ORIGINAL ARTICLE

Physical activity is associated with a reduced risk of atrial fibrillation in middle-aged and elderly women

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ABSTRACT

Objective Previous studies have found that regular participation in intense physical activity increases the risk of developing atrial fibrillation (AF) in men, but it remains unclear how physical activity influences the risk of AF in women. We aimed to examine whether physical activity of different types and at different ages influences the development of AF in women.

Methods In the population-based Swedish Mammography Cohort, information about physical activity was obtained from 36 513 AF-free women (49–83 years old, median age 60 years) who had completed a questionnaire at study entry (1997). Participants reported their time spent on leisure-time exercise and on walking or bicycling throughout their lifetime (at study entry, and at 30 and 50 years of age). We used the Swedish National Inpatient Register (IPR) to determine whether the participants were diagnosed with AF. Cox proportional hazards regression models were used to estimate relative risks (RR) with 95% CI, adjusted for potential confounders.

Results During a median follow-up of 12 years (10th percentile 7.5 years, 90th percentile 12.0 years), 2915 cases of AF were diagnosed. The risk of AF decreased with increasing levels of leisure-time exercise at study entry (RR 0.85, 95% CI 0.75 to 0.95 for ≥4 h/week vs <1 h/week) and walking/bicycling (RR 0.81, 95% CI 0.72 to 0.92, for ≥40 min/day vs almost never).

Conclusions Physical activity is associated with a reduced risk of AF in women. Moderate amount of physical activity was sufficient to significantly reduce AF risk.

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice.[1] It is associated with decreased quality of life and work capacity as well as with increased risk of stroke, heart failure and mortality.[2–4] In young and middle-aged men, long-term regular sport activity increases the risk of developing AF, whereas in older men moderate physical activity seems to decrease the risk.[5–8] Very few studies have assessed the association between physical activity and the risk of AF in women.[9 10] Everett *et al* showed that in middle-aged women, physical activity was associated with a small reduction in the risk of AF; however, this association was no longer significant after controlling for body mass index (BMI).[10] Thelle *et al* were not able to show any association between the risk of being prescribed flecainide (an antiarrhythmic drug mainly being used for prevention of AF) and physical activity in women.[9] Given the lack of data on the role of physical activity with respect to AF risk in women, we examined the influence of different types of physical activity and at different ages on the risk of developing AF in a large population-based cohort of Swedish women.

METHODS

Study population

Established 1987–1990, the Swedish Mammography Cohort included all women born between 1914 and 1948 living in Västmanland and Uppsala counties (Central Sweden).[11] These women completed a diet questionnaire. In the autumn of 1997, the 56 030 participants who were still alive and residing in the study area received an expanded self-administered questionnaire that asked about their physical activity and other risk factors for chronic diseases. Because data on physical activity were included for the first time in the 1997 questionnaire, only women who completed the 1997 questionnaire (n=39 227 women, 70% response rate) were eligible for inclusion in the present study. We excluded women with an incorrect or a missing Swedish Personal Identification Number (n=243), women who died before the start of follow-up (1 January 1998) (n=26), and women diagnosed before study entry with AF (n=634) as recorded in the Swedish Inpatient Register (IPR) or cancer (n=1811), except non-melanoma skin cancer, as recorded in the Swedish Cancer Registry. As a result, 36 513 women were eligible for the analyses. The Regional Ethical Review Board at Karolinska Institute in Stockholm, Sweden, has approved this study on physical activity and risk of AF as well as record linkage of the study population to Swedish registries.

Case ascertainment and follow-up

AF cases were identified by computerised linkage of the study cohort to the Swedish IPR using the Swedish Personal Identification Number. Diagnoses in the Swedish IPR are coded according to the Swedish International Classification of Disease (ICD) (modified from the WHO ICD classification system). Incident cases of AF and atrial flutter were identified using the codes 427.92 for ICD-8, 427D for ICD-9 and I48 for ICD-10. Because AF and atrial flutter are very similar, making it difficult to ascertain a diagnosis, we defined both as a diagnosis of AF. Currently, more than 99% of all somatic and psychiatric hospital discharges are registered in the IPR.[12] Since 2001, the register also includes outpatient visits from public and private care providers. The validity of an AF diagnosis in the IPR is high (95%–97%).[12] Information on dates of deaths for deceased participants was obtained from the Swedish Death Registry. Participants were followed up from 1 January 1998 to the date of AF diagnosis, death or the end of follow-up (31 December 2009), whichever came first.

Baseline data

Through a self-administered questionnaire, all participants reported information on education, body weight and height, alcohol consumption, smoking status and history, family history of myocardial infarction before 60 years of age, history of hypertension and history of diabetes. BMI was estimated from self-reported weight and height (weight in kg/height in m^2). 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 heart failure was obtained from the Swedish IPR. We calculated pack-years of smoking by multiplying the number of packs of cigarettes smoked per day by the number of years of smoking. Twenty pack-years of smoking correspond to smoking one pack (20 cigarettes) per day for 20 years.

Assessment of physical activity

Information on time spent on walking or bicycling as for everyday transport and leisure-time exercise reported separate from the time reported for walking/bicycling was collected in the 1997 questionnaire. Activity during work hours was not included in this analysis. For this baseline data, participants retrospectively reported their leisure-time exercise and walking/bicycling habits throughout their lifetime (at study entry, and at 30 and 50 years of age). Leisure-time exercise was reported as one variable, without specific information about types of exercise (eg, running, swimming, etc.).

The physical activity questions were validated using two 7-day activity records that were performed 12 months apart in 116 women (aged 56–75 years) randomly selected from the cohort. Validity of combined exercise and walking/bicycling was 0.42; this was measured by deattenuated concordance correlations comparing the records with the questionnaire.[13]

Statistical analysis

Follow-up time for each woman was aggregated from study entry to the date of diagnosis of AF, death or 31 December 2009, whichever came first. We categorised the women into four groups depending on their self-reported leisure-time exercise level in hours/week (<1, 1, 2–3, >4) at study entry (median age 60) and at age 30 years as well as into four groups according to their walking/bicycling level (almost never, <20 min/day, 20–40 min/day or >40 min/day) at study entry and at age 30 years. If information about walking/bicycling or leisure-time exercise at study entry was missing, we used data for walking/bicycling and leisure-time exercise at age 50 years. Women with missing data for walking/bicycling or leisure-time exercise at both time periods were excluded. Women with missing data on leisure-time exercise (n=2473 for exercise at study entry and n=7458 for exercise at 30 years old) or walking/bicycling (n=1271 for walking/bicycling at study entry and n=4655 for walking/bicycling at age 30 years) were excluded from the corresponding analysis. Relative risks (RR) with 95% CIs were estimated using Cox proportional hazards regression models.[14] We tested the proportional hazards assumption using the likelihood ratio test; there was no departure from the assumption.

All models were adjusted for age (in months) at study entry. 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, 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) and alcohol consumption (never drinkers, past drinkers and current drinkers of <1 drink/day, 1–2 drinks/day and ≥3 drinks/day).

Since participants with a history of coronary heart disease or heart failure (ascertained through the Swedish IPR) at study entry (n=1640) may have changed their physical activity levels due to their disease, we also conducted a separate analysis excluding those diagnosed with these diseases before study entry.

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 conducted using 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

During a median follow-up of 12 years (10th percentile 7.5 years, 90th percentile 12.0 years; 402 369 person-years), 2915 cases of AF were diagnosed in the cohort, which corresponds to 7.2 cases of AF per 1000 person-years. The mean age at first diagnosis of AF was 76.0 (SD±8.6) years. Table 1 shows the baseline characteristics of the study population according to leisure-time exercise and walking/bicycling. As expected, women who reported a high level of leisure-time exercise or walking/bicycling were on average leaner, and were less likely to be a current smoker or have diabetes, hypertension, coronary heart disease or heart failure compared with women with a low level of leisure-time exercise or walking/bicycling.

There was no association between risk of AF and leisure-time exercise or walking/bicycling at age 30 years (reported retrospectively at study entry). For example, the multivariable RR of AF for the highest compared with the lowest category (same categories as in table 2) were 1.00 (95% CI 0.86 to 1.16) for exercise and 0.97 (95% CI 0.78 to 1.21) for walking/bicycling.

The risk of AF was inversely associated with leisure-time exercise at study entry with a trend from lowest to highest category, but only women in the highest category (≥4 h/week) had a statistically significant risk reduction (15% lower risk of AF) compared with women in the lowest category (<1 h/week) (table 2 and figure 1). Walking/bicycling at study entry was also inversely associated with risk of AF (table 2 and figure 1). Compared with women who almost never walked or bicycled, women who walked or bicycled 20–39 min/day and ≥40 min/day had a 14% and 19% lower risk of AF, respectively. The association between walking/bicycling and leisure-time exercise at study entry was not modified by previous coronary heart disease or heart failure (p for interaction walking/bicycling=0.60 and p for interaction leisure-time exercise=0.39).

In women, even extreme physical activity/exercise for more than 5 h/week is inversely associated with risk of AF. The multivariable RR of AF for women who exercise >5 h/week (11% of all women), compared with <1 h/week, is 0.85 (95% CI 0.74

Table 1 Baseline characteristics* of participants of the Swedish Mammography Cohort by categories of exercise and walking/bicycling at study entry

Characteristics	Exercise at study entry (h/week) <1 (n=6624)†	1 (n=8120)	2–3 (n=11 523)	≥4 (n=7773)	Walking/bicycling at study entry (min/days) Almost never (n=3776)†	<20 (n=6650)	20–39 (n=12 141)	≥40 (n=12 675)
Age, mean (years)	61.1	60.3	61.2	62.6	64.0	60.5	60.8	62.0
Height (cm)	164.7	164.8	164.9	164.6	164.2	164.8	165.0	164.6
Body mass index, mean (kg/m^2)	25.7	25.3	24.9	24.4	26.1	25.5	24.9	24.6
Postsecondary education (%)	18.1	20.2	20.3	17.9	14.9	19.0	21.2	18.1
Current smoking (%)	29.7	23.2	20.2	22.2	32.1	25.1	21.4	22.0
History of hypertension (%)	23.4	21.9	20.4	19.1	25.5	21.8	20.5	19.4
History of type 2 diabetes (%)	4.9	3.9	3.7	4.2	6.5	4.3	3.6	3.9
History of coronary heart disease or heart failure (%)	5.6	4.7	3.9	3.7	6.9	5.0	4.0	3.7
Family history of myocardial infarction (%)	17.4	17.2	16.5	18.0	19.3	17.8	17.3	16.5
Alcohol intake, mean (g/day)	5.4	5.3	5.3	5.5	5.4	5.3	5.5	5.3

*Age standardised to the age distribution of the study population at study entry.
†The number of women does not sum up to the total number because of missing data on exercise (n=2473) and walking/bicycling (n=1271).
g/day; gram/day.

to 0.98), which is identical to those who exercise 4–5 h/week (RR=0.85; 95% CI 0.74 to 0.98).

DISCUSSION

In this cohort of women, both walking/bicycling and leisure-time exercise were associated with a reduced risk of AF. A significant reduction in AF risk was observed for a leisure-time exercise level of four or more hours per week or daily walking/bicycling for at least 20–39 min/day.

Previous studies done on younger and middle-aged men have reported an increased risk of AF with high levels of intense physical activity, while moderate levels of light-to-moderate intense physical activity in older adults seem to decrease the risk.[6–8] In our previous study of Swedish men, we observed an increased risk of AF in men who reported high levels (>5 h/week) of leisure-time exercise at 30 years of age, but we also observed that more light-intense physical activity like walking and bicycling at

Table 2 Relative risks (RR) (95% CI) of atrial fibrillation by categories of exercise and walking/bicycling in the Swedish Mammography Cohort, 1998–2009

	Cases*	Age-adjusted RR	Multivariable RR†
Exercise at study entry (h/week)			
<1	555	1.00 (reference)	1.00 (reference)
1	564	0.85 (0.75–0.95)	0.89 (0.79–1.00)
2–3	888	0.84 (0.75–0.93)	0.92 (0.82–1.02)
≥4	601	0.75 (0.67–0.84)	0.85 (0.75–0.95)
p For trend		<0.0001	0.02
Walking/bicycling at study entry (min/day)			
Almost never	421	1.00 (reference)	1.00 (reference)
<20	524	0.88 (0.78–1.01)	0.94 (0.82–1.07)
20–39	880	0.77 (0.68–0.89)	0.86 (0.76–0.97)
≥40	937	0.71 (0.63–0.80)	0.81 (0.72–0.92)
p For trend		<0.0001	0.0002

*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) and alcohol consumption (never drinkers, past drinkers and current drinkers of <1 drink/day, 1–2 drinks/day and ≥3 drinks/day).

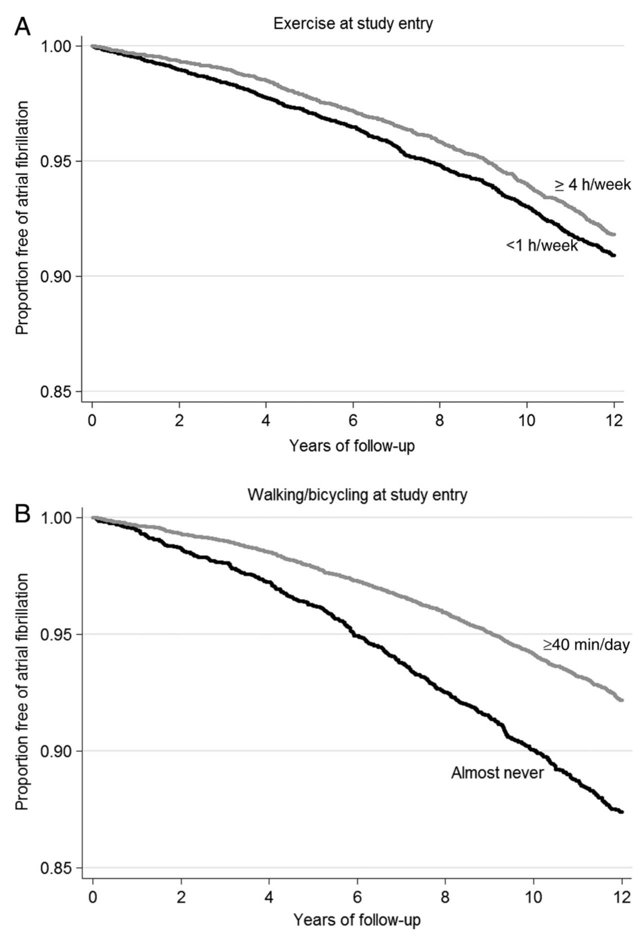

Figure 1 Kaplan–Meier survival curves (unadjusted) (ie, free of atrial fibrillation (AF)) for the two extreme groups of leisure-time exercise (A) and walking/bicycling (B) at study entry.

older age (mean age 60 years) reduced the risk of AF.[5] High levels of leisure-time exercise at older age were not associated with AF risk in men. In the current study of Swedish women, we were not able to observe any association between risk of AF and leisure-time exercise at age 30 years. At study entry when the median age was 60, we observed an inverse associated risk of AF with walking/bicycling and even in the most extreme leisure-time-exercise category (>5 h/week). Wilhelm *et al* observed a sex difference for atrial and ventricular remodelling and autonomic tone with respect to endurance training. Male athletes had larger atrial volume, longer p-wave duration on signal-averaged ECG and a larger LV mass index as well as greater relative wall thickness and sympathovagal balance as represented by the low/high-frequency power ratio.[15] All these factors could influence the risk of developing AF.

Walking/bicycling 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 different results for men and women could be explained by the fact that exercise intensity in men was higher than in women. Very high-intensity exercise at younger age could potentially increase the risk of AF while lighter exercise at older age could potentially decrease the risk.

In a large female cohort study, Everett *et al*[10] observed that physical activity was associated with a modest reduced risk of AF, although this association was not significant after adjusting for BMI. In the present study, the inverse association between physical activity and AF remained after adjusting for multiple factors, including BMI, hypertension, diabetes and cardiovascular disease. This inverse association could imply that positive effects of physical activity are not entirely mediated by the positive effect of physical activity on these well-known risk factors for AF.

The strengths of this study include its large study population and the complete follow-up, both made possible because of access to high-quality nationwide and population-based registries. In addition, this prospective study used validated data on physical activity. This study has a few limitations. The assessment of physical activity was self-reported, and the intensity of the exercise levels was not measured. In addition, there is also a possibility that some of the participants who were classified as non-cases had asymptomatic AF, leading to an underestimation of the incidence of AF.

In conclusion, physical activity is associated with a reduced risk of AF in middle-aged and elderly women. Moderate amount of physical activity was sufficient to reduce risk significantly.

Key messages

What is already known on this subject?

Previous studies have found that regular participation in intense physical activity increases the risk of developing atrial fibrillation (AF) in men. Very few studies have assessed the association between physical activity and the risk of AF in women. It is unclear how physical activity influences the risk of AF in women.

What might this study add?

This study found that physical activity was associated with a reduced risk of AF in middle-aged and elderly women. Moderate amount of physical activity was sufficient to reduce risk significantly. High levels of exercise were not a risk factor for AF in women as previously described in men.

How might this impact on clinical practice?

These findings indicate that physical activity may prevent development of AF in middle-aged and elderly women. Physical activity should be encouraged.

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

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Competing interests MJ-U has received consultancy fees from Medtronic, and ND has received consultancy fees from Biosense Webster.

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