Title page

Physical activity modifies the risk of atrial fibrillation in obese individuals: the HUNT3 study

Lars E. Garnvik[a], Vegard Malmo[a,b], Imre Janszky[c], Ulrik Wisløff[a,d], Jan P. Loennechen[a,b] and Bjarne M. Nes[a,b]

[a]The K.G. Jebsen Center for Exercise in Medicine at Department of Circulation and Medical Imaging, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Trondheim, Norway: [b]Clinic of Cardiology, St Olav's Hospital, Trondheim, Norway; [c]Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Trondheim, Norway. [d]School of Human Movement & Nutrition Sciences, University of Queensland, Australia.

Correspondence and reprints to: Bjarne M. Nes, Department of Circulation and Medical Imaging, NTNU, Medisinsk Teknisk Forskningssenter, Post box 8905, 7491 Trondheim, Norway. E-mail: bjarne.nes@ntnu.no.

The authors are supported by grants from the K.G. Jebsen Foundation and the Liason Committee between the Central Norway Regional Health Authority and the Norwegian University of Science and Technology. There are no disclosures to report or conflict of interests.

Word count: 3878

Abstract

Background

Atrial fibrillation (AF) is the most common heart rhythm disorder and high body mass index (BMI) is a well-established risk factor for AF. The objective was to examine the associations of physical activity (PA) and body mass index (BMI) and risk of atrial fibrillation (AF), and the modifying role of PA on the association between BMI and AF.

Design

Prospective cohort study

Methods

This study followed 43 602 men and women from the HUNT3 study in 2006-2008 until first AF diagnosis or end of follow up in 2015. AF diagnoses were collected from hospital registers and validated by medical doctors. Cox proportional hazard regression analysis was performed to assess the association between PA, BMI and AF.

Results

During a mean follow up of 8.1 years (352 770 person-years), 1459 cases of AF were detected (4.1 events per 1000 person-years). Increasing levels of PA were associated with gradually lower risk of AF (*p* trend 0.069). Overweight and obesity were associated with an 18% (HR 1.18, 95% CI 1.03-1.35) and 59% (HR 1.59, 95% CI 1.37-1.84) increased risk of AF, respectively. High levels of PA attenuated some of the higher AF risk in obese (HR 1.53, 95% CI 1.03-2.28 in active and 1.96, 95% CI 1.44-2.67 in inactive) compared to normal weight individuals.

Conclusion

Overweight and obesity were associated with increased risk of AF. PA offsets some, but not all AF risk associated with obesity.

Word count: 234

Keywords: Atrial fibrillation, physical activity, body mass index, obesity.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with increased morbidity and mortality.[1] The risk of AF rises exponentially after 70 years of age and the AF prevalence is therefore expected to rise substantially in the years to come due to the aging of the population.[2]

High body mass index (BMI) is a well-established risk factor for AF[3]. Considering that overweight and obesity has reached pandemic proportions, with an estimated prevalence of 2.1 billion in 2013[4], identifying potential modifiers of the association between high BMI and AF is important.

Physical activity (PA) protects against many cardiovascular risk factors related to overweight and obesity. Moreover, a recent review suggests that moderate levels of PA is also beneficial for AF prevention[5]. However, it is not clear whether PA modifies the risk of AF associated with high BMI. One study showed that PA attenuated the risk of AF in postmenopausal obese women,[6] whereas another study found similar results in obese men, but not in obese women.[7] Furthermore, the literature on PA and incident AF has shown divergent results. While numerous studies have shown that moderate to high levels of PA is associated with lower risk of AF,[8, 9] some report increased risk of AF with vigorous leisure time PA[10, 11] or with high levels of occupational PA[12]. Therefore, it has been suggested that there is a U- or J-shaped association between PA and AF.[5]

In this study, we investigate the role of PA and BMI on incident AF in men and women from a general population, and further examine whether PA modifies the association between BMI and AF. We hypothesized that PA and BMI are both associated with risk of AF, and that PA attenuates some of the AF risk conferred by overweight and obesity.

Methods

Study population and design

The third wave of the HUNT study (HUNT3), was carried out between October 2006 and June 2008 in Nord-Trøndelag County, Norway. All residents aged 18 years or older (n=93 860) were invited, of whom 50 803 (54.1%) participated. Details about study procedures and methods have previously been described[13]. We included 43 602 participants after excluding participants with AF diagnosed before baseline (n=1438), underweight (<18.5 kg/m^{-2}) (n=303) or missing

baseline data (n=5460). All participants signed a written informed consent before participating in the study. The regional committee for medical and health research ethics approved the study.

Assessment of physical activity

Participants reported their average leisure-time PA by answering three questions concerning frequency, intensity and duration; 1: "How often do you exercise?" with the response alternatives "never" [0], "less than once a week" [0], "once a week" [1], "two to three times per week" [2.5], and "almost every day" [5]. 2: "If you do such exercise as frequently as once or more times a week, how hard do you push yourself?" with the response alternatives "I take it easy, I don't get out of breath or break a sweat [1], "I push myself until I'm out of breath and break into a sweat" [2] and "I practically exhaust myself" [3]. Question 3: "How long does each session last?" with the response alternatives "less than 15 min" [0.1], "15-29 min" [0.38], "30 min to 1 h" [0.75], and "more than 1 h" [1.0]. We calculated a PA summary score by multiplying each participant's response (i.e., numbers in brackets) to the tree questions. The PA score have previously been found to be reliable and valid[14]. Those who responded "never" or "less than once a week" were given a score of 0 and classified as inactive. The remaining participants were classified into tertiles based on the distribution of their score values, where "low PA" had an index score from 0.05 to 1.88, "medium PA" from 1.89 to 3.75 and "high PA" from 3.76 to 15.00.

Clinical and questionnaire-based information

Trained nurses conducted standardized measurements of height, weight, and blood pressure. Height and weight were measured to the nearest centimeter and half kilogram, respectively, with participants wearing light clothes without shoes. BMI was calculated as weight divided by the square of the height (kg/m^2). Participants were classified as normal weight (18.5-25.9 kg/m^2), overweight (25-29.9 kg/m^2) and obese ($\geq$30 kg/m^2) according to World Health Organization's standard classification. Blood pressure was measured three times using a Dinamap 845XT (Citikon, Tampa, USA), with the mean values of the second and third measurement used. Obese participants were classified as metabolically unhealthy if they had two or more of the following criteria: nonfasting triglycerides >1.7 mmol/l, nonfasting glucose $\geq$11.1 mmol/l, high-density lipoprotein <1.03 mmol/l for men and <1.29 mmol/l for women, blood pressure $\geq$130/85 mm Hg or use of hypertension medication, or self-reported diabetes diagnosis.

From a self-administered questionnaire, we obtained information on current smoking, alcohol use in the past two weeks, self-reported cardiovascular disease (CVD), diabetes, and occupational status according to international standard classification of occupations.

Follow up and ascertainment of AF

We followed the participants from the date of examination until first onset of validated AF or atrial flutter diagnosis or the end of follow-up in November 2015, whichever came first. To identify persons with AF, information on ICD-10 code I48 atrial fibrillation/atrial flutter was retrieved from diagnosis registers at the two hospitals in the county. All AF diagnoses were validated by medical doctors using recorded ECGs according to standard criteria.[15] In cases where the ECG was unavailable, medical records were reviewed and AF was verified when a physician had described the ECG as AF or atrial flutter according standard criteria. A study validating hospital-diagnoses of AF in this population has been published elsewhere.[16]

Statistical analysis

Descriptive data are presented as means ± standard deviations for continuous variables and percentages for categorical variables. We used Cox proportional hazard regression with 95% confidence intervals, using attained age as time scale, to assess the association between physical activity, BMI and AF. We tested the proportional hazard assumptions by using Schoenfeld residuals and found evidence of non-proportionally by sex. Therefore, we used a stratified Cox regression analysis conditioning on sex. We developed sex- and age-adjusted models and multivariable models adjusting for potential confounding factors, including current smoking, alcohol use, self-reported CVD and occupational status. In order to obtain a valid estimate of the causal effect of physical activity and BMI on incident AF, we did not adjust for potential mediators in the multivariable models, such as hypertension and diabetes, because conditioning on intermediate variables within the causal path are likely to give biased estimates.[17]

To study the interaction between physical activity and BMI on AF risk, we performed analysis on the combined association between physical activity and AF across 9 subgroups of BMI and PA with highest PA levels and normal BMI as reference. Further, we did stratified analysis of PA and AF risk by level of BMI. In addition, we stratified obese individuals into metabolically healthy and unhealthy individuals and examined whether the association between PA and AF were different between the groups. Finally, we used a method described by Andersson et al. to calculate relative excess risk due to interaction (also known as interaction contrast ratio)

between physical inactivity and obesity with 95% confidence intervals, with the following formula[18]:

$$\text{Relative excess risk due to interaction} = RR_{11} - RR_{10} - RR_{01} + 1$$

Where RR_{11} = the relative risk when physical inactivity and obesity is present; RR_{10} = the relative risk when physical inactivity is present but obesity is absent; RR_{01} = the relative risk when obesity is present but physical inactivity is absent.

Results

In total 20 016 (45.9%) men and 23 586 (54.1%) women with a mean age at baseline of 52.1±15.0 and 50.9±15.5 years, respectively, were included. Further baseline characteristics according to sex and physical activity levels are shown in Table 1. During a mean follow up of 8.1 years (352 770 total person-years), 1459 new cases of AF were documented, corresponding to an incidence rate of 4.1 events per 1000 person-years.

Higher levels of PA were associated with a gradually lower risk of AF (Table 2, *p*-trend 0.061). After multivariable adjustment, participants with the highest levels of PA had 14% lower risk of AF compared to inactive participants (HR 0.86, 95% CI 0.72-1.02). Additional adjustment for baseline BMI weakened the association.

Hazard ratios for incident AF associated with BMI is shown in Table 3. In the multivariable model, overweight and obesity were associated with an 18% and 59% higher risk of AF, respectively, compared to normal BMI (HR 1.18, 95% CI 1.03-1.35 and 1.59, 95% CI 1.37-1.84). Further adjustment for PA did not influence the estimates.

The combined analysis showed that obesity was associated with increased risk of AF, compared to the normal weight group across all PA categories (Figure 1 and Supplemental Table 1). However, higher levels of PA attenuated the AF risk in the obese group and inactive obese had HR of 1.96 (95% CI 1.44-2.67) compared to active normal weight participants, while the corresponding HR for active obese were 1.53 (95% CI 1.03-2.28). Stratified analyses showed similar results with a 22% lower risk of AF in active versus inactive obese participants (HR 0.78, 95% CI 0.55-1.09) and no apparent association between PA and AF in normal and overweight individuals (*p*-trend 0.76 and 0.96, respectively, Supplemental table 2). There were neither any differences in risk reduction in metabolically healthy versus unhealthy obese individuals.

Finally, the relative excess risk due to interaction between physical inactivity and obesity were calculated. Obesity and inactivity alone was associated with 32.2% and 6% higher risk of AF, respectively. When both risk factors were present, i.e., being obese and inactive, there was an additional 25.6% increased risk of AF beyond the effect of these factors alone (RERI 0.256, 95% CI -0.08-0.59).

Discussion

In this prospective cohort study of 43 602 men and women, overweight and obesity were both associated with increased risk of developing AF. Higher PA levels attenuated some of the AF risk in obese individuals, with a lower risk in highly active compared to inactive counterparts. Overall, higher levels of PA were associated with a moderate, gradually lower risk of AF, although not statistically significant.

Our results are in agreement with two previous studies suggesting that PA reduces the risk of AF in obesity. In a study of ~80 000 postmenopausal women,[6] the risk of AF was greater for sedentary obese women than for physical active obese women. Moreover, Huxley et al.[7] found a similar reduction in AF risk with increasing levels of PA in obese men, but not in obese women.

We found no association between PA and AF in the normal and overweight group. Although the normal BMI group showed a trend towards increased risk of AF with low to moderate PA, the low precision of the estimates precludes any firm conclusions. Our results suggest that obese individuals are likely to benefit the most from being physically active concerning AF risk.

The pathophysiology behind obesity and AF risk is likely to be multifactorial, including changes in hemodynamics, cardiac structural remodeling, autonomic dysfunction and inflammation, as well as an increased prevalence of AF risk factors such as hypertension, type 2 diabetes, dyslipidemia and cardiovascular disease.[19] PA may reduce AF occurrence in obesity directly by its ability to reduce these major AF risk factors[20]. Moreover, PA possesses anti-inflammatory properties[21] which may potentially influence AF risk conferred by obesity. Indeed, both systemic inflammation[22] and local inflammation in pericardial fat[23] has been shown to be associated with the development of AF. In a Korean cohort of ~ 390 000 adults, metabolically unhealthy obese individuals had greater risk for AF than their metabolically healthy counterparts. A greater risk reduction would be expected among metabolically unhealthy obese individuals if PA mediates some of its beneficial effects by reducing metabolic

risk factors. However, we found no particular difference in risk reduction associated with PA for metabolically healthy versus unhealthy obese individuals.

Further, PA may protect against AF development by improving cardiorespiratory fitness. Qureshi et al.[24] showed that each metabolic equivalent higher fitness was associated with a 7% reduced risk of AF, and this association was even stronger for obese than for non-obese individuals. In addition, Grundvold et al.[25] reported that unfit men had higher risk of AF with increasing BMI, compared to physically fit men where no such association were found.

The relation between PA and AF is complex and not fully understood. It has consistently been shown that long-term participation in endurance sports is associated with increased prevalence of AF.[26, 27] The pathophysiology behind arrhythmogenesis in healthy athletes with few CVD risk factors is, however, likely to be different from AF development in nonathletic individuals[10, 11] and most evidence points towards a protective effect of moderate to high levels of PA on AF incidence.[8, 28] Our results, although not compelling, indicate that the protective effect of PA on AF risk is more pronounced in obese individuals and that the combination of obesity and an inactive lifestyle confers a higher risk than either risk factor alone.

There are both strengths and limitations in this study that warrant mention. This study cohort consisted of a large population sample including both men and women, and complement the few other studies conducted on this topic.[6, 7] Further, we consider the use of validated diagnosis as a major advantage of this study that ensures high specificity[16]. Still, about one third of AF cases may be asymptomatic and undetected which cause lower sensitivity [16, 29]. However, imperfect specificity is generally a greater threat to validity than imperfect sensitivity in epidemiological studies[30]. The assessment of PA was based on a self-reported questionnaire, which is a limitation. However, the questionnaire used has previously been validated and shown to be reproducible.[14] Lastly, we cannot exclude the possibility of residual confounding in both measured and unmeasured covariates.

Conclusion

In a large cohort of men and women, overweight and obesity were strongly associated with increased risk of developing AF. PA attenuated some of the AF risk associated with obesity. Hence, increasing PA levels should be considered as a strategy for prevention of AF in this high-risk group.

Acknowledgement

We would like to thank all the participants and technicians of the HUNT study for their contributions.

Funding

This work was supported by grants from the K.G. Jebsen Foundation and the Liasion Committee between the Central Norway Regional Health Authority and the Norwegian University of Science and Technology.

Conflict of interest

None declared

Author contributions

LEG, BMN, JPL and VM contributed to conception or design of the work. LEG and BMN acquired data and did the analyses, and IJ and UW contributed to interpretation. LEG and BMN drafted the manuscript and all authors critically revised it and gave final approval.

References

1. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. *Circulation*. 2014; 129: 837-47.
2. Krijthe BP, Kunst A, Benjamin EJ, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J*. 2013; 34: 2746-51.
3. Aune D, Sen A, Schlesinger S, et al. Body mass index, abdominal fatness, fat mass and the risk of atrial fibrillation: a systematic review and dose–response meta-analysis of prospective studies. *Eur J Epidemiol*. 2017; 32: 181-92.
4. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*. 2014; 384: 766-81.
5. Gorenek B, Pellicia A, Benjamin E, et al. European Heart Rhythm Association (EHRA)/European Association of Cardiovascular Prevention and Rehabilitation (EACPR) position paper on how to prevent atrial fibrillation endorsed by the Heart Rhythm Society (HRS) and Asia Pacific Heart Rhythm Society (APHRS). *Europace*. 2017; 19: 190-225.
6. Azarbal F, Stefanick ML, Salmoirago-Blotcher E, et al. Obesity, physical activity, and their interaction in incident atrial fibrillation in postmenopausal women. *J Am Heart Assoc*. 2014; 3.
7. Huxley RR, Misialek JR, Agarwal SK, et al. Physical activity, obesity, weight change, and risk of atrial fibrillation: the Atherosclerosis Risk in Communities study. *Circ Arrhythm Electrophysiol*. 2014; 7: 620-5.
8. Drca N, Wolk A, Jensen-Urstad M and Larsson SC. Physical activity is associated with a reduced risk of atrial fibrillation in middle-aged and elderly women. *Heart*. 2015; 101: 1627-30.
9. Everett BM, Conen D, Buring JE, Moorthy MV, Lee I-M and Albert CM. Physical Activity and the Risk of Incident Atrial Fibrillation in Women. *Circ Cardiovasc Qual Outcomes*. 2011; 4: 321-7.
10. Thelle DS, Selmer R, Gjesdal K, et al. Resting heart rate and physical activity as risk factors for lone atrial fibrillation: a prospective study of 309,540 men and women. *Heart*. 2013; 99: 1755-60.
11. Aizer A, Gaziano JM, Cook NR, Manson JE, Buring JE and Albert CM. Relation of vigorous exercise to risk of atrial fibrillation. *Am J Cardiol*. 2009; 103: 1572-7.
12. Skielboe AK, Marott JL, Dixen U, Friberg JB and Jensen GB. Occupational physical activity, but not leisure-time physical activity increases the risk of atrial fibrillation: The Copenhagen City Heart Study. *Eur J Prev Cardiol*. 2016; 23: 1883-93.
13. Krokstad S, Langhammer A, Hveem K, et al. Cohort Profile: The HUNT Study, Norway. *Int J Epidemiol*. 2013; 42: 968-77.
14. Kurtze N, Rangul V, Hustvedt BE and Flanders WD. Reliability and validity of self-reported physical activity in the Nord-Trondelag Health Study: HUNT 1. *Scand J Public Health*. 2008; 36: 52-61.
15. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010; 31: 2369-429.
16. Malmo V, Langhammer A, Bønaa KH, Loennechen JP and Ellekjaer H. Validation of self-reported and hospital-diagnosed atrial fibrillation: the HUNT study. *Clinical Epidemiology*. 2016; 8: 185-93.
17. VanderWeele TJ. On the relative nature of overadjustment and unnecessary adjustment. *Epidemiology (Cambridge, Mass)*. 2009; 20: 496-9.
18. Andersson T, Alfredsson L, Källberg H, Zdravkovic S and Ahlbom A. Calculating measures of biological interaction. *Eur J Epidemiol*. 2005; 20: 575-9.
19. Lavie CJ, Pandey A, Lau DH, Alpert MA and Sanders P. Obesity and Atrial Fibrillation Prevalence, Pathogenesis, and Prognosis: Effects of Weight Loss and Exercise. *J Am Coll Cardiol*. 2017; 70: 2022-35.
20. Myers J, McAuley P, Lavie CJ, Despres J-P, Arena R and Kokkinos P. Physical Activity and Cardiorespiratory Fitness as Major Markers of Cardiovascular Risk: Their Independent and Interwoven Importance to Health Status. *Prog Cardiovasc Dis*. 2015; 57: 306-14.
21. Fleg JL. Physical activity as anti-inflammatory therapy for cardiovascular disease. *Preventive cardiology*. 2005; 8: 8-10.

22. Conen D, Ridker PM, Everett BM, et al. A multimarker approach to assess the influence of inflammation on the incidence of atrial fibrillation in women. *Eur Heart J*. 2010; 31: 1730-6.
23. Al Chekakie MO, Welles CC, Metoyer R, et al. Pericardial fat is independently associated with human atrial fibrillation. *J Am Coll Cardiol*. 2010; 56: 784-8.
24. Qureshi WT, Alirhayim Z, Blaha MJ, et al. Cardiorespiratory Fitness and Risk of Incident Atrial Fibrillation: Results From the Henry Ford Exercise Testing (FIT) Project. *Circulation*. 2015; 131: 1827-34.
25. Grundvold I, Skretteberg PT, Liestol K, et al. Importance of physical fitness on predictive effect of body mass index and weight gain on incident atrial fibrillation in healthy middle-age men. *Am J Cardiol*. 2012; 110: 425-32.
26. Karjalainen J, Kujala UM, Kaprio J, Sarna S and Viitasalo M. Lone atrial fibrillation in vigorously exercising middle aged men: case-control study. *Bmj*. 1998; 316: 1784-5.
27. Myrstad M, Nystad W, Graff-Iversen S, et al. Effect of years of endurance exercise on risk of atrial fibrillation and atrial flutter. *Am J Cardiol*. 2014; 114: 1229-33.
28. Morseth B, Graff-Iversen S, Jacobsen BK, et al. Physical activity, resting heart rate, and atrial fibrillation: the Tromso Study. *Eur Heart J*. 2016; 37: 2307-13.
29. Svennberg E, Engdahl J, Al-Khalili F, Friberg L, Frykman V and Rosenqvist M. Mass Screening for Untreated Atrial Fibrillation: The STROKESTOP Study. *Circulation*. 2015; 131: 2176-84.
30. Rothman K, Greenland S and Lash T. *Modern Epidemiology*. 3 ed. Philadelphia, USA: Lippincott Williams & Wilkins, 2008.

Tables

Table 1 Baseline characteristics according to sex and physical activity level

	Men (n=20 016)				Women (n=23 586)			
	Inactive (n=5415)	Low (n=5332)	Medium (n=5116)	High (n=4153)	Inactive (n=3937)	Low (n=7793)	Medium (n=7310)	High (n=4546)
Age, mean (SD), y	50.5 (14.6)	54.4 (14.6)	52.8 (14.5)	50.4 (16.2)	51.8 (16.6)	53.1 (15.3)	50.3 (14.9)	47.5 (14.4)
Height, mean (SD), cm	177.8 (6.6)	177.5 (6.7)	178.4 (6.6)	178.5 (6.6)	164.4 (6.3)	164.4 (6.4)	165.4 (6.1)	165.9 (5.9)
Weight, mean (SD), kg	88.8 (14.3)	87.1 (12.9)	86.8 (12.5)	85.3 (12.1)	75.6 (15.6)	74.0 (13.7)	72.6 (12.7)	70.9 (11.9)
BMI, mean (SD) ,kg/m^2	28.1 (4.1)	27.6 (3.7)	27.3 (3.5)	26.7 (3.4)	28.0 (5.5)	27.3 (4.8)	26.6 (4.5)	25.7 (4.1)
SBP, mean (SD), mmHg	133.0 (16.3)	134.3 (16.9)	133.5 (16.6)	132.6 (16.3)	128.4 (19.6)	128.6 (19.4)	126.4 (18.6)	124.2 (17.4)
DBP, mean (SD), mmHg	76.7 (10.9)	77.3 (10.9)	76.6 (10.7)	74.6 (11.2)	70.9 (11.0)	71.1 (10.7)	70.7 (10.5)	70.1 (10.4)
Antihypertensive medication, %	19.0	23.8	20.4	17.2	22.9	22.8	16.1	13.9
Hypertension[a], %	41.0	46.9	41.9	38.0	37.7	37.7	30.7	25.2
CVD[b], %	10.4	12.7	11.1	9.6	8.6	7.6	4.6	3.7
MI, %	4.0	5.4	4.2	3.8	2.0	1.7	0.7	0.5
HF, %	0.8	1.0	0.7	0.7	0.9	0.5	0.3	0.2
AP, %	4.1	5.0	4.1	3.5	3.1	2.7	1.4	0.9
Stroke, %	2.5	2.9	2.6	2.0	2.6	2.2	1.6	1.1
Diabetes, %	4.6	5.1	4.3	4.1	4.6	3.8	3.1	2.0
Current smoking, %	33.4	23.3	18.4	16.1	38.5	26.6	21.7	19.6
Alcohol use[c], %	83.8	85.4	87.0	86.3	64.0	70.8	77.5	79.2

Data are presented as means (SD) or percentages. BMI indicates body mass index; SBP, systolic blood pressure, DBP, diastolic blood pressure; mmHg, millimeter of mercury; CVD, cardiovascular disease, MI, myocardial infarction; HF, heart failure; AP, angina pectoris.

[a] Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or self-reported use of antihypertensive medication.

[b] Comprises self-reported MI, HF, stroke, AP and/or other CVD.

[c] Alcohol use 2 weeks before examination.

Table 2: Hazard ratios of incident atrial fibrillation according to physical activity level

PA-I	*N*	AF events	Person-Years	Model 1[a]	Model 2[b]	Model 3[c]
Inactive	9352	362	75 556	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
Low	13 125	506	106 111	0.90 (0.79-1.04)	0.92 (0.80-1.05)	0.94 (0.82-1.08)
Medium	12 426	371	100 662	0.87 (0.75-1.0)	0.89 (0.77-1.03)	0.93 (0.81-1.08)
High	8699	220	70 441	0.82 (0.69-0.97)	0.86 (0.72-1.02)	0.91 (0.77-1.09)
				P-trend 0.015	*P*-trend 0.061	*P*-trend 0.305

Data are presented as hazard ratios (95% confidence intervals). PA-I indicates physical activity index score; low equals an index score from 0.05 to 1.88, medium from 1.89 to 3.75 and high from 3.76 to 15.00. AF, atrial fibrillation.

[a] Adjusted for sex and age.

[b] Adjusted for sex, age, current smoking, alcohol use, self-reported CVD and occupational status.

[c] Adjusted for model 2 + BMI

Table 3: Hazard ratios of incident atrial fibrillation according to body mass index

BMI, kg/m^2	*N*	AF events	Person-Years	Model 1[a]	Model 2[b]	Model 3[c]
18.5-24.9	14 323	312	116 308	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
25-29.9	19 488	701	157 567	1.19 (1.04-1.36)	1.18 (1.03-1.35)	1.18 (1.03-1.35)
>30	9791	446	78 895	1.62 (1.40-1.88)	1.59 (1.37-1.84)	1.58 (1.36-1.83)
				P-trend <0.001	*P*-trend <0.001	*P*-trend <0.001

Data are presented as hazard ratios (95% confidence intervals). BMI indicates body mass index, AF, atrial fibrillation.

[a]Adjusted for sex and age.

[b]Adjusted for sex, age, current smoking, alcohol use, self-reported CVD and occupational status.

[c]Adjusted for model 2 + physical activity

Figure legend Figure 1

Hazard ratios of incident atrial fibrillation according to category of physical activity index score and BMI. High physical activity and normal BMI is used as reference group. Hazard ratios are adjusted for sex, age, current smoking, alcohol use, self-reported CVD and occupational status. P for trend <0.001.

Figure 1

Physical activity, body mass index and risk of atrial fibrillation