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A 3-year population-based study of exercise-related sudden cardiac arrest among 12- to 50-year-old Norwegians

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Introduction: Regular exercise is associated with reduced risk of cardiovascular disease. Paradoxically, an increased risk of sudden cardiac arrest (SCA) is documented during or immediately after exercise and in athletes compared to the non-athletic population. Our objective was to identify, through multiple sources, the total number of exercise-related versus non-exercise-related SCA in the young population in Norway.

Methods: We collected primary data from the prospective Norwegian Cardiac Arrest Registry (NorCAR) for all patients aged 12–50 suffering SCA of presumed cardiac cause from 2015 to 2017. We collected secondary data about prior physical activity and the SCA, through questionnaires. We searched media reports for SCA incidents in sports. Exercise-related SCA is defined as SCA during or <1 h after exercise.

Results: Overall, 624 patients, median age 43 years, were included from NorCAR. Two thirds (393) replied to the study invitation, of whom 236 answered the questionnaires: 95 survivors and 141 next of kin. The media search resulted in 18 relevant hits. With a multiple source approach, we identified 63 cases of exercise-related SCA, equivalent to an incidence of 0.8/100 000 person-years, versus 7.8/100 000 person-years of non-exercise-related SCA. Among those who answered ($n = 236$), almost two thirds (59%) exercised regularly, most commonly (45%) 1–4 h/week. Endurance exercise (38%) was the most prevalent type of regular exercise and the most common activity during exercise-related SCA (53%).

Conclusion: The burden of exercise-related SCA was low (0.8 per 100 000 person-years) and ten times lower than non-exercise-related SCA in the young population in Norway.

KEYWORDS
athlete, cardiology, epidemiology, exercise, out-of-hospital cardiac arrest, registry, sudden cardiac arrest, sudden cardiac death

1 | INTRODUCTION

Sudden cardiac arrest (SCA) represents a significant disease burden in Europe with poor odds of survival.[1] Exercise is essential for health and longevity,[2–4] and is associated with reduced risk of cardiovascular disease.[5] Even so, there is a transient increased risk of SCA during and immediately after cessation of exercise.[6,7]

The reported incidence of exercise-related SCA in the general population range from 0.1 to 2.2 per 100 000 person-years.[8–17] Historically, an increased risk of SCA and sudden cardiac death (SCD) is reported in the ultimate group of exercisers, athletes.[4] The reported risk of SCA/SCD varies considerably from 0.02 in American youth athletes to 89.05 per 100 000 person-years in Belgian cyclists. A recent systematic review and meta-analysis reported <2 per 100 000 for SCD.[18,19] The distinction between regular exercisers and athletes on different levels is not straightforward, and the trend of increased exercise volume and intensity among recreational athletes/regular exercisers adds to the complexity.[20,21]

To learn whether excessive exercise and athletic activity increase the risk of SCA, the first step is to assess the true incidence of exercise-related SCA compared to the age-equivalent general population. The main aim of this study was to identify, through multiple sources, the total number of exercise-related versus non-exercise-related SCA in the general 12- to 50-year-old population in Norway, and secondary to assess the exercise habits of the young SCA population.

2 | MATERIALS AND METHODS

We based this study on data from three sources: the Norwegian Cardiac Arrest Registry (NorCAR), a questionnaire follow-up of cases in NorCAR, and a media search.

2.1 | The Norwegian Cardiac Arrest Registry

In 2013 reporting out-of-hospital cardiac arrest to NorCAR became mandatory for Norwegian health trusts, making Norway the only country in the world where cardiac arrest is a reportable condition.[22] In 2015, the registry covered 96% of the population, and from May 2016 the entire country. Inclusion criteria in NorCAR are cardiopulmonary resuscitation (CPR) or defibrillation by bystanders, first responders or professional healthcare workers on an unresponsive patient without normal breathing. NorCAR does not register SCD where no-one has started resuscitation. Local data processors enter variables from Emergency Medical Service (EMS) records. Data in the registry adhere to the Utstein definitions.[23] An event is registered as exercise-related if it happened during or <1 h after exercise.

2.2 | Inclusion and exclusion criteria

We included patients aged 12–50 registered in NorCAR from January 1, 2015 to December 31, 2017. We included Norwegian Citizens with SCA confirmed by EMS, with an arrest of presumed cardiac cause, or cases registered as drowning accidents or respiratory failure. We did not include patients receiving CPR by bystander only, if the cardiac arrest could not be confirmed by EMS.

2.3 | Questionnaire follow-up of cases

For additional information, we tracked patients identified from NorCAR, or next of kin of the deceased, through the National Population Register. An invitation to answer a consent-based questionnaire covering the SCA and the following exercise-related issues: type of sport, volume (0, 1–4, 5–10 or >10 h of exercise/week), and level (recreational or competitive)[24] was sent by mail. Respondents reported circumstances around SCA as exercise-related or not based on a definition of exercise as "training resulting in sweating or increased heart rate." As for NorCAR, an event was exercise-related if it occurred during or <1 h after exercise. For further classification by the study panel (first and last author), exercise was defined as an activity performed in order to maintain- or increase physical capacity.[25] Based on the activity described in free-text answers, the study panel re-classified cases that did not fit this description. Cases confirmed as exercise-related were used to validate exercise-related SCA in NorCAR. We sent one reminder to most of the potential participants. Patients missing a postal address, or for deceased, an identifiable next of kin could not receive a questionnaire.

2.4 | Media search

We did a world wide web media search (Retriever, Tekinetics) for SCA in Norway from January 1, 2015, through December 31, 2017, using the search terms (in Norwegian) "cardiac arrest" OR "cardiac death" AND sport*, training*, "physical activity," recreational*, run*, as well as the names of the 57 sports registered by the Norwegian Olympic and Paralympic Committee and Confederation of Sports as of 2017. Words ending with "*" were truncated to include words beginning with the syllable before the truncation.

2.5 | Calculations and statistical analyses

We present data as median with interquartile range (IQR) or as numbers (%). The population incidence of SCA is calculated based on cases reported to NorCAR divided by population numbers from Statistics Norway, adjusted to the population covered by NorCAR during the study period.[22]

2.6 | Ethical approval

Norwegian Law regulates data collection in NorCAR, and patient consent is not needed for inclusion or research using registry data only. The use of data and collection of supplementary data from the patients and next of kin were based on written informed consent. The study was approved by the Regional Committees for Medical and Health Research Ethics (REC) (2016/671). Data handling and privacy issues were discussed and approved by the Data Security and the Data Protection Officer at Oslo University Hospital.

2.7 | Patient and public involvement

Before sending out the questionnaire, we consulted an adult survivor, a next of kin to a child (defined as 12–15 years) who survived and a next of kin for a deceased child and a deceased adult. Based on their feedback, we modified the study invitations and questionnaires.

3 | RESULTS

3.1 | Inclusion and characteristics of the study population

During the study period, a total of 9248 cases of SCA were registered in NorCAR from a total of 15 288 394 person-years at risk.[26] Among these, we identified 720 Norwegian Citizens (12–50 years) without an apparent external cause of cardiac arrest (Figure 1). We excluded 96 patients, leaving 624 patients as our main study population. Their median age was 43 years (33–47), and 29% were women.

We found current addresses for 588: 175 survivors and 413 next of kin. We received a reply from 393 (67%), of whom 236 (40%) answered the questionnaire; 95 (40%) survivors and 141 next of kin (Figure 1, Table 1). The response rate was significantly higher among survivors (54%) than next of kin (34%) ($p < 0.001$). Among those who replied but did not answer the questionnaire, 91 did not want to participate, most often due to "too painful memories", 63 did not fill the inclusion criteria and three were excluded for other reasons. Among next of kin that responded, 73 (52%) were parents, 42 (30%) partners, 13 (9%) children >18 years, and 13 (9%) were siblings or had other connections to the deceased. The distribution of age and gender among responders to the questionnaire were representative of the population eligible for inclusion from NorCAR, and almost all reported white as ethnicity (Table 1). Among responders to the questionnaire, overall 30-day survival was 40% (95/236), and almost 1.5 times higher in exercise-related (54%, $n = 21/39$) versus non-exercise-related SCA (38%, $n = 74/197$).

3.2 | Identification and validation of cases registered as exercise-related SCA in NorCAR

From NorCAR, 49 out of the 624 (7.9%) cases eligible for inclusion were registered as exercise-related SCA (Figure 2). Among these 49 cases, there were 34 responders to the questionnaire, of whom 30 confirmed the SCA to be exercise-related, and four refuted it. Based on free-text answers, five of these 30 cases were reclassified as non-exercise-related physical activity by the study panel, resulting in 25 cases of exercise-related SCA registered in NorCAR and confirmed in the questionnaire.

We could not validate the 15 cases registered as exercise-related in NorCAR without response to the questionnaire but included these in the final pool of cases recognized as exercise-related SCA from only one source.

3.3 | Detection and validation of additional cases not registered as exercise-related in NorCAR

The remaining 575 cases of SCA eligible for inclusion were registered as non-exercise-related in NorCAR. Among these, 202 responded to the questionnaire and 23 reported the SCA as exercise-related. Nine of these were reclassified as non-exercise-related physical activity by the study panel, resulting in 14 cases of exercise-related SCA identified from the questionnaire in patients registered with non-exercise-related SCA in NorCAR.

3.4 | Comparison with results from the systematic media search

There were 4079 hits in Retriever, 17 describing exercise-related SCA, and one occurring in a team sport player during daily life activity. Among the 17 exercise-related SCA reported by media, 11 were registered in NorCAR, and eight matched with cases confirmed by questionnaire and panel review (Figure 2), leaving nine

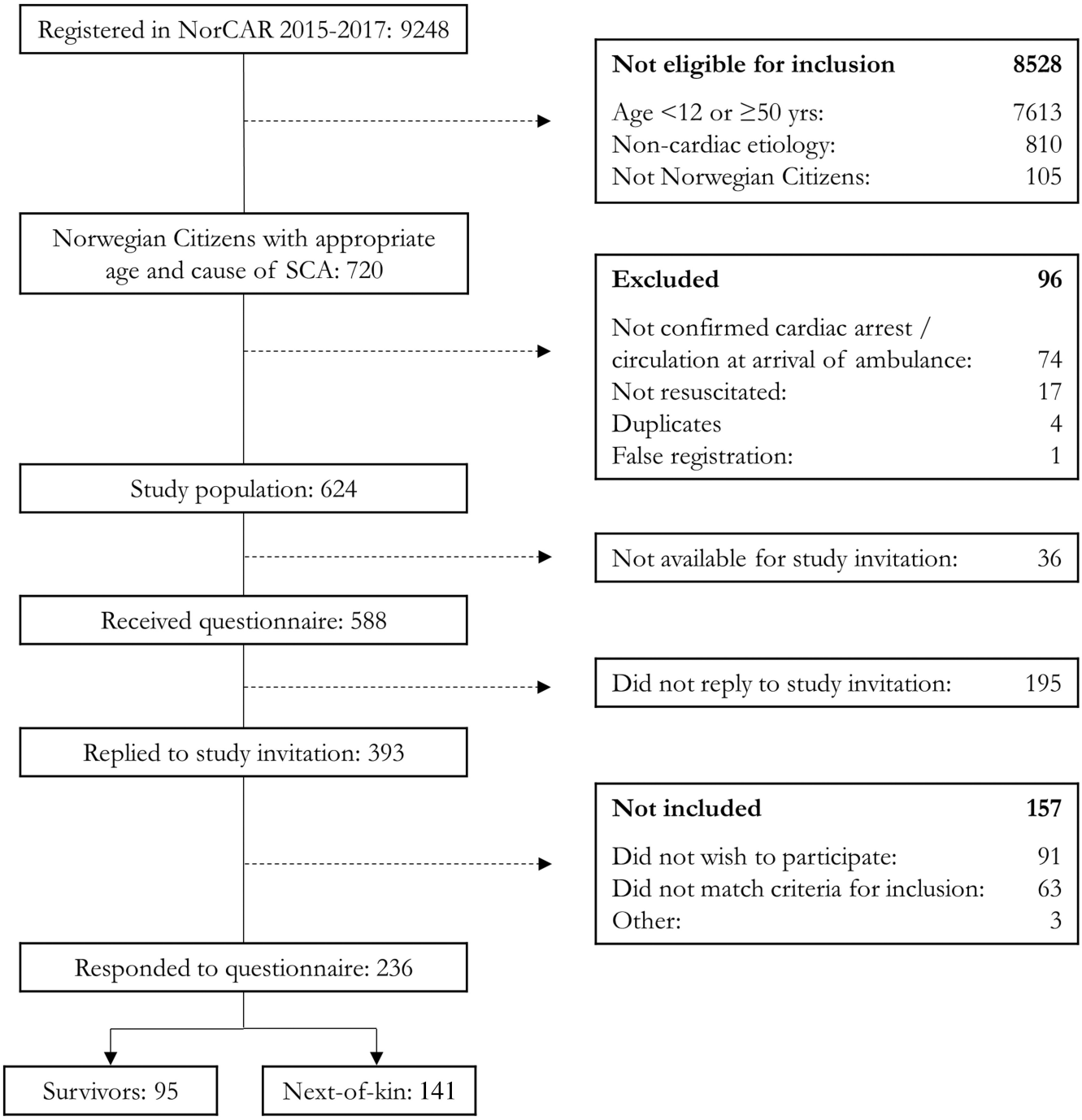

FIGURE 1 Flowchart of the inclusion of patients from NorCAR (2015–2017) to the study population ($n = 624$), through feedback and response to the study invitation, ending up with 236 responders to the questionnaire (95 survivors and 141 next of kin). NorCAR, the Norwegian Cardiac Arrest Registry; SCA, Sudden Cardiac Arrest.

additional cases of exercise-related SCA found by the media search only.

3.4.1 | Incidence of exercise-related SCA

Summarized from all three sources during the three years study period, we found 63 unique cases (average 21 cases/year) of exercise-related SCA (Figure 2). Of these, only five cases were identified through all three sources, another 23 in two, and 35 only in one (Figure 3).

The population incidence of exercise-related SCA was calculated to 0.8 (95% CI 0.5–1.1) per 100 000 person-years, 0.4 for persons ≤35 years and 1.3 for persons >35. The overall incidence of out-of-hospital cardiac arrest of presumed cardiac cause was 7.8 (95% CI 6.8–8.9) per

TABLE 1 Characteristics of patients 12–50 years old registered with exercise- or non-exercise-related sudden cardiac arrest in the Norwegian Cardiac Arrest Registry.

	Overall	Exercise-related	Non-exercise-related
	n = 236	*n* = 39	*n* = 197
Age, median (IQR)	43.7 (36.0–47.1)	42.9 (35.7–46.3)	43.8 (36.1–47.5)
Age groups (years)			
12–15	4 (2)	1 (3)	3 (2)
16–35	55 (23)	9 (23)	46 (23)
36–49	177 (75)	29 (74)	148 (75)
Gender (female)	72 (31)	6 (15)	66 (34)
30th days survival	95 (40)	21 (54)	74 (38)
Country of Origin[b]			
Norway	218 (94)	34 (87)	184 (95)
Other	15 (6)	5 (13)	10 (5)
Ethnicity[c]			
Caucasian	229 (98)	38 (97)	191 (98)
Other	4 (2)	1 (3)	3 (2)
Hours of exercise/week[a,d]			
No regular exercise	74 (35)	2 (5)	72 (41)
<5 h	96 (45)	21 (55)	75 (43)
5–10 h	33 (15)	13 (34)	20 (11)
>10 h	10 (5)	2 (5)	8 (5)
Performance level (self-reported)[a,e]			
No regular exercise	70 (37)	2 (5)	68 (45)
Recreational athlete	98 (52)	29 (76)	69 (46)
Competitive athlete	20 (11)	7 (18)	13 (9)
Membership in sports club[f]	33 (14)	10 (26)	23 (12)
Number of respondents reporting			
Regular endurance exercise	90 (25)	28 (72)	62 (31)
Regular strength exercise	56 (24)	15 (38)	41 (21)
Regular technical exercise	24 (10)	9 (23)	15 (8)

Note: Data reported as *n* (%), if not otherwise specified. [a]Sum differs from 100 due to rounding. The denominator equals the number of answers per group, "Overall"/"Exercise-related SCA"/"Non-exercise-related SCA": [b]233/39/194, [c]233/39/194, [d]213/38/175, [e]188/38/150, [f]232/38/194.

Abbreviations: NorCAR, the Norwegian Cardiac Arrest Registry; SCA, sudden cardiac arrest.

100 000 person-years, 3.9 for ≤35 years and 13.5 for persons >35.

3.5 | Exercise habits and self-reported athletic level before SCA

Among responders to the questionnaire, 139 (59%) reported regular exercise the last year before SCA (Table 1). Endurance exercise (38%) was the most common type, followed by strength (24%). During exercise-related SCA, activities categorized as endurance- (16/30) or team sport (9/30) dominated.

Primary sport or recreational activity was reported in free text by 108 (46%) exercisers (Figure 4). The self-reported athletic level was recreational for 98 patients, of whom 27 (28%) exercised ≥5 h/week, and competitive for 20 athletes, of whom 9 (45%) exercised 5–10 h/week and 5 (25%) >10 h/week. Fourteen of the competitive athletes had participated in one or more competitions the previous year.

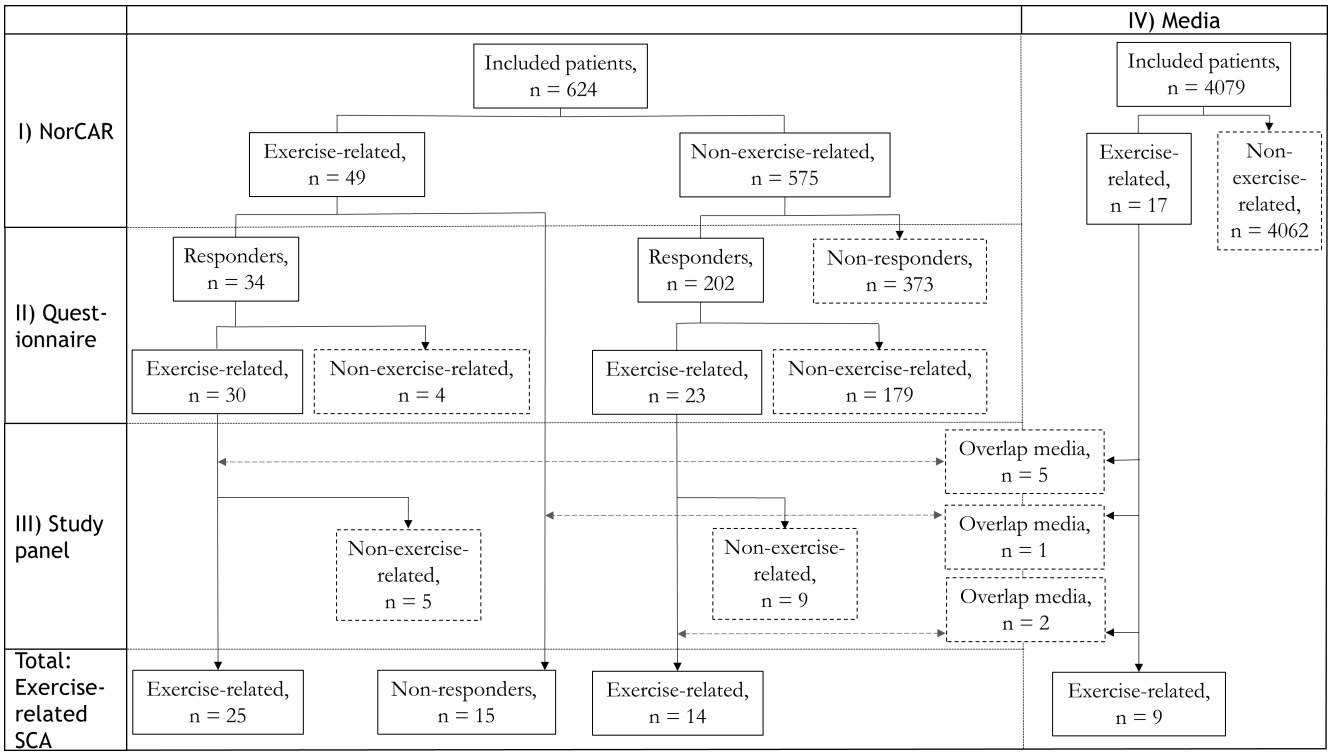

FIGURE 2 Flowchart of 63 exercise-related SCA in Norway, identified through four sources (NorCAR, questionnaire, study panel and media) starting with (I) cases included from NorCAR registered as exercise-related and non-exercise-related, respectively, (II) validation of cases from NorCAR based on answers from responders to the questionnaire (information from non-responders to the questionnaire were not possible to validate), (III) exclusion of cases considered as ordinary physical activity by the study panel, and (IV) addition of cases identified only through the systematic media search. NorCAR, the Norwegian Cardiac Arrest Registry; SCA, sudden cardiac arrest.

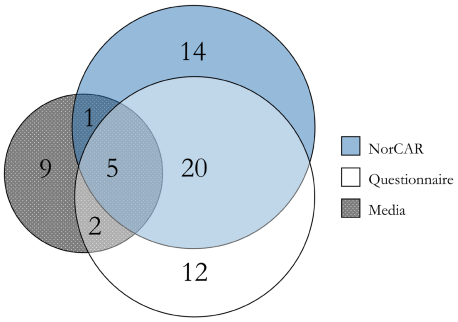

FIGURE 3 Venn diagram illustrating the overlap and mismatch between the multiple sources (NorCAR, questionnaire and media) used to identify the 63 cases of exercise-related SCA during the 3 years study period. NorCAR, the Norwegian Cardiac Arrest Registry; SCA, sudden cardiac arrest.

4 | DISCUSSION

We identified 63 cases of exercise-related SCA in almost the entire Norwegian population, aged 12–50, over three years. The incidence of exercise-related SCA was low (0.8 per 100 000 person-years), only one-tenth of non-exercise-related SCA.

For non-responders, which constituted almost two-thirds of the 624 included patients, we had to rely on data from our main source, NorCAR. Among the 40% of cases validated by answers to the questionnaires, exercise-related SCA was confirmed by 25 (74%) patients registered with exercise-related SCA in NorCAR, and in addition, reported by 14 (7%) patients registered with non-exercise-related SCA. Based on our results, we consider the population incidence of 0.8 per 100 000 person-years with a reported 95% CI of 0.5–1.1 of exercise-related SCA as trustworthy, and the presented number of 21 cases of exercise-related SCA per year as reliable.

4.1 | How does the incidence of exercise-related SCA in Norway compare to the published literature?

In population studies, the incidence of exercise-related SCA ranges from 0.1 to 2.2 per 100 000 person-years.[8–17] Berdowski et al. in Holland reported 0.3 cases, quite similar to our 0.4 cases per 100 000 person-years for the age group under 35, but 3.0 cases, compared to our 1.3 cases

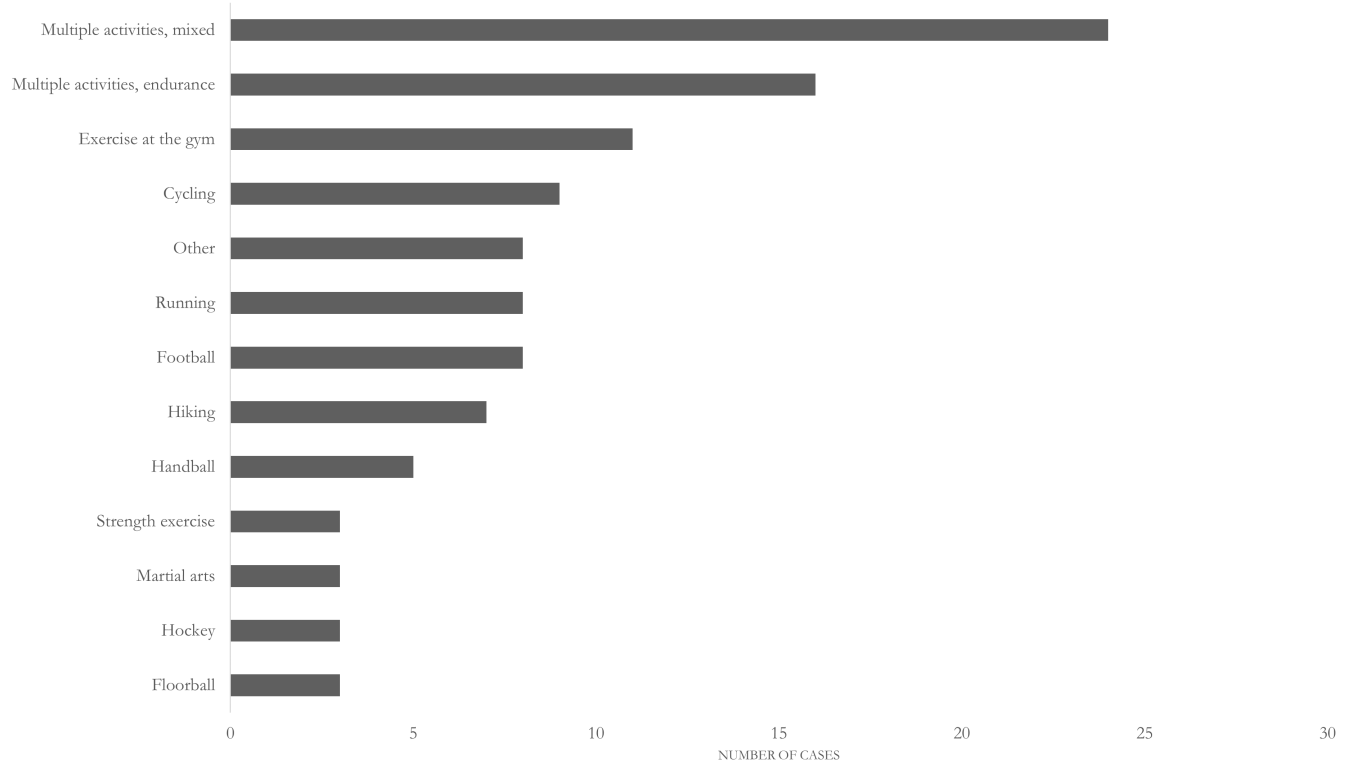

FIGURE 4 Main sport—or exercise activity were reported in 108 regular exercisers, among the 236 responders to the questionnaire, representing the young Norwegian SCA population. If more than one activity were listed, the reported activities were categorized as "multiple," and as "mixed" if different types of sports were listed, and "endurance," if only activities categorized as endurance were listed. Activities with $n \leq 2$ were reported in the common group "other" and included activities as dance, cross country skiing, boccia, squash, volleyball and Zumba. SCA, sudden cardiac arrest.

per 100 000 person-years above 35 years. This difference is probably fully explained by our upper age limit of 50, while they had no upper age limit. Lifestyle-related cardiovascular diseases increase with age, followed by an increase in SCA.[27] Population studies from France, Australia, England, Sweden, Holland, and Denmark also include older age cohorts, with mean age 46.0–61 in patients suffering exercise-related SCA.

4.2 | Is the risk of suffering exercise-related SCA related to exercise habits?

Wisten et al.[28] found that exercise-related SCD was more common in Swedish athletes than in non-athletes in the age group 12–35 years during 2000–10. In our study, the prevalence of exercise-related SCA was twice as high among patients that exercised 5–10 versus 1–4 h/week (13 [39%] vs. 22 [22%]). The mechanisms for a relationship between SCA and physical exercise are open for discussion. The biological mechanisms may be related to acute challenges of myocardial perfusion and provocation of inherited or acquired arrhythmic diseases, but we can also speculate that time spent on physical training may increase the risk of cardiac arrest during training by purely non-biological causes. In the latter case, we would expect a proportional increase in exercise-related SCA with increasing number of hours/week spent exercising.

Historically, athletes have been estimated to have two to three times higher risk of SCA than non-athletes, but recent results are conflicting.[29] A nationwide registry study from Denmark presented a reduced risk of SCA in athletes compared to non-athletes,[30] and Maron et al.[31] found the incidence of SCD from a forensic registry in Minnesota to be threefold higher in non-athletes than athletes. We believe the reasons for conflicting results regarding the risk of SCA in athletes are linked to methodological challenges like the lack of a uniform definition of athletes and exercise, a mixture of SCA and SCD, data collection from different types of sources, as well as different populations with regard to ethnicity, age, and healthcare systems.

4.3 | How does the definition of athletic level and exercise affect the incidence?

Exercise-related SCA and SCD in athletes are rare events, and different definitions of the key elements of athletic

level and exercise may lead to significant variations in reported incidence. For example, the European Society of Cardiology (ESC) defines athletes as "an individual of young age or adult age, either amateur or professional, who is engaged in regular exercise training and participates in official sports competitions."[24,32] In addition, in the 2020 guidelines on sports cardiology, the ESC refers to the editorial from McKinney et al. where they proposed a classification of minimum volume of exercise of ≥10 h/week in elite athletes, ≥6 h/week in competitive athletes, and ≥4 h/week in recreational athletes.[21,33] Among the 20 respondents who self-categorized the patient as competitive athletes, only half reported examples of competitions *and* at least 5 h of exercise/week.

The second crucial definition is "exercise." After user involvement in our study, we added examples of physical activities as "walk to the bus," or "gardening" in the questionnaire, and described "exercise" as any training resulting in sweating or increased heart rate. Still, we had to reclassify 14 cases from exercise-related to physical activity. Without corrections based on free text, the incidence of exercise-related SCA would have been 29% higher.

4.4 | The incidence of SCA versus SCD

A challenge in the published literature is the mixture of SCA and SCD in studies.[34] The crucial number is the incidence of SCA, representing the population available for successful resuscitation. SCD does not include SCA patients that are successfully resuscitated.[35,36] Among the 39 cases of exercise-related SCA confirmed in the questionnaires, 21 (54%) were alive at 30 days post-arrest. Hence, counting only SCDs would lead to an underestimation of the number of exercise-related SCA (Table 1). However, SCD may also include sudden death where no treatment was offered or available. These cases would not be included in a cardiac arrest registry, but an autopsy could confirm a cardiac cause. The number of patients in this latter group is likely low in exercise-related cardiac arrest but may complicate counting and comparison for non-exercise-related SCA in athletes.

4.5 | Data source

Harmon et al.37 reported media to identify 44%–87% of cases registered in the National Collegiate Athletic Association database of SCD, with an increased detection rate in high-profile athletes.38 The detection rate of only 27% of exercise-related SCA in our media search makes media searches in Norway a poor source of information.

As a mandatory cardiac arrest registry prospectively recording all cases of SCA in Norway, NorCAR is superior as a source to assess the incidence of SCA in general. However, the purpose of the registry is to monitor the quality of treatment provided to patients suffering SCA.[23] Since the ability of the registry to detect cases of exercise-related SCA is not validated, we chose to reach out to all patients eligible for inclusion to detect potentially missed cases and also to discover SCA in athletes during rest or daily life activity. We believe that applying this thorough method to the data available from NorCAR, gives us the most precise and reliable estimate of the incidence of exercise-related SCA and the number of SCA in athletes available to date from Norway.

4.6 | Limitations

We found that the incidence of exercise-related events is underreported in NorCAR. Still, the proportion of exercise-related events reported among responders to the questionnaire is probably too high and not representative of the SCA population due to selection bias. Possible selection bias limited our analyses of relationship between exercise, exercise habits, and athletic level with SCA incidence. Data from the questionnaire were collected retrospectively, were self-reported, and for the deceased, filled in by a next of kin, and the risk of response- and recall bias is present. We also experienced difficulties in categorizing the level of sport and exercise. Overlapping reported hours of exercise between recreational and competitive athletes, as well as categorizing athletes only by their participation in competitions, illustrates this problem. Lastly, we were not able to identify the denominator necessary to calculate an incidence of SCA in athletes, which is recognized as one of the major challenges in sports cardiology.[34,37]

4.7 | Perspective

Our study confirms the complexity of assessing the incidence of SCA related to exercise and in athletes. Primary data collection from NorCAR made it possible to identify all cases of SCA in Norwegians 12–50 years old, and supplemental information from survivors or next of kin of the deceased increased the validity of the data.

We found that the risk of suffering SCA for young Norwegians in general is low, and even ten times lower in exercise-related SCA. Our data do not allow us to assess with certainty the potential increased risk of exercise-related SCA, but given the confirmed rarity of the event, young Norwegians should in general feel safe to exercise. However, awareness of symptoms of SCA and early

cardiopulmonary resuscitation and available defibrillators are crucial for the safety of young athletes and exercisers; still, similar measures targeted at the general population are equally important to minimize the numbers of young lives lost to SCA.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest relevant for this study are declared by the authors.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are partly available from the Norwegian Cardiac Arrest Registry and partly from the authors. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of The Norwegian Institute of Public Health and the Norwegian Regional Ethical Committee.

PATIENT CONSENT STATEMENT

Norwegian Law regulates data collection in NorCAR, and patient consent is not needed for inclusion or research using registry data only. The use of data and collection of supplementary data from the patients and next of kin were based on written informed consent.

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