

Physical activity, resting heart rate and atrial fibrillation: The Tromsø Study

Authors: Bente Morseth^{1,2,3}, Sidsel Graff-Iversen^{1,4}, Bjarne K. Jacobsen¹, Lone Jørgensen^{5,6}, Audhild Nytnes¹, Dag S. Thelle^{4,7,8}, Peter Vestergaard⁹, Maja-Lisa Løchen^{1,10}

UiT The Arctic University of Norway

Corresponding author:

Bente Morseth

School of Sport Sciences, UiT The Arctic University of Norway, 9037 Tromsø, Norway

E-mail: bente.morseth@uit.no

Telephone +47 77 660769

Author affiliations:

¹Department of Community Medicine, UiT The Arctic University of Norway, Tromsø, Norway

²School of Sport Sciences, UiT The Arctic University of Norway, Tromsø, Norway

³Centre for Clinical Research and Education, University Hospital of North Norway Trust, Tromsø, Norway

⁴Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway

⁵Department of Health and Care Sciences, University of Tromsø, Tromsø, Norway

⁶Department of Clinical Therapeutic Services, University Hospital of Northern Norway, Tromsø, Norway

⁷Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway

⁸Department of Community Medicine and Public Health, Institute of Medicine, Gothenburg University, Gothenburg, Sweden

⁹Departments of Clinical Medicine and Endocrinology, Aalborg University Hospital, Aalborg, Denmark

¹⁰Department of Cardiology, University Hospital of North Norway, Tromsø, Norway

Abstract

Aims: The objective was to examine the association of physical activity and resting heart rate (RHR) with hospital-diagnosed atrial fibrillation (AF) in a Norwegian cohort.

Methods and Results: This prospective study included 20 484 adults (50.3% men) who participated in the third Tromsø Study survey in 1986-1987. At baseline, physical activity was assessed by a validated questionnaire, and RHR was objectively measured. Participants were followed from baseline through 2010 with respect to incident cases of hospital-diagnosed AF documented on an electrocardiogram. During a mean follow-up period of 20 years (409 045 person-years), 750 participants (70.5% men) were diagnosed with AF. Compared with the low physical activity group, moderately active individuals had a 19% lower risk of any AF (adjusted HR 0.81, 95% CI 0.68-0.97), whereas highly active had similar risk of AF. Vigorously active individuals showed a non-significantly higher risk of AF (adjusted HR 1.37, 95% CI 0.77-2.43). Risk of AF increased with decreasing RHR (adjusted HR 0.92, 95% CI 0.86-0.98 for each 10 beats/minutes increase in RHR), and RHR <50 beats/minute was a risk factor for AF (P<0.05).

Conclusion: In this prospective cohort study, leisure time physical activity was associated with AF in a J-shaped pattern. Moderate physical activity was associated with a reduced risk of AF, whereas higher activity levels attenuated the benefits of moderate activity. Low RHR was a risk factor for AF. Our results support the hypothesis that moderate and vigorous physical activity may affect AF risk via different pathophysiological mechanisms.

Keywords: Exercise; Physical activity; Atrial fibrillation; Resting heart rate; Arrhythmia;

Introduction

Atrial fibrillation (AF) is a cardiac arrhythmia with a prevalence of 0.5-1% at age 40-50 years, increasing to 5-15% at age 70-80 years.¹ Typically, AF progresses from short, infrequent to longer, more frequent episodes, and eventually, the patient may develop permanent AF.¹ AF is most commonly associated with cardiovascular disease or other medical conditions, but may also occur in individuals without any underlying medical conditions,¹ and factors such as alcohol consumption and endurance training have been linked to development of AF.²

In recent decades, studies have demonstrated high prevalences of AF in male endurance athletes.²⁻⁷ However, these studies are mainly conducted among men with a history of sport practice and demanding competitions at rather high level. Only recently, studies embracing a wider range of physical activity have addressed the issue, and the findings vary from increased risk^{8,9} or a gradually decreasing risk of AF with increasing physical activity level,¹⁰⁻¹³ to a U-shaped relationship between physical activity and risk of AF.^{14,15} Very few studies have examined risk of AF in relation to occupational activity.¹⁶

Therefore, we aimed to examine the associations between leisure time and occupational physical activity, resting heart rate (RHR), and hospital-diagnosed AF in a community-based cohort of Norwegian men and women.

Methods

Study population

The Tromsø Study is a prospective, community-based cohort study with repeated surveys, conducted in the municipality of Tromsø, Norway. The study is described in detail elsewhere.¹⁷ The present study consists of participants from the survey in 1986-1987 (Tromsø 3), which comprised 21 733 men and women aged 12-67 years (participation rate 75%). Follow-up data on AF was derived from medical hospital records at the University Hospital of North Norway, by linking the participants to the hospital's diagnosis registry using their national 11-digit identification number.

Participants who also had reported physical activity level 7 years prior to Tromsø 3 (data from the second Tromsø Study in 1979-1980) were included in a subcohort in order to study AF in relation to change in physical activity.

The Tromsø Study has been approved by the Norwegian Data Inspectorate and recommended by the Regional Committee of Research Ethics. Participants were informed that data would be treated in strict confidence.

Analytical sample

After excluding participants younger than 20 years (n=1054), participants with missing baseline data (n=83), AF diagnosed prior to baseline (n=25), migrating during the study (n=35) or before participating in the baseline examination (n=52), the present study includes 20 484 men and women (Figure 1). Of these, 12 121 persons also participated in the second Tromsø Study survey in 1979-80, generating a subcohort with two assessments of physical activity.

Baseline data collection

At baseline in 1986-1987, data were collected by questionnaire and physical examinations. From the questionnaire we extracted self-reported data on current smoking (yes/no), CVD, i.e. heart attack, stroke and/or angina (yes/no), diabetes (yes/no), educational level (years), use of heart medicine or hypertension treatment during the last 14 days (yes/no), teetotaller (yes/no), and physical activity. Physical activity was assessed with separate questions on leisure time and occupational physical activity, which have both been used in several other health surveys.^{8, 16, 18-20} Leisure time physical activity was graded from 1 to 4 with the following categories; (1) Reading, watching TV, or other sedentary activity (“*Low activity*”), (2) Walking, cycling, or other forms of exercise at least four hours a week (“*Moderate activity*”), (3) Participation in recreational sports, heavy gardening etc. at least four hours a week (“*High activity*”), and (4) Participation in hard training or sports competitions regularly several times a week (“*Vigorous activity*”). The occupational activity question was also graded from 1 to 4, using the following response options: (1) Mostly sedentary work, (2) Work requiring a lot of walking, (3) Work requiring a lot of walking and lifting, and (4) Heavy manual labour.

Physical activity was measured with similar questions in Tromsø 2. In a subsample comprising participants with physical activity data from both the second and third Tromsø Study, we categorized the participants into four categories according to change in leisure time physical activity from 1979-80 to 1986-87: (1) Low physical activity (*Low* at both examinations), (2) Reduced activity (from *Moderate/High/Vigorous* to *Low*), (3) Increased activity (from *Low* to *Moderate/High/Vigorous*), and finally (4) Active (*Moderate/High/Vigorous* at both examinations).

Height and weight were measured to the nearest centimetre and half-kilogram, with subjects wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight (kg)/height² (m²). Blood pressure was measured using standard procedures (Dinamap, Criticon, Tampa, FL), and RHR was derived during the time of the blood pressure measurement after 2 minutes rest. Three recordings of heart rate were made with 2 minutes' interval, and the lowest recorded measurement was used.

Follow-up and detection of AF

The participants were followed from the date of examination in 1986–87 (Tromsø 3) until the date of first documented AF, or date of censoring due to migration or death, or end of follow-up at 31 December 2010, whichever came first. Deaths and migration from Tromsø during follow-up were identified through the Population Register of Norway.

Incident cases of AF documented on an electrocardiogram (ECG) were retrieved from medical hospital records at the University Hospital North Norway (UNN), which is the only hospital within a radius of 250 km. For participants without arrhythmia, but with diagnoses of cerebrovascular or cardiovascular events, text search in electronic records were performed, along with a manual search in paper versions of hospital records, aiming at documenting further AF events. Adjudication of AF events was performed by an independent endpoint committee.²¹

AF type was categorized into any, paroxysmal/persistent and permanent. Subjects with transient AF occurring only during an acute myocardial infarction or cardiac surgery, and persons with AF documented only in the last week of life were classified as non-cases.

Statistical analyses

Cox proportional hazard regression was used to assess the association between AF and leisure time and occupational physical activity and RHR. Proportional hazard assumptions were tested by inspecting log minus log plots. The lowest physical activity level was used as reference group. RHR was treated as both a continuous and categorical variable (<50, 50-59, 60-69, 70-79, 80-89, ≥ 90 beats/minute, with the lowest RHR group (<50 beats/minute, n=286) as reference group). All analyses were adjusted for baseline age, sex, daily smoking, BMI, height, CVD, systolic and diastolic blood pressure, diabetes, and hypertension treatment. Secondary analyses were conducted in a subcohort (n=12 121), using change in physical activity with four categories as exposure.

Sensitivity analyses were performed to assess the robustness of the leisure time physical activity model, with the following additional adjustments: 1) RHR was added to the model, 2) Alcohol consumption, education and use of heart medication was added to model (n=15 685), 3) Exclusion of participants using heart medication and participants with baseline CVD, and 4) Interim myocardial infarction was added to the model. Finally, use of heart medication was added to the RHR model.

Possible interactions were assessed by adding multiplicative interaction terms to the main multivariable model. No significant interactions were indicated between sex and physical activity, age and physical activity, or physical activity and RHR ($P > 0.2$).

Two-sided P values < 0.05 were considered statistically significant. All analyses were performed using SPSS (Statistical Package for Social Sciences, Chicago, IL, USA), version 22.

Results

Baseline characteristics

In total, 10 300 men (mean age 39.1 years at baseline) and 10 184 women (mean age 36.9 year at baseline) were included in the analyses. Further baseline characteristics of the participants are given in Table 1. During a mean follow-up period of 20.0 years (409 045 person-years), 750 participants (529 men and 221 women) were diagnosed with AF, of which 408 were paroxysmal/persistent and 342 permanent. Incidence of AF was 1.83/1000 person-years (2.62/1000 person-years in men and 1.07/1000 person-years in women).

[Table 1]

Self-reported physical activity and AF

The nature of the relationship between leisure time physical activity and AF followed a J-shape (Figure 2). In the main multivariable model, moderately active individuals had a 19% lower risk of any AF (HR 0.81, 95% CI 0.68-0.96) than those reporting low activity (Model 2, Table 2). The HRs for paroxysmal/persistent and permanent AF varied slightly from any AF. Highly active individuals had similar risk of any, paroxysmal/persistent or permanent AF as the low activity group. Vigorously active individuals showed a non-significantly higher risk of AF than the low activity group (HR 1.37, 95% CI 0.77-2.43), although they had a significantly higher risk when analysing permanent AF separately (HR 2.28, 95% CI 1.08-4.82). Adding RHR produced virtually similar results as the main multivariable model (Model 3, Table 2). Occupational physical activity was not related to risk of AF (Figure 4, Table 3S). Adjusted cumulative risk of AF according to leisure time physical activity during follow-up is displayed in Figure 3.

[Table 2] [Figure 2] [Figure 3] [Figure 4]

Changes in physical activity and AF

In a subsample comprising participants with an additional assessment of physical activity 7 years prior to the baseline examinations (n=12 121), we analysed changes in leisure time physical activity level in relation to risk of AF (Figure 5). We found no significant differences between those who were sedentary at both assessments and those who were active at one or both assessments (Table 2S).

[Figure 5]

RHR and AF

There was a significant, but weak inverse correlation between physical activity and RHR (Table 1, Spearman's rho -0.185). Among those reporting vigorous physical activity, 10% had an RHR <50 beats/minute. Using RHR as exposure in the main multivariable model, we found that risk of AF increased with decreasing RHR (HR 0.92, 95% CI 0.86-0.98 for each 10 beats/minutes increase in heart rate) (Figure 6). Individuals with a RHR <50 beats/minute had higher risk of AF than those with a RHR >60 beats/minute (P <0.05) (Table 4S). Adding physical activity to the model did not change the estimates (Table 4S).

[Figure 6]

Sensitivity analyses

In general, the main results were robust to addition of potential confounders. Additional adjustment for baseline alcohol consumption, education, and heart medication or interim myocardial infarction only slightly affected the effect estimates in a subsample of participants with valid data on these variables (Table 5S). Moreover, excluding participants using heart

medication and participants with CVD did not alter the estimates (Table 5S).

Discussion

Previous cohort studies of physical activity and AF have shown divergent results,^{6, 8, 10-14} and this study adds to the current knowledge by suggesting a J-shaped relationship between leisure time physical activity and AF. Our main finding was that moderately active individuals were at reduced risk of AF, whereas higher activity attenuated the benefits of moderate activity. It is worth stressing that vigorous activity did not confer a significant increased risk of AF beyond being sedentary. However, low RHR (<50 beats/minute) was a risk factor for AF, and RHR showed an inverse association with risk of AF. The fact that self-reported physical activity and RHR show a different nature of relationship to AF is intriguing and in our analyses RHR did not mediate the established association between moderate physical activity and AF.

Self-reported physical activity and AF

In accordance with the present study, most previous cohort studies have found that moderate physical activity is related to a reduced risk of AF.^{6, 10-14} However, the shape of the relationship between AF and physical activity varies largely. Our results are in accordance with a study of participant from the sixth Tromsø and endurance athletes, showing a J-shaped association similar to the one we suggest in our study.⁶ Moreover, Drca et al.¹⁴ reported a comparable U-shaped relationship between physical activity and AF. Our study further accentuates the likelihood of a J-shaped relationship, by studying a cohort of both women and men with a large age span, using ECG validated AF endpoints and a prospective study design. In contrast, Thelle et al.⁸ did not find a reduced risk of AF with moderate physical activity, although they found a higher risk of AF in both the high and vigorous groups in

men, in a large cohort of women and men aged 40-42 years. It is worth notice that while Thelle et al.⁸ restricted their study to subjects with “lone” AF, i.e. AF that occurs due to mechanisms related to exercise training, such as structural cardiac adaptations and lower RHR (“athlete’s heart”), the present study aimed to include all diagnosed AF. As suggested in a recent review²² and supported by the present study, the mechanisms explaining the relationship of physical activity with AF could involve two distinct pathways.²² Moderate physical activity may reduce AF risk via improved cardiovascular risk factors. However, this beneficial effect of moderate physical activity on AF may be mitigated by years of endurance training, which generates structural and functional cardiac adaptations that increase the risk of AF, including lower RHR.

Yet a different pattern was found in cohort studies reporting a gradually decreasing risk of AF with increasing physical activity level in men and women of various ages.¹⁰⁻¹³ However, self-reported physical activity, widely varying categorizing of the activity, and different cultural patterns of sport seem to limit the comparative interpretation of existing studies.²³

As in our study, a Danish study found no association between physical activity during working hours and risk of AF.¹⁶ As occupational activity is less likely to result in high demands on the heart, these results are not surprising.

Resting heart rate and AF

Given the methodological weaknesses of self-reported physical activity, RHR might serve as an alternative measure of physical activity, as RHR in general is reversely related to physical activity and physical fitness.^{8, 24, 25} This pattern was demonstrated in this study as well, although only a small proportion of the vigorously active individuals reported an RHR <50 beats/minute. Our analyses with RHR as exposure showed that risk of AF increased with

decreasing RHR, in agreement with most previous studies.^{8,26} Physical activity did not moderate the association between RHR and AF in the present study.

Limitations and strengths

Our study has some limitations. Even with a participation rate of 75%, individuals with poor health were presumably underrepresented, introducing potential selection bias. In the Tromsø Study, non-attendees tend to be male, younger and more likely single than attendees.^{17,27} However, bias due to non-participation is probably of less concern in prospective studies.^{28,29}

The use of self-reported physical activity has most likely introduced misclassification errors. Given that people tend to overestimate their activity level,²⁴ misclassification will probably underestimate the real effects of physical activity.³⁰ The validity of our physical activity questions has been ensured in several studies^{8,31,32} and found to be positively associated with objectively measured physical activity and physical fitness in a dose-response relationship.²⁴

Our results are based on AF diagnosed in hospital, which implies there are most certainly asymptomatic, undiagnosed and non-referred cases of AF.³³ Assuming that such a misclassification is non-differential, inclusion of undiagnosed cases would presumably strengthen the observed relationship between physical activity and AF. However, athletes may more often experience paroxysmal AF or hesitate to seek care, which may introduce differential misclassification, which could weaken the association.

Furthermore, we cannot exclude residual confounding by measured and unmeasured variables. This includes lack of data on the specific types of heart medication in use; for example, people diagnosed with AF might have been prescribed negative chronotropes, resulting in lower RHR, which could possibly have confounded the association between RHR

and AF. Finally, the generalizability of the data beyond the Tromsø community and the examined age range is uncertain.

On the other hand, cohort studies resemble real life and our study had the advantage of a large cohort, with a prospective design and a long follow-up period. Another strength of this study is that AF events were ascertained with ECG.

Conclusion

This prospective study suggests a J-shaped relationship between leisure time physical activity and AF. Moderate physical activity was associated with reduced risk of AF, whereas higher activity levels attenuated the benefits of moderate activity. Low RHR was a risk factor for AF. Our results support the hypothesis that there may be two contradictory pathophysiological mechanisms behind the association of physical activity with AF;²² a protective effect of moderate physical activity via reduced cardiovascular risk, and an increased risk of AF associated with more vigorous physical activity via cardiac adaptations and low RHR. Further research is recommended to clarify the association between physical activity and AF, preferably with objective measures of physical activity.

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Conflict of interest

Conflict of interest: none declared.

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Figure legends

Figure 1 Flow chart showing the selection process for the present study.

Figure 2 Risk of AF in relation to leisure time physical activity level at baseline, a) Overall, b) Stratified by sex*, c) Stratified by age*.

*“*High activity*” and “*Vigorous activity*” were merged into a new “*High/Vigorous activity*” category due to few participants undertaking vigorous activity.

Figure 3 Adjusted probability of AF in relation to physical activity

Figure 4 Risk of AF in relation to occupational physical activity level at baseline.

Figure 5 Risk of AF in relation to change in leisure time physical activity level.

Figure 6 Risk of AF in relation to resting heart rate at baseline.

Table 1. Baseline characteristics by physical activity level

	Men (n=10 300)				Women (n=10 184)		
	Low activity	Moderate activity	High activity	Vigorous activity	Low activity	Moderate activity	High/vigorous activity ^a
<i>n</i>	2371	5110	2358	461	2420	6708	1056
Age (years)	39.0 (11.0)	40.8 (11.2)	37.4 (10.3)	30.1 (8.5)	36.8 (9.8)	37.3 (9.9)	34.5 (9.7)
Body height (cm)	177.0 (6.9)	177.1 (6.8)	178.1 (6.6)	178.6 (7.0)	164.0 (6.3)	164.4 (6.1)	165.6 (5.9)
Body weight (kg)	78.1 (12.2)	77.5 (10.8)	77.2 (9.7)	75.6 (9.0)	62.7 (11.0)	62.6 (9.8)	62.1 (8.5)
BMI (kg/m ²)	24.9 (3.4)	24.7 (3.1)	24.3 (2.6)	23.7 (2.3)	23.3 (3.9)	23.2 (3.4)	22.6 (2.9)
Systolic blood pressure (mmHg)	130 (15)	130 (14)	129 (13)	129 (13)	120 (15)	120 (14)	118 (13)
Diastolic blood pressure (mmHg)	77 (11)	77 (11)	74 (11)	69 (10)	73 (11)	72 (10)	70 (10)
RHR (beats/min)	75 (13)	73 (13)	68 (12)	63 (12)	78 (12)	77 (13)	72 (12)
Education (years) ^b	11.1 (4.0)	11.2 (3.9)	12.1 (3.9)	12.6 (3.4)	10.8 (3.6)	11.2 (3.7)	12.2 (3.8)
RHR, % (<i>n</i>)							
<50	0.8 (18)	1.4 (72)	3.9 (92)	11.7 (54)	0.4 (10)	0.4 (28)	1.1 (12)
50-59	8.2 (194)	11.8 (603)	20.3 (479)	32.3 (149)	4.3 (104)	5.6 (377)	9.7 (102)
60-69	27.0 (641)	30.4 (1553)	33.7 (794)	30.8 (142)	19.2 (464)	23.1 (1549)	30.9 (326)
70-79	33.7 (798)	30.9 (1578)	25.4 (598)	15.4 (71)	35.0 (846)	34.6 (2320)	33.4 (353)
80-89	18.7 (444)	16.0 (819)	11.7 (275)	6.7 (31)	24.5 (592)	21.2 (1424)	17.5 (185)
≥90	11.6 (276)	9.5 (485)	5.1 (120)	3.0 (14)	16.7 (404)	15.1 (1010)	7.4 (78)

Smokers	59.8 (1418)	47.8 (2442)	37.4 (883)	21.3 (98)	56.7 (1372)	43.8 (2937)	37.5 (396)
CVD	3.7 (88)	3.5 (181)	1.6 (38)	0.0 (0)	1.2 (29)	0.6 (39)	0.0 (0)
Diabetes	1.1 (25)	0.9 (48)	0.3 (8)	0.2 (1)	0.4 (10)	0.4%(25)	0.3 (3)
Mostly sedentary work	50.7 (1203)	42.1 (2152)	37.5 (884)	36.4 (168)	45.0 (1088)	34.1 (2289)	34.3 (362)
Teetotaller ^b	5.9 (108)	6.8 (275)	4.8 (91)	5.2 (20)	9.2 (158)	9.8 (488)	7.4 (60)
Heart medicine use ^b	2.1 (39)	2.2 (91)	0.7 (14)	0.3 (1)	1.2 (21)	0.5 (27)	0.0 (0)
Treatment for hypertension	3.3 (78)	3.4 (172)	1.9 (45)	0.7 (3)	2.3 (56)	2.1 (138)	0.9 (9)

Data are presented as mean (SD) or % (n). BMI: body mass index; CVD: cardiovascular disease; RHR: resting heart rate.

^an=High and vigorous activity were combined due to a low number of AF events (<10)

^bn=15 685

Table 2. Risk of AF in relation to leisure time physical activity

Physical activity level	N	AF events	Sex- and age-adjusted HR (95% CI)	Adjusted HR (95% CI)			Adjusted HR (95% CI)
			Model 1 ^a (n=20 484)	Model 2 ^b (n=20 484)		Model 3 ^c (n=20 415)	
				All AF cases	Paroxysmal/persistent AF	Permanent AF	
Low	4791	188 (3.9%)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Moderate	11818	422 (3.6%)	0.76 (0.64-0.90)	0.81 (0.68-0.97)	0.76 (0.60-0.96)	0.88 (0.68-1.15)	0.81 (0.68-0.96)
High	3303	127 (3.8%)	0.87 (0.69-1.09)	0.97 (0.77-1.22)	0.99 (0.73-1.35)	0.95 (0.67-1.36)	0.94 (0.75-1.19)
Vigorous	572	13 (2.3%)	1.19 (0.68-2.11)	1.37 (0.77-2.43)	0.84 (0.34-2.08)	2.28 (1.08-4.82)	1.29 (0.73-2.30)

^aModel 1 adjusted for age and, sex

^bModel 2 adjusted for age, sex, BMI, height, daily smoking, CVD, systolic blood pressure, diastolic blood pressure, diabetes, hypertension treatment (main multivariable model)

^cModel 3 adjusted for age, sex, BMI, height, daily smoking, CVD, systolic blood pressure, diastolic blood pressure, diabetes, hypertension treatment, RHR