.5)	
PEA/Asystole	17 (37.7)	537 (69.8)	<0.001
Defibrillation			
By Bystander	14 (31.1)	44 (5.7)	<0.001
Missing	2 (4.0)	16 (2.1)	
By EMS	16 (35.6)	134 (17.4)	0.005
Missing	0 (0.0)	16 (2.0)	
ROSC at Any Time	37 (82.2)	286 (37.2)	<0.001
Missing	0 (0.0)	9 (1.2)	
30-day Survival	36 (80.0)	192 (25.0)	<0.001

Missing data are excluded from the denominator. Summary statistics are presented as numbers (%) or mean (SD) of patients. yr. years; EMS. Emergency Medical Service; VT. Ventricular tachycardia; VF Ventricular Fibrillation; PEA. Pulseless Electrical Activity; ROSC. Return of Spontaneous Circulation.



OHCA. Out-of-Hospital Cardiac Arrest; Yrs. Years; DC. Defibrillation.

Fig. 2 – Multvarate analysis for 30 day survival.

Discussion

This study found that the incidence of OHCA related to exercise was at 1.9 per 100.000 person-years in Denmark, particularly within the male population. Exercise-related OHCAs had a more favourable outcome when compared to the overall cases of OHCAs.

The reported incidence rates in this study are comparable to the findings in other studies.[3–5] Similarly, the increased 30-day survival found among patients with OHCA related to exercise is consistent with previous findings when compared to OHCAs not related to exercise. A 2013 study conducted in the Netherlands reported a survival-to-discharge rate of 46.2%.[5] Further, Edwards et al.[4] reported a survival-to-discharge rate of 31.6% from London, whereas this study demonstrated a 30-day survival rate of 57.7%. These differences could be explained by the large sample size of this study, together with higher rates of bystander CPR and the use of AED, when compared to the data from Edwards et al.s' study. Furthermore, differences in the cohorts studied may also be significant.

Further, OHCA related to exercise was associated with greater odds for 30-day survival compared to non-exercise-related OHCA after adjusting for identified predictors of survival. This indicates that there are confounding factors yet to be identified.

This study found that OHCA related to exercise is predominantly observed in middle-aged men, consistent with established literature.[3–6] It has previously been speculated that the over-representation of males is caused by greater male participation in exercise, combined with a greater prevalence and the early onset of underlying heart diseases in males.[17,18] However, with increasing age, the aetiology might be more likely to originate from atherosclerotic coronary artery disease and other lifestyle-dependent pathologies.[19] Nevertheless, within 15–35 years of age, males were also overrepresented in exercise-related OCHA. This could be explained

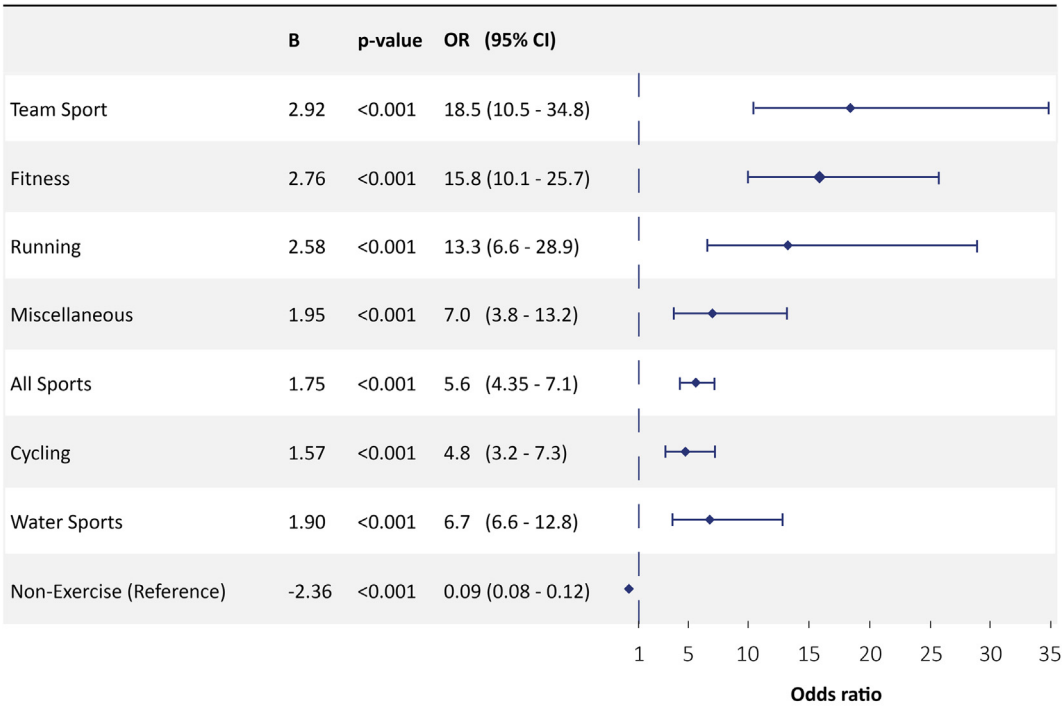


Fig. 3 – Odds ratio 30 day survival in different sport categories compaired to Inon exercise.

by an increased prevalence among younger men with hypertrophic cardiomyopathy compared to the female population.[20] While the male sex was associated with increased survival in this study, the literature reveals conflicting results.[3,5] Moreover, some trials have reported that no conclusions were possible due to the predominance of males in the sample size, and thus, the lacking numbers of female fatalities.[4] Additionally, it should be considered that the population of OHCA related to exercise represents a selected group within the general population. Confounding factors related to lifestyle might be present in this subgroup of patients with OHCA related to exercise, and this could influence outcomes after cardiac arrest.

Exercise might trigger cardiac arrest in patients suffering from undiagnosed cardiovascular diseases.[21] In particular, vigorous-intensity physical activities have been shown to induce a transient increased risk of cardiac arrest.[22] However, this study failed to prove any difference between the moderate and vigorous intensity of exercise. A German trial from 2008 reported positive effects on potentially modifiable risk factors associated with cardiovascular disorders (e.g. blood pressure and cholesterol levels). Nevertheless, they found a greater prevalence of severe coronary artery calcification among male marathon participants aged > 50 years compared to the control group.[23] Calcification of the coronary arteries might be interpreted as a surrogate of the cumulative degree of cardiovascular injury. Thus, these findings could illustrate the apparent paradox of exercise and the risk of cardiovascular events. Nonetheless, exercise is fundamental to the enhancement of health, including cardiovascular status. This is further corroborated by Hamer et al., who investigated seven major causes of death related to cardiovascular disease. They found that exercise was associated with reduced risk of all the investigated cardiovascular diseases.[24] Pre-existing morbidity was not adjusted in this study. Additionally, exercise-induced cardio protection based on sub-lethal ischaemia has been proposed.[25] However, patients who have symptoms such as syncope, presyncope, fatigue, chest pain, etc., should be advised for further examination.[26].

The reported rate of initial shockable rhythms recorded by the EMS personnel was low in our study (45.0%) compared to existing literature, with reported rates between 68% and 85%.[3–6] This might be explained by the considerable number of patients who were already subjected to defibrillation before the arrival of EMS personnel. Some of these patients likely underwent ROSC during the first ECG rhythm check. This explanation is further substantiated by the relatively small number of cases with non-shockable rhythm as the primary rhythm recorded by EMS personnel (29.8%). Furthermore, the use of AEDs by bystanders was associated with increased survival and was consistent with the recent trials from Italy and Japan.[6,27] Access to and use of AEDs in settings other than OHCA related to exercise have been associated with better outcomes throughout the existing literature.[28,29]

The distribution of OHCAs within different sports disciplines is similar to findings reported in the Netherlands and Sweden.[5,30] Both of these studies attributed a large proportion of OHCAs in cycling to the frequent use of bicycles for transportation, which could be extrapolated to the Danish population. The extent of witnesses present, access to AEDs, and the degree of bystander CPR among team sports might explain the differences in survival within the various sports categories.

Strength and limitations

The nationwide sample size and use of an electronic reporting system enhanced the robustness of the findings reported in this study. Although the overall number of OHCA cases was greater in this study than in the established literature, the number of patients, who are younger than 35 years of age, are limited. This hinders fur-

ther logistic analysis and thereby the conclusions of this subgroup. Further, the retrospective observational design has biases; hence, caution should be exercised when inferring any statistical causality. The EMS reporting system does not collect the exact level of intensity, which may be an important factor in OHCA related to exercise. Limitations also include the lack of access to post-mortem analyses, which restricts information on pre-existing morbidity, including underlying heart disease and other risk factors. Furthermore, knowing the treatment and diagnoses after admission to the hospital could contribute to a better understanding of OHCA related to exercise and the factors that improve chances of survival.

Perspectives

Currently, data on OHCA related to exercise have been evaluated in different studies. Although the Utstein template has been established, inconsistent classifications have been reported in the literature. Among patients with OHCA related to exercise, subjects in this study had a median age of 61 years and were predominantly male (75.3%). Around 80% of the OHCA cases were witnessed, the rate of CPR performed by bystanders was 95%, and an AED was used in more than a third of the cases. Early interventions such as CPR to minimise no-flow time and defibrillation are important to improve survival. The study findings could have implications for campaigns, programmes, and health services to prevent death from OHCA related to exercise.

Conclusion

OHCA related to exercise in the general population is uncommon; however, survival is significantly higher than that in non-exercise-related OHCA. The rates of bystander CPR and use of AEDs in this study emphasise their respective importance regarding survival, and these findings might indicate positive effects from campaigns and education over the last decades. Nevertheless, underlying factors such as prior patient morbidity, treatment, and diagnosis after admission to hospital and factors associated with better survival require further evaluation in randomised trials.

CRediT authorship contribution statement

Signe Amalie Wolthers: Data curation, Formal analysis, Funding acquisition, Methodology, Software, Project administration, Validation, Writing – original draft, Writing – review & editing. **Theo Walther Jensen:** Conceptualization, Data curation, Formal analysis, Methodology, Software, Validation. **Stig Nikolaj Blomberg:** Conceptualization, Data curation, Methodology. **Mathias Geldermann Holgersen:** Supervision, Validation, Software. **Freddy Lippert:** . **Søren Mikkelsen:** Methodology. **Ole Mazur Hendriksen:** . **Christian Torp-Pedersen:** Validation. **Helle Collatz Christensen:** Conceptualization, Data curation, Validation, Methodology, Funding acquisition, Project administration, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

This work was supported by the TrygFonden Foundation. The funding source had no role in the study design, collection, management, analysis, interpretation of data, writing of the report, or the decision to submit the report for publication.

A special thanks to the members of the collaboration group from the Danish Cardiac Arrest Registry Group in the acquisition, analysis, and interpretation of data. All members of the Danish Cardiac Arrest Registry validation group are affiliated to The Danish Clinical Quality Program, National Clinical Registries, Copenhagen, Denmark: Gunhild Kjærgaard-Andersen, René Arne Bergmann, Heinrich Dedenroth Larsen, Lars Borup, Theo Walther Jensen, Mathias Geldermann Holgersen, Stig Nikolaj Fasmer Blomberg, Julie Linding Bogh Kjerulf, Kristian Bundgaard Ringgren, and Kenneth Lübcke.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2022.01.021.

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