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ORIGINAL ARTICLE

Atrial fibrillation is associated with different levels of physical activity levels at different ages in men

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ABSTRACT

Objective This study examines the influence of physical activity at different ages and of different types, on the risk of developing atrial fibrillation (AF) in a large cohort of Swedish men.

Methods Information about physical activity was obtained from 44 410 AF-free men, aged 45–79 years (mean age=60), who had completed a self-administered questionnaire at baseline in 1997. Participants reported retrospectively their time spent on leisure-time exercise and on walking or bicycling throughout their lifetime (at 15, 30 and 50 years of age, and at baseline (mean age=60)). Participants were followed-up in the Swedish National Inpatient Register for ascertainment of AF. Cox proportional hazards regression models were used to estimate relative risks (RR) with 95% CIs, adjusted for potential confounders.

Results During a median follow-up of 12 years, 4568 cases of AF were diagnosed. We observed a RR of 1.19 (95% CI 1.05 to 1.36) of developing AF in men who at the age of 30 years had exercised for >5 h/week compared with <1 h/week. The risk was even higher (RR 1.49, 95% CI 1.14 to 1.95) among the men who exercised >5 h/week at age 30 and quit exercising later in life (<1 h/week at baseline). Walking/bicycling at baseline was inversely associated with risk of AF (RR 0.87, 95% CI 0.77 to 0.97 for >1 h/day vs almost never) and the association was similar after excluding men with previous coronary heart disease or heart failure at baseline (corresponding RR 0.88, 95% CI 0.77 to 0.998).

Conclusions Leisure-time exercise at younger age is associated with an increased risk of AF, whereas walking/bicycling at older age is associated with a decreased risk.

INTRODUCTION

Regular physical activity contributes to the prevention and management of many diseases and medical conditions, such as cardiovascular disease, cerebrovascular disease, hypertension, obesity, diabetes mellitus, osteoporosis, some malignancies and mental illness.[1–6] The impact of physical activity on the risk of atrial fibrillation (AF) appears to be more complex. Several small case-control studies have reported that long-term regular sport activity elevates the risk of AF in young and middle-aged men.[7–10] One recent large cohort study of men and women participating in a 90 km cross-country skiing event reported elevated risk of arrhythmias including AF among men and women with the fastest finishing times and greatest number of completed races.[11] On the other hand, a prospective study of older men and women observed a reduction in risk of AF with moderate-intensity physical activity, including leisure-time exercise and walking, but found no increase in risk with high-intensity physical activity.[12] This implies that physical activity of different intensities could have different effects on the risk of developing AF later in life.

The vast majorities of previous studies investigated athletes and individuals participating in sport competitions. Large studies investigating the association between physical activity and AF in a general population are lacking.

This study examines the associations of physical activity at different ages and of different types, with risk of developing AF in a large general population. We examined the relationship between various types of physical activity at different ages and the risk of AF in a large population-based prospective cohort of Swedish men. We hypothesised that leisure-time exercise (considered as moderate-intensity to high-intensity activity) increases the risk of developing AF later in life, while walking/bicycling for transportation (low-intensity to moderate-intensity) decreases the risk.

METHODS

Study population

The population-based cohort of Swedish men was established in 1997–1998, when all men (n=100 303) aged 45–79 years and residing in Västmanland and Örebro counties (central Sweden) received an invitation to participate in the study along with a self-administered questionnaire. Of the eligible men, 48 850 (49%) completed the questionnaire. For the current analyses, we excluded men with missing data (n=297), men who died before start of follow-up (n=55), and men with a diagnosis of AF (n=1496), recorded in the Swedish Inpatient Register (IPR), or cancer (n=2592) (except non-melanoma skin cancer), recorded in the Swedish Cancer Registry, before baseline. This left 44 410 men eligible for the analyses.

Assessment of physical activity

Participants reported their time spent walking or bicycling for everyday transportation purposes and leisure-time exercise (such as running, soccer, bicycling, swimming, floorball, gymnastics, cross-country skiing, etc) throughout their lifetime (at 15, 30 and 50 years of age, and at baseline in 1997). Walking/bicycling (one question for walking and bicycling combined) for transportation was considered to be low-intensity to moderate-intensity physical activity, while leisure-time exercise was considered to be moderate-intensity to high-intensity physical activity.

The validity of the assessment of physical activity through the questionnaire used in this cohort was tested in 111 men, aged 44–78 years, from the study area, by comparison with two seven-day activity records performed 6 months apart.[13] The Spearman correlation coefficients (adjusted for within-person and between-person variations in the records) between the questionnaire and activity records were 0.4 for combined walking/bicycling and exercise.[13]

Assessment of body size and other information

Self-reported information on weight and height at age 20 years, and weight at baseline, was obtained through a questionnaire. Body Mass Index (BMI) was estimated from self-reported weight and height (kg/height in m^2). Self-reported height (r=0.9) and weight (r=0.9) have a high validity compared with actual measurement among Swedish men.[14] Information was collected on smoking status and smoking history, family history of myocardial infarction, history of hypertension, history of diabetes, history of coronary heart disease, alcohol consumption, and aspirin use. Participants were classified as having diabetes if they self-reported diabetes on the questionnaire or had a diagnosis of diabetes recorded in Swedish IPR or the Swedish National Diabetes Register. Information on coronary heart disease and congestive heart failure was obtained from the Swedish IPR. Pack-years of smoking history were calculated as the number of packs of cigarettes smoked per day multiplied by the number of years of smoking at different ages (10-year age groups).

Case ascertainment and follow-up

Incident cases of AF were identified through computerised linkage of the study cohort to the Swedish IPR. Diagnoses in the IPR are coded according to the Swedish International Classification of Disease (ICD) system (adapted from WHO ICD classification system). We used the codes 427.92 from ICD-8, 427D from ICD-9, and I48 (I48.0, I48.1, I48.2, I48.3, I48.4, I48.9) from ICD-10 to identify the diagnosis of AF and atrial flutter. The outcome of AF was defined as either a diagnosis of AF or of atrial flutter because of their close inter-relationship and the difficulties differentiating between these conditions. The Swedish IPR has complete national coverage since 1987.[15] In Sweden, the vast majority of care providers are public. Currently, more than 99% of all somatic and psychiatric hospital discharges are registered in the IPR.[15] Since 2001, the register also includes outpatient visits from public and private care providers. The validity of a diagnosis of AF in IPR is high (95–97%), indicating only a small impact of case misclassification bias.[16] Follow-up of the cohort through 31 December 2009 revealed 4563 cases of AF. Ascertainment of deaths in the cohort was accomplished through linkage to the Swedish Death Registry at Statistics Sweden.

Statistical analysis

Follow-up time for each individual was accrued from baseline to the date of diagnosis of AF, death, or 31 December 2009, whichever came first. We categorised the individuals into five groups depending on their self-reported leisure-time exercise level in hours/week (<1, 1, 2–3, 4–5, or >5) at the ages of 15, 30, 50 years, and at baseline (mean age 60 years) as well as into five groups according to walking/bicycling level (almost never, <20, 20–40, 40–60 min/day, or >1 h/day) at 15, 30, 50 years of age and at baseline. If information about physical activity at baseline were missing, we used information for physical activity at age 50 years. Men with missing data on leisure-time exercise or walking/bicycling were excluded from the corresponding analysis. For the physical activity variables used in this study, data were missing for 4.7% (n=2092) (walking/bicycling at baseline) to 11.6% (n=5152) (leisure-time exercise at age 30 years).

Relative risks (RR) with 95% CIs were estimated using Cox proportional hazards regression models.[17]

All models were adjusted for age (in months) at baseline. Multivariable models were further adjusted for education (primary school, high school and university), smoking status and pack-years of smoking (never smoker; past smoker and <20 pack-years; past smoker and 20–39 pack-years; past smoker and ≥40 pack-years; current smoker and <20 pack-years; current smoker and 20–39 pack-years; and current smoker and ≥40 pack-years), BMI (<23.0, 23.0–24.9, 25.0–29.9, and ≥30 kg/m^2), diabetes (yes/no), history of hypertension (yes/no), history of coronary heart disease or heart failure (yes/no), family history of myocardial infarction (yes/no), aspirin use (yes/no), and alcohol consumption (g/day, in quartiles). Leisure-time exercise and walking/bicycling were mutually adjusted. A separate multivariable model was conducted excluding those with previous coronary heart disease or heart failure at baseline (n=4172) because they may have changed their physical activity levels due to their disease.

Analysis was also done without adjustment for BMI, diabetes and hypertension, as these factors are potential mediators of the association between physical activity and AF risk. We tested the proportional hazards assumption using the likelihood ratio test; there was no departure from the assumption.

Tests of linear trends across exposure categories were assessed by fitting ordinal exposure variables as continuous terms. We used the likelihood ratio test to assess statistical interaction. All analyses were performed using the statistical software SAS (V.9.3; SAS Institute, Cary, North Carolina, USA). All statistical tests were two-sided, and p values <0.05 were considered statistically significant.

RESULTS

Baseline characteristics of the study population for the lowest and highest categories of leisure-time exercise and walking/bicycling are shown in table 1. The groups with high physical activity levels for walking/bicycling and leisure-time exercise were older and had generally fewer cardiovascular risk factors, including less current smoking and lower prevalence of diabetes mellitus and hypertension.

During a median follow-up of 12 years (476 112 person-years), 4568 cases of AF were diagnosed in the cohort, which corresponds to 9.6 cases of AF per 1000 person-years. The associations of leisure-time exercise and walking/bicycling at age 30 years (reported retrospectively at baseline) and at baseline with risk of AF, are presented in table 2, figures 1 and 2.

There was a positive association between leisure-time exercise at age 30 years and risk of AF. Men who engaged in exercise for 5 h or more per week at age 30 years had a RR of 1.19 (95% CI 1.05 to 1.36) compared with men who engaged in leisure-time exercise for less than 1 h/week to develop AF, after adjustment for other risk factors, and excluding men with coronary heart disease or heart failure at baseline. Walking/bicycling at the age of 30 was not associated with risk of AF. However, walking/bicycling at baseline (mean age 60 years) was inversely associated with risk of AF (RR 0.87, 95% CI 0.77 to 0.97 for >1 h/day vs almost never) and the association was similar after excluding men with previous coronary heart disease or heart failure at baseline (corresponding RR 0.88, 95% CI 0.77 to

Table 1 Age-standardized baseline characteristics for the lowest and highest categories of leisure-time exercise and walking/bicycling, in the cohort of Swedish men

	Exercise at age 30 years		Exercise last year		Walking/bicycling at age 30 years		Walking/bicycling last year	
Characteristic	<1 h/week	>5 h/week	<1 h/week	>5 h/week	Almost never	>1 h/day	Almost never	>1 h/day
Age, mean (years)	57.1	60.9	57.9	63.6	55.9	62.8	59.9	62.8
Height, mean (cm)	177	178	177	177	177	177	177	177
Body Mass Index, mean (kg/m^2)	25.9	25.9	26.3	26.2	26.1	25.9	26.5	25.5
Postsecondary education (%)	13.2	14.7	13.7	10.7	14.8	12.7	14.2	12.5
Current smoking (%)	27.5	23.9	30.8	23.2	29.6	25.8	32.7	25.0
Aspirin use (%)	36.9	35.0	37.5	34.1	37.2	35.8	38.4	34.4
History of coronary heart disease or heart failure (%)	8.1	8.9	9.4	8.5	10.0	8.9	10.7	8.2
History of hypertension (%)	24.0	21.5	26.2	22.0	26.1	23.6	27.8	21.6
History of type 2 diabetes (%)	9.7	7.8	10.8	8.4	10.8	8.7	12.0	8.2
Family history of myocardial infarction (%)	14.0	15.7	14.9	18.2	15.6	15.3	15.6	15.1
Alcohol intake, mean (g/day)	9.8	10.7	10.2	10.8	10.4	10.1	10.7	9.9

0.998). Leisure-time exercise at baseline was inversely associated with risk of AF in the age-adjusted analysis, but the association was attenuated and not statistically significant after adjustment for other risk factors for AF. All results were similar without adjustment for BMI, diabetes mellitus and history of hypertension.

Table 2 Relative risks (RR) of atrial fibrillation by leisure-time exercise and walking/bicycling at age 30 years and at baseline, in the cohort of Swedish men, 1998–2009

Variable	Cases*	Person-years	Age-adjusted RR	Multivariable RR†	Multivariable RR†‡
Exercise at age 30 years (h/week)					
<1	499	69 469	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	695	83 297	1.06 (0.94–1.19)	1.07 (0.95–1.20)	1.08 (0.95–1.22)
2–3	1267	140 057	1.02 (0.92–1.14)	1.04 (0.93–1.16)	1.06 (0.94–1.20)
4–5	619	63 208	1.07 (0.95–1.20)	1.09 (0.96–1.23)	1.13 (0.98–1.29)
>5	790	70 719	1.15 (1.02–1.29)	1.17 (1.03–1.32)	1.19 (1.05–1.36)
p for trend			0.11	0.01	0.008
Exercise at baseline (h/week)					
<1	821	97 499	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	740	86 712	0.92 (0.83–1.02)	0.96 (0.86–1.06)	0.98 (0·87–1.10)
2–3	1369	140 318	0.90 (0.83–0.98)	0.97 (0.89–1.07)	1.01 (0·91–1.12)
4–5	582	55 875	0.83 (0.75–0.93)	0.91 (0.81–1.02)	0.96 (0·84–1.09)
>5	802	64 638	0.90 (0.81–0.99)	1.00 (0.90–1.12)	1.05 (0.92–1.18)
p for trend			0.01	0.76	0.60
Walking/bicycling at age 30 years					
Almost never	259	38 662	1.00 (reference)	1.00 (reference)	1.00 (reference)
<20 min/day	717	96 153	1.02 (0.89–1.18)	1.03 (0.89–1.19)	1.08 (0.92–1.26)
20–40 min/day	1151	134 281	0.93 (0.81–1.07)	0.96 (0.84–1.10)	0.98 (0.84–1.15)
40–60 min/day	786	76 069	0.98 (0.85–1.13)	0.99 (0.86–1.15)	1.03 (0.88–1.21)
>1 h/day	1223	101 287	1.04 (0.91–1.20)	1.04 (0.90–1.20)	1.08 (0.93–1.27)
p for trend			0.30	0.45	0.35
Walking/bicycling at baseline					
Almost never	603	59 085	1.00 (reference)	1.00 (reference)	1.00 (reference)
<20 min/day	1011	112 429	0.90 (0.81–1.00)	0.96 (0.86–1.06)	0.96 (0.85–1.08)
20–40 min/day	1216	133 991	0.83 (0.75–0.91)	0.89 (0.80–0.99)	0.90 (0.80–1.01)
40–60 min/day	740	68 753	0.87 (0.78–0.97)	0.95 (0.85–1.07)	0.97 (0.86–1.11)
>1 h/day	851	79 369	0.79 (0.71–0.87)	0.87 (0.77–0.97)	0.88 (0.77–0.998)
p for trend			<0.0001	0.03	0.09

*The sum does not add up to the total owing to missing data for the exposure variable.
†Multivariable models were adjusted for age, education (primary school, high school, university), smoking status and pack years of smoking (never smoker, past smoker and <20 pack-years, past smoker and 20–39 pack-years, past smoker and ≥40 pack-years, current smoker and <20 pack-years, current smoker and 20–39 pack-years, current smoker and ≥40 pack-years), body mass index (<23.0, 23.0–24.9, 25.0–29.9, ≥30 kg/m^2), diabetes (yes/no), history of hypertension (yes/no), history of coronary heart disease or heart failure (yes/no), family history of myocardial infarction (yes/no), aspirin use (yes/no), and alcohol consumption (g/day, in quartiles). Leisure-time exercise and walking/bicycling were mutually adjusted in the multivariable model.
‡Excluding men with previous coronary heart disease or heart failure at baseline.

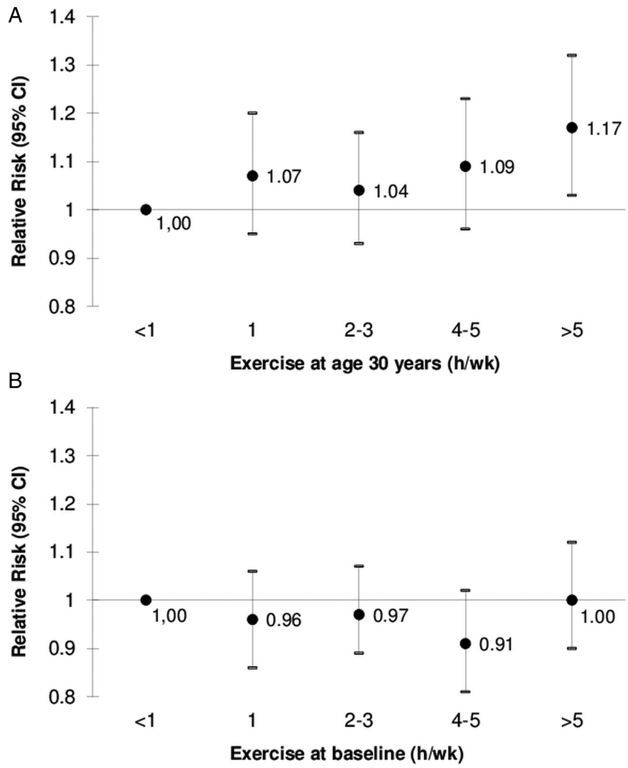

Figure 1 Multivariable relative risks* of atrial fibrillation by exercise at age 30 years (A) and at baseline (B) in the cohort of Swedish men, 1998–2009 *Multivariable relative risks were adjusted for the same variables as in table 2.

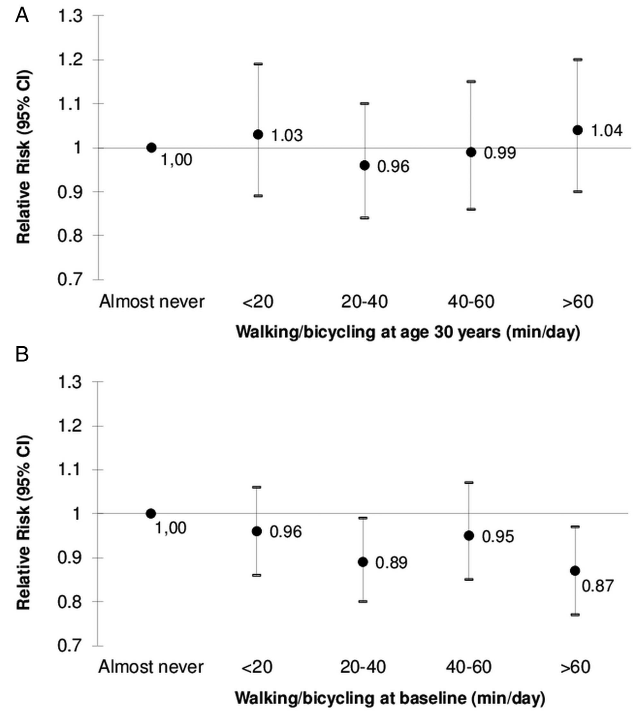

Figure 2 Multivariable relative risks* of atrial fibrillation by walking/bicycling at age 30 years (A) and at baseline (B) in the cohort of Swedish men, 1998–2009 *Multivariable relative risks were adjusted for the same variables as in table 2.

There was no association between risk of AF and leisure-time exercise or walking/bicycling at the age of 15 years and 50 years (data not shown).

To investigate how the amount of leisure-time exercise throughout life influences the risk of developing AF, we categorised the population into five groups: Group 1 (reference group): exercise <1 h/week at age 30 years and at baseline; Group 2: exercise >5 h/week at age 30 years and <1 h/week at baseline; Group 3: exercise >5 h/week at age 30 years and at baseline; Group 4: exercise: <1/week at age 30 years and >5 h/week at baseline; and Group 5: exercise 1–5 h/week at age 30 years and at baseline. A statistically significant association between leisure-time exercise and risk of AF was only observed among men who had a high level of exercise at age 30 years (>5 h/week) and became inactive at an older age (exercise <1 h/week at baseline) (Group 2). This group had a RR of 1.49 (95% CI 1.14 to 1.95) to develop AF compared with Group 1 (exercise <1 h/week at age 30 years and at baseline).

DISCUSSION

This study, comprising 44 010 men followed for a median of 12 years, showed a complex association between physical activity and development of AF. High levels of leisure-time exercise (ie, exercising for more than 5 h a week), considered as moderate to high-intensity physical activity at the age of 30 years, was associated with an increased risk of AF later in life. These men had a RR of 1.19 to develop AF compared with those who exercised less than 1 h a week at age 30 years. The risk of AF was even greater (RR 1.49) among men who had exercised more than 5 h/week at the age of 30 years, and were inactive when they were older (mean age 60 years).

Our finding of an increased risk of AF with a high level of leisure-time exercise at a younger age is in agreement with the Physicians' Health Study, a large prospective cohort study where subgroup analyses showed a 74% increased risk of AF associated with a high frequency of vigorous exercise (5–7 days/week) in men <50 years of age.[18] Furthermore, previous case series and retrospective studies have found an increased risk of AF in young athletes and middle-aged men engaged in high-intensity exercise or endurance training.[7–10] However, this finding differs from a previous observation by Elosua *et al*[10] who found that present engagement in endurance training was an independent risk factor for AF. An explanation for the discrepancy may be that Elosua studied younger men: mean age was 42 years compared with our study where the mean age was 60 years. Another difference is that the study by Elosua only included lone AF.

Our data did not show that leisure-time exercise in older age (mean age in the cohort at baseline is 60 years) increased the risk for AF. Furthermore, our data showed no increase in risk of AF with walking or bicycling at any age. In fact, walking or bicycling in older age was inversely associated with risk of AF, a finding that is consistent with the results found in the Cardiovascular Health Study.[12]

There are several possible mechanisms by which physical activity could influence the risk of AF. Exercise has positive effects on traditional cardiovascular risk factors such as hypertension, diabetes, hypercholesterolaemia and obesity.[19 20] Furthermore, it has a positive effect on age-related decline in arterial elasticity.[21] All these factors protect against AF. On the other hand, there are many mechanisms through which frequent high-intensity exercise might increase the risk of AF, including left atrial enlargement, left ventricular hypertrophy, left ventricular dilation, inflammatory changes in the atrium, and the most commonly cited mechanism, an increase in parasympathetic tone.[22 23] We observed an increased risk of AF associated with high levels of leisure-time exercise at age 30 years but not at an older age. We think that a potential explanation for the different effects of exercise on the risk of AF depending on age could be because in older ages, the positive effects of physical activity on risk factors for AF dominate over the potential negative effects. Moreover, leisure-time exercise may be of lower intensity at an older age than at age 30 years.

The present study is a population-based study with a large sample size, and it has a prospective design with validated data on physical activity. Because of the large sample size, especially the large number of AF cases, we had high statistical power and could also detect weak associations. Additionally, this study includes complete follow-up through nationwide and population-based registries, which limits selection and surveillance bias. To our knowledge, this is the largest population-based study investigating the relationship between physical activity and AF.

Limitations

Measurements of physical activity were self-reported, and the information regarding physical activity at age 30 years was reported retrospectively at baseline. This could lead to misclassification of exposures. However, because information on exposures was collected before the diagnosis of AF in our main analyses, any misclassification would most likely have attenuated rather than exaggerated any true relationships and, thus, is unlikely to explain the observed associations. Assessment of the intensity of the physical activity was also self-reported. Another limitation is that we cannot rule out the possibility that some of the participants who were classified as non-cases had asymptomatic AF, leading to an underestimation of the incidence of AF. Cases in our cohort are mainly symptomatic cases. Furthermore, we did not assess or adjust for other chronic diseases like pulmonary disease and valvular heart disease which influence the risk of developing AF and the ability to perform physical activity. We also did not have information regarding sleep apnoea, which is a risk factor for AF.

When giving advice to the public regarding physical activity, it is important to consider all the positive effects of physical activity on several medical conditions and even on extended life expectancy.[1–6 24 25] Physical inactivity and a sedentary lifestyle is a far bigger health problem for the general population then excessive physical activity. However, frequent high-intensity exercise could be associated a with negative health impact. Results from subanalysis of The Copenhagen City Heart Study suggested that jogging at a slow to moderate pace not more frequent then three times a week was associated with the lowest mortality, while no survival benefit was seen when jogging at a fast pace, or more than three times a week.[24]

In conclusion, our results suggest that a high level of leisure-time exercise (moderate-intensity to high-intensity physical activity) in younger men is associated with an increased risk of AF later in life, and that the increase in risk becomes even higher for those who quit exercising later in life. On the other hand, walking/bicycling (low-intensity to moderate-intensity) at an older age seems to reduce the risk of AF, a finding that might be due to positive effects on several traditional cardiovascular risk factors.

Contributors ND and SCL designed the study. SCL and AW obtained the data. ND, AW, MJU and SCL analysed the data. ND wrote the report. ND, AW, MJU and SCL critically revised the report. SCL did the statistical analysis. All authors approved the final report submission.

Key messages

What is already known on this subject

- Results from previous studies indicate that long-term regular exercise elevates the risk for atrial fibrillation (AF) among athletes. The vast majorities of previous studies investigated athletes and individuals participating in sport competitions. Large studies investigating the association between physical activity and AF in a general population are lacking.

How might this impact on clinical practice

- The aetiology and pathogenesis of atrial fibrillation (AF) is still largely unclear. Several conditions, such as ageing, hypertension, heart failure, valvular heart disease and diabetes are associated with AF. However, in addition to these well-known risk factors for AF, vigorous long-time physical activity seems to increase the risk for AF.
- When giving advice to the public regarding physical activity, it is important to consider all the positive effects of physical activity on several medical conditions and even on extended life expectancy. Physical inactivity with a sedentary lifestyle is a far bigger health problem for the general population than excessive physical activity. However, frequent high-intensity exercise could be associated with negative health impact, and patients with such lifestyle should be informed. It will also help physicians give plausible aetiological explanations to patients with AF and a history of long-time vigorous exercise.

What this study adds

- This is by far the largest study on a general population that has examined the association between physical activity and the risk of atrial fibrillation.
- We found that intense physical activity, like leisure-time exercise of more than 5 h/week at the age of 30 years, increased the risk of developing atrial fibrillation later in life. By contrast, moderate-intensity physical activities, like walking or bicycling of more than 1 h/day later in life at older age decreased the risk.

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Competing interests MJ-U has received consultancy fees from Medtronic.

Ethics approval The study was approved by the Ethical Review Board at the Karolinska Institute in Stockholm, Sweden.

Provenance and peer review Not commissioned; externally peer reviewed.

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Atrial fibrillation is associated with different levels of physical activity levels at different ages in men

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Notes