Physical Activity and the Risk of Incident Atrial Fibrillation in Women

Brendan M. Everett, MD, MPH[*,†], **David Conen, MD, MPH**[†,‡], **Julie E. Buring, ScD**[†,¶], **MV Moorthy, PhD**[†], **I-Min Lee, MBBS, ScD**[†,¶], and **Christine Albert, MD, MPH**[*,†]

[*] Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, Massachusetts 02115 [†] Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, 900 Commonwealth Avenue, Boston, Massachusetts 02215 [‡] Department of Medicine, University Hospital Basel, Basel, Switzerland [¶] The Department of Epidemiology, Harvard School of Public Health, 677 Huntington Avenue, Kresge Building, Boston, Massachusetts 02115

Abstract

Background—Physical activity (PA) is well known to reduce the risk of cardiovascular disease. We hypothesized that regular PA, possibly acting through reductions in blood pressure and body mass index (BMI), would reduce the risk of incident atrial fibrillation (AF) in women.

Methods and Results—We prospectively followed 34,759 women who reported their leisure-time PA levels for the occurrence of AF. We estimated energy expenditure in metabolic equivalent (MET)-hrs/wk, and validated self-reported AF with medical records. The mean (SD) age of the 34,759 participants was 54.6 (7.0) years, the mean BMI was 26.0 (5.0) kg/m^2, 26.5% had hypertension, and the median (IQR) PA was 8.4 (2.8, 20.4) MET-hrs/wk. After a median of 14.4 years of observation, 968 women developed AF. In age, cholesterol, smoking, alcohol, diabetes, and race adjusted models, increasing quintiles of PA were associated with reduced risks of AF (hazard ratio (HR) for extreme quintiles, 0.82, 0.66–1.01, P-trend = 0.007 over quintiles). While this association was not substantially different after adjusting for hypertension (0.87, 0.70–1.07, P-trend 0.02), it was attenuated after adjustment for BMI (0.99, 0.80–1.23, P-trend= 0.22). Women who achieved the federal government's recommendation of 7.5 MET-hrs/wk of PA were at reduced risk of AF compared to those who did not (0.86, 0.75–0.98, P=0.03). This association was also attenuated by BMI (0.96, 0.84–1.10, P=0.57).

Conclusions—In middle-aged women, physical activity was associated with a modestly reduced risk of AF. However, this relationship was no longer significant after controlling for body mass index.

Keywords

arrhythmia; exercise; obesity; hypertension; lifestyle

Corresponding author: Brendan M. Everett, MD, MPH, Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, 900 Commonwealth Avenue East, Boston, MA 02215, Ph: 617-732-4969, Fax: 617-232-3541, beverett@partners.org.

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, and is associated with large societal costs, including an increased risk of stroke, congestive heart failure, and death.[1–5] Established risk factors for atrial fibrillation include hypertension, coronary heart disease, heart failure, valvular heart disease, and obesity.[4, 6–10]

Regular physical activity is well known to have a beneficial impact on many of these cardiovascular risk factors. For example, physical activity is associated with a 3 to 5 mm Hg reduction in systolic blood pressure,[11] a reduction in both body weight and body mass index (BMI),[12] and a 30–50 percent reduction in the risk of coronary heart disease.[13–15] However, the impact of physical activity on the risk of AF seems to be more complex. A number of studies have reported that vigorous exercisers and elite athletes are at an elevated risk of lone AF.[16–23] By contrast, work-related physical activity had no impact on AF risk in a middle-aged population, and light to moderate physical activity was associated with a reduction in the risk of AF among participants in the Cardiovascular Health Study, who are all over age 65.[24, 25]

Whether physical activity might alter the risk of AF among otherwise healthy, middle aged women – among whom the prevalence of coronary heart disease is low – is less well known. We hypothesized that regular physical activity, possibly acting through reductions in blood pressure and BMI, would reduce the risk of incident AF in women.

Methods

Study Population

Study participants were enrolled in the Women's Health Study (WHS) a completed randomized, double-blind, placebo-controlled 2×2 factorial design trail of aspirin and vitamin E in the prevention of cardiovascular disease and cancer. Beginning in 1993, a total of 39876initially health women who were at least 45 years old enrolled in the WHS. The randomized treatment portion of the study was completed in March 2004, and participants were invited to participate in continued observational follow-up. Of the original cohort, 4324 women opted out and were excluded because their atrial fibrillation could not be reliably confirmed, such that 35,552 women were eligible for this study. Follow-up information from randomization through February 29, 2008 was used for this analysis.

At enrollment, women completed questionnaires on demographics, anthropometrics, medical history, medications, and lifestyle factors. Of the 35,552 women eligible for this study, we excluded women with atrial fibrillation (n=783) or cardiovascular disease (n=9) and those who did not report physical activity level (n=1) for a total sample size of 34,759. All participants provided written informed consent, and the study was approved by the institutional review board of the Brigham and Women's Hospital.

Assessment of Physical Activity

At baseline and again at months 36, 72, and 96 and at the end of the randomized portion of the study, and at 2 years of the observational follow up study, each participant was asked to report her approximate average time per week during the previous year spent on 8 or 9 groups of recreational activities on a questionnaire. Recreational activities included on the questionnaires were walking, jogging, running, bicycling, aerobic exercise or dance, racquet sports, lap swimming, weight lifting, and yoga or stretching. Each participant was also asked to report the average number of flights of stairs climbed daily and her usual walking pace at randomization, at 96 months, at the end of the randomized study, and during the observational follow-up portion of the study. After assigning a metabolic equivalent task

(MET) score to each activity based on its hourly energy cost,[26] we estimated the energy expended on each activity by multiplying the associated MET score by the hours spent on the activity, and summed the energy expended across all activities to estimate the total energy expenditure per week. Vigorous physical activity was defined as any activity requiring at least 6 METs. Jogging, running, aerobic exercise or dance, racquet sports, and lap swimming were all considered vigorous exercise. Finally, in a separate question on the baseline questionnaire, distinct from the leisure-time physical activities described above, women were also asked to report the number of times per week they engaged in strenuous (aerobic) physical activity such as swimming, aerobics, cycling, or running.

This assessment of physical activity has been previously found to be valid and reliable.[27] The test-retest correlation coefficient over 2 years in a random sample of nurses was 0.59 (95% CI, 0.48–0.69). Self-reported estimates of physical activity compared with 4 past-week recalls of physical activity collected during the year prior to questionnaire administration had a correlation coefficient of 0.79 (0.64–0.88). When compared to activity diaries kept for 4 separate weeks during the same year, the correlation was 0.62 (0.44–0.75).

Ascertainment of Incident Atrial Fibrillation

Women were asked to report the month and year of any diagnosis of AF at the time of enrollment and again at 48 months, and then annually thereafter. Women enrolled in the continued observational follow-up who reported an incident AF event on at least one yearly questionnaire were mailed supplementary questionnaires and requests for permission to review medical documentation. Those reporting events, including next-of-kin of decedents, were asked for permission to obtain medical records. An endpoint committee of physicians reviewed these records and confirmed an incident atrial fibrillation event if there was electrocardiographic evidence of atrial fibrillation or if the medical record clearly indicated a personal history of atrial fibrillation. The earliest date when AF was documented in the medical record was established as the date of onset of atrial fibrillation. Only confirmed events are included in the present analysis.

Data Analysis

Physical Activity Measures—In order to evaluate the long-term impact of leisure-time physical on AF risk and to reduce measurement error, for our primary analysis, we calculated the cumulative average of physical activity in MET-hrs/week from the baseline, months 36, 72, 96 and the end of the randomized study, and observational follow-up questionnaires and divided the population distribution at each time point into quintiles of cumulative average physical activity. In secondary analyses, we created a similar cumulative MET-hrs/wk variable limited to the time spent in vigorous physical activity (> 6 METs), and performed a separate analysis to explore the association between vigorous activities and AF. Since a minority of women in this cohort engaged in physical activity categorized as vigorous, we elected to use tertiles rather than quintiles for this analysis. We also tested a threshold category of 7.5 MET-hrs/week of physical activity, as recommended by the federal government.[28]

Additionally, because of prior data from the Physicians' Health Study, we specifically investigated whether the time spent jogging or running, or the frequency of aerobic exercise (in times per week) altered AF risk.[23] Finally, we tested whether categories of increasing frequency (in times/week) of baseline strenuous activity was associated with AF risk.

Statistical Analysis—Characteristics of the study population and unadjusted incidence rates were computed across baseline quintiles of physical activity. Time-varying Cox proportional hazards models were used to calculate hazard ratios (HR) and 95% confidence

intervals (CI) for relationships between the various measures of physical activity and incident AF. Multivariable proportional hazards models were adjusted for age, randomized treatment assignment, race, hypercholesterolemia, diabetes, current smoking, past smoking, and alcohol intake. Age and randomized treatment assignment were available for all participants, and participants with missing values for other covariates at the baseline were not included in the multivariable analysis. In addition to physical activity as described above, several of these covariates (hypercholesterolemia, diabetes, smoking status, and alcohol intake) were updated at various time points throughout the study. If data on physical activity or other covariates were missing at a given time point(2.9% of observations), the information from the last questionnaire was carried forward except for smoking. Participants with missing values for smoking during follow-up contributed observation time until the time period when the values were missing, at which point they were dropped from the analysis. In order to exclude the possibility that missing or imputed data might bias our results, we conducted sensitivity analyses that used only non-imputed data and incorporated missing covariate terms to include all participants. We observed no substantial change in our results. Participants who did not develop AF were censored at the time of death or at the last available contact.

We then considered the possibility that hypertension, body mass index (BMI), or cardiovascular disease (CVD), which are influenced by physical activity[13, 29, 30] and in turn influence AF risk [4, 10, 31], might mediate any observed relationship between physical activity and incident AF. In order to evaluate this possibility, time-varying covariates for hypertension and BMI were added individually and then in combination to the adjusted model. In order to determine their effect on the relationship between physical activity and AF we examined the change in the HRs for the highest category of physical activity as compared to the lowest category, and evidence of attenuation of these HRs was considered supportive of this hypothesis.[29, 32] Then, in order to evaluate the possibility that the development of cardiovascular disease (CVD) might mediate any observed associations between physical activity and AF, we performed secondary analyses in which women were censored when they developed CVD.

To test for trend, we used a single score variable equal to the median value of each tertile, quintile or category.[28] On an a priori basis, we tested for evidence of a non-linear relationship between physical activity level and incident AF with a 2 degree of freedom likelihood ratio test. We also tested for an interaction between age and physical activity level and incident AF using a cross-product interaction term.

Results

During a total of 480,509person-years of follow up (median 14.4 years, IQR 13.7, 14.8), we observed 968 incident cases of AF, for an overall incidence rate of 2.01 cases per 1,000 person-years. Of the 968 cases, 743 (76.8%) were confirmed by electrocardiogram and 225 (23.2%) were confirmed by a physician's report in the medical record. Forty three cases were characterized as lone AF.

Baseline characteristics stratified by baseline physical activity level are displayed in Table 1. As anticipated, women who reported higher levels of physical activity tended to have lower body weight and body mass index than those with lower levels of physical activity. The proportion of women with masters or doctorate degrees increased as physical activity level increased, while the proportion with some college education declined. Women with high levels of physical activity were more likely to drink at least one alcoholic drink per week. Many risk factors for coronary heart disease, including hypertension, diabetes, hypercholesterolemia, and current smoking, were concentrated in women with the lowest

levels of physical activity. Unadjusted AF incidence rates were highest amongst those with the lowest physical activity levels (2.43 cases per 1,000 person-years) and ranged from 1.81 to 1.87 cases per 1,000 person-years among women in the top three quintiles (≥5.9 MET-hrs/wk).

After adjustment for age, cholesterol, current and past smoking, alcohol use, diabetes, race, and randomized treatment, increasing levels of physical activity were associated with a statistically significant reduction in the rates of AF (P-trend = 0.007; Table 2). Specifically, relative to women in the lowest category of physical activity, the rates of AF were 18% lower among women in the highest category of physical activity (hazard ratio (HR) 0.82, 95% CI 0.66–1.01), a finding of borderline statistical significance (P = 0.06). After adjustment for hypertension, the effect of physical activity on the rates of AF was somewhat attenuated, but the trend remained statistically significant (P-trend = 0.03; HR for extreme quintiles 0.87, 95% CI 0.70–1.07, P = 0.18). By contrast, after adjustment for body mass index, no statistically significant relationship between physical activity levels and incident atrial fibrillation was observed (P-trend = 0.22; HR for extreme quintiles 0.99, 95% CI 0.80–1.23, P = 0.91). The addition of hypertension to a model including BMI did not substantially alter those point estimates (Table 2). Tests for deviation from linearity and an age-activity level interaction were not statistically significant. After adjusting for all covariates except hypertension and BMI and censoring follow-up at the time women developed CVD, estimates of the HR for each of the physical activity quintiles were similar to those calculated without censoring for incident CVD (Supplementary Table 1).

The risks of AF for women whose physical activity level met or exceeded the United States government's recently published guidelines for physical activity are displayed in Table 3. In updating models adjusting for all covariates except hypertension and BMI, the rate of AF was 14% lower in women with at least 7.5 MET-hrs/wk of physical activity (HR 0.86, 95% CI 0.75–0.98, P=0.03). While this risk estimate did not change substantially after adjusting for hypertension (HR 0.89, 95% CI 0.78–1.02, P=0.09), the relationship was no longer statistically significant. By contrast, adjusting for BMI markedly attenuated the reduction in AF risk observed with physical activity (HR 0.96, 95% CI 0.84–1.10, P=0.57). Results from analyses that censored women at the time they developed CVD were not substantially different (Supplementary Table 2).

Table 4 reports the adjusted risk of incident atrial fibrillation for women who reported engaging in vigorous activity. As shown, we did not observe an increased risk of atrial fibrillation for any of the levels of vigorous activity as compared with no vigorous activity. For example, when compared to women who did not engage in any vigorous physical activity, those reporting the highest levels of vigorous activity (tertile 3) were at modestly lower, statistically non-significant risk of AF (Model 1 HR 0.90, 95% CI 0.75–1.08, P=0.26). That relationship was attenuated somewhat by the addition of either hypertension (HR 0.93, 0.81–1.17, P=0.44) or BMI (HR 0.98, 95% CI 0.81–1.18, P=0.76) to the model. Time spent jogging or running was not associated with AF risk. We did not observe an association between lone atrial fibrillation and any threshold of vigorous activity, although the total number of lone AF cases was small (N=43), so our power to detect such an association is low.

Increasing frequency of strenuous activity at baseline was associated with a statistically significant reduction in the risk of AF in models adjusted for age, cholesterol, current and past smoking, alcohol use, diabetes, race, and randomized treatment(Table 5). Women who engaged in strenuous physical activity 1–3 times/week appeared to be at the lowest risk (HR 0.78, 95% CI 0.67–0.91, P=0.002). This relationship was largely unchanged after adjusting for hypertension (HR 0.80, 95% CI 0.69–0.94, P=0.006), and was attenuated but remained

statistically significant after adjustment for BMI (HR 0.85, 95% CI 0.73–1.00, P=0.04). In models adjusted for both hypertension and BMI, women engaging in strenuous activity 1–3 times/week remained at statistically lower risk of AF (HR 0.85, 95% CI 0.73–1.00, P=0.05). Tests for a U-shaped trend across all categories of aerobic exercise frequency in each model were not significant.

Discussion

In this prospective analysis of initially healthy women, we report that regular physical activity is associated with a modest reduction in the risk of AF. However, that relationship was no longer significant after controlling for body mass index, suggesting that reductions in body mass index associated with increasing physical activity may underlie the association. Similarly, the modest reduction in AF incidence observed among women who met the federal government's recommendation of 7.5 MET-hrs/wk of physical activity (equivalent to at least 150 minutes/wk of moderate-intensity activity) was also no longer significant after the addition of body mass index to adjusted models. Finally, women who reported vigorous physical activity or frequent aerobic exercise did not appear to be at increased risk of atrial fibrillation when compared to women who reported no such activity.

We believe these data are of interest because they expand our understanding of the complex role of physical activity in modifying the risk of AF to a population of middle-aged women. Physical activity has both acute and chronic effects on cardiovascular physiology. With respect to ventricular arrhythmias, vigorous exertion can transiently increase the risk of sudden cardiac death,[33, 34] but chronic exposure to moderate levels of exercise can lower this risk. [35, 36] Chronic physical activity also has beneficial effects on atherothrombotic risk factors such as obesity, blood pressure, tobacco use, lipids, and diabetes, each of which can also affect AF risk.[11–15, 33] Given these prior associations, in this study, we chose to focus on the association between chronic exposure to regular physical activity and AF risk, and observed a modest decrease in AF risk among those reporting regular physical activity that was no longer significant after controlling for body mass index..

While these data may appear to conflict with published results of the Cardiovascular Health Study (CHS) and Physicians Health Study (PHS), we believe the 3 studies provide complimentary information obtained in different patient populations.[23, 25] In the middle-aged men enrolled in PHS, vigorous exercise (and jogging in particular) was associated with a modest increased risk of AF, an observation similar to that reported in case-series and retrospective analyses of endurance athletes and military recruits. [16–22] Interestingly, in PHS, this elevation in risk was limited to men less than 50 years old (RR 1.74, 95% CI 1.23–2.47, P<0.01 for 5–7 days/week of vigorous activity vs. no exercise).[23] The authors of that study hypothesize that the exercise-induced modifications of parasympathetic tone dominate in younger men, but as the prevalence of other cardiovascular disorders linked with AF rise with increasing age, the deleterious effects of physical activity on AF risk are counterbalanced by more beneficial effects. Our data support this hypothesis, as do data from the Danish Diet, Cancer, and Health Study, in which no adverse relationship between work-related physical activity and AF risk was observed in a population similar in age to our own. Alternatively, physical activity reduced the risk of AF by approximately 36% (HR for extreme quintiles = 0.64, 95% CI 0.52–0.79, P-trend < 0.001) in an elderly population [mean (SD) age 72.8 (5.6) years] enrolled in the CHS.[24, 25] Taken together, these 4 large, prospective studies suggest that the factors underlying AF risk may differ in men and women, and may shift as patients age.

Unlike prior studies in men, [16, 18–21, 23] we did not observe an increased risk of AF among women who reported a broad spectrum of vigorous physical levels, or among women who

reported engaging in strenuous activity at least 4 times/week. In fact, we noted a statistically significant 16% reduction in the risk of AF amongst women who engaged in strenuous activity 1–3 times per week, but no statistically significant reduction in AF risk among those in other categories of strenuous activity. There are a number of plausible explanations for this discrepancy. First, the women enrolled in the WHS resemble women in the general population, and did not, in general, engage in high intensity physical activity. Participants in all but one of the previous studies reporting an increased risk of AF with vigorous activity were highly trained athletes who had engaged in high-intensity endurance training for a number of years. [16–21, 23] Therefore, we do not believe any firm conclusions about the relationship between vigorous physical activity and AF can be drawn from our study. Second, if WHS participants who engaged in intense physical activity developed AF before the start the WHS, they would have been excluded from this study of incident AF. Lastly, we have relatively few cases of lone AF, where intense physical activity may be more likely to play an important pathophysiologic role, but which represents only a minority of AF cases.

There are many mechanisms by which physical activity is thought to influence AF risk. Habitual vigorous exertion can result in increases in left atrial size, which may lead to atrial fibrosis and AF.[37] Regular physical activity alters the balance of sympathetic and parasympathetic stimulation to the heart,[38] and an increase in vagal tone can lead to a shorter atrial refractory period with greater dispersion and a higher risk of reentrant rhythms. [39] Elevated vagal tone has been associated with AF onset in patients with structurally normal hearts and in experimental studies.[40–42] On the other hand, even moderate levels of physical activity are associated with reductions in weight, blood pressure and inflammation, [29, 30] which counterbalance potentially adverse consequences of vigorous activity on atrial remodeling and electrophysiology.

Strengths and Limitations

The strengths of our study include its prospective design, its sample size, the long-term follow-up of an initially healthy population of women, and the large number of confirmed events. However, a number of important limitations should be considered. First, because the study is composed of initially healthy women, generalizing the study to other populations should be done with caution. Second, physical activity was collected by self-report, albeit with methods shown to be reproducible and reliable.[13, 27] Third, incident atrial fibrillation was collected by self-report and validated by medical record review. While it is possible that cases of AF were missed because no routine screening electrocardiograms were performed as part of this study, the rates of asymptomatic AF in our study are similar to those in other studies that did employ screening electrocardiograms.[7] Fourth, determining the precise time and date of when AF developed was often difficult. This imprecision may have introduced some bias towards the null in this time-to-event analysis, but we would anticipate that this effect would be small. Finally, while our results support the hypothesis that BMI mediates the effects of physical activity on AF, we cannot exclude correlation between those two exposures or an alternative causal model as possible explanations for our observations.

Conclusions

In summary, these prospective data suggest that modest amounts of regular physical activity is associated with a reduced risk of atrial fibrillation in a population of middle-aged, initially healthy women. In this population, the effects of physical activity on AF risk appear to be mediated by body mass index, but not by hypertension or cardiovascular disease. We did not observe an increased risk of AF among women reporting vigorous exercise, but few women engaged in high levels of vigorous exercise.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Baseline characteristics of the study population

	Quintile of Weekly Physical Activity Level at Baseline				
	1	**2**	**3**	**4**	**5**
Range (MET-hours/week)	<2.0	2.0 to < 5.9	5.9 to < 12.0	12.0 to < 23.0	≥ 23.0
N	6957	6956	6957	6947	6942
Age, median (IQR), y	53 (49, 59)	53 (49, 58)	53 (49, 58)	53 (49, 59)	53 (49, 59)
Weight, median (IQR), lb	159 (138, 185)	150 (135, 175)	150 (133, 170)	145 (130, 165)	140 (128, 160)
Body mass index, median (IQR), kg/m^2	26.6 (23.3, 31.0)	25.6 (22.9, 29.2)	24.9 (22.6, 28.3)	24.4 (22.3, 27.4)	23.6 (21.6, 26.5)
White race, N (%)	6485 (94.1)	6564 (95.3)	6583 (95.5)	6604 (95.9)	6543 (94.9)
Education, No. (%)					
Some college	2136 (31.3)	1650 (24.1)	1547 (22.6)	1430 (20.9)	1431 (21.0)
Bachelor's degree	3662 (53.7)	3875 (56.7)	3833 (56.0)	3883 (56.7)	3708 (54.4)
Master's or doctorate degree	1025 (15.0)	1315 (19.2)	1463 (21.4)	1531 (22.4)	1679 (24.6)
Alcohol use, >once/week, No. (%)	2342 (33.7)	2792 (40.1)	3022 (43.5)	3187(45.9)	3430 (49.4)
Coronary heart disease risk factors, No. (%)					
History of hypertension	2271 (32.6)	1886 (27.1)	1787 (25.7)	1734 (25.0)	1517 (21.8)
History of diabetes	277 (4.0)	189 (2.7)	181 (2.6)	181 (2.6)	120 (1.7)
Cholesterol > 240 mg/dL, No. (%)	2306 (33.2)	2076 (29.9)	2004 (28.8)	2004 (28.9)	1742 (25.1)
Current smoking	1356 (19.5)	981 (14.1)	746 (10.7)	666 (9.6)	567 (8.2)
Parental history of myocardial infarction at age < 60 years	869 (13.8)	800 (12.8)	738 (11.8)	771 (12.4)	806 (12.9)
Post-menopausal	3832 (55.2)	3725 (53.6)	3683 (53.0)	3807 (54.9)	3782 (54.6)
All AF events, N	231	201	181	175	180
Incidence rate *	2.43	2.09	1.87	1.81	1.87
CVD-censored AF events, N	215	185	169	164	172
Incidence rate *	2.32	1.96	1.77	1.73	1.82

Abbreviations: AF, atrial fibrillation; CVD, cardiovascular disease; MET, metabolic equivalent task.

*
Incidence rate is presented in events per 1,000 person-years of observation

Table 2

Risk of incident atrial fibrillation according to level of physical activity.

	Quintile of Cumulative Average Weekly Physical Activity Level					P-trend
	1	2	3	4	5	
Model 1 Hazard Ratio (95% CI)	1.0	1.04 (0.85–1.27)	0.89 (0.73–1.10)	0.86 (0.70–1.06)	0.82 (0.66–1.01)	0.007
P-value		0.69	0.28	0.16	0.06	
Model 2 Hazard Ratio (95% CI)	1.0	1.06 (0.87–1.29)	0.92 (0.75–1.13)	0.90 (0.73–1.10)	0.87 (0.70–1.07)	0.03
P-value		0.59	0.41	0.30	0.18	
Model 3 Hazard Ratio (95% CI)	1.0	1.12 (0.92–1.37)	1.00 (0.82–1.23)	1.00 (0.81–1.23)	0.99 (0.80–1.23)	0.22
P-value		0.26	0.98	0.98	0.91	
Model 4 Hazard Ratio (95% CI)	1.0	1.12 (0.92–1.37)	1.01 (0.82–1.24)	1.01 (0.82–1.24)	1.00 (0.81–1.25)	0.28
P-value		0.25	0.96	0.96	0.97	

Model 1: Age, randomized treatment, cholesterol, current smoking, past smoking, alcohol, diabetes, and race adjusted

Model 2: Model 1plus hypertension

Model 3: Model 1 plus body mass index (kg/m2)

Model 4: Model 1 plus hypertension and body mass index.

Abbreviations: AF, atrial fibrillation; CI, confidence interval; MET, metabolic equivalent task.

Table 3

Risk of incident atrial fibrillation according to the United States government's recommended level of weekly physical activity.

	Cumulative Average Physical Activity Level (MET-hours/week)		
	<7.5	7.5+	P
Model 1 Hazard Ratio (95% CI)	1.0	0.86(0.75–0.98)	0.03
Model 2 Hazard Ratio (95% CI)	1.0	0.89 (0.78–1.02)	0.09
Model 3 Hazard Ratio (95% CI)	1.0	0.96 (0.84–1.10)	0.57
Model 4 Hazard Ratio (95% CI)	1.0	0.97 (0.84–1.11)	0.65

Model 1: Age, randomized treatment, cholesterol, current smoking, past smoking, alcohol, diabetes, and race adjusted

Model 2: Model 1plus hypertension

Model 3: Model 1plus body mass index (kg/m2)

Model 4: Model 1plus hypertension and body mass index

Abbreviations: AF, atrial fibrillation; CI, confidence interval; CVD, cardiovascular disease; MET, metabolic equivalent task.

Table 4

Risk of atrial fibrillation according to three categories of weekly vigorous activity. Vigorous activity is defined as those activities that require at least 6 metabolic equivalent task units of energy expenditure per hour, such as running, jogging, swimming, aerobic dance, and racquet sports.

| | No vigorous activity (referent) | Tertile of Vigorous Physical Activity* | | | P-trend |
		1	2	3	
Model 1 Hazard Ratio (95% CI)	1.0	1.01 (0.85–1.20)	0.96 (0.80–1.14)	0.90 (0.75–1.08)	0.09
P-value		0.94	0.62	0.26	
Model 2 Hazard Ratio (95% CI)	1.0	1.02 (0.86–1.21)	0.97 (0.81–1.17)	0.93 (0.81–1.17)	0.17
P-value		0.84	0.78	0.44	
Model 3 Hazard Ratio (95% CI)	1.0	1.03 (0.86–1.22)	1.00 (0.83–1.19)	0.98 (0.81–1.18)	0.37
P-value		0.73	0.96	0.76	
Model 4 Hazard Ratio (95% CI)	1.0	1.03 (0.87–1.23)	1.01 (0.84–1.20)	0.99 (0.82–1.19)	0.44
P-value		0.73	0.95	0.93	

Model 1: Age, randomized treatment, cholesterol, current smoking, past smoking, alcohol, diabetes, and race adjusted

Model 2: Model 1plus hypertension

Model 3: Model 1plus body mass index (kg/m2)

Model 4: Model 1plus hypertension and body mass index

*
The tertile cutpoints for vigorous activity varied according to follow-up questionnaire. However, in order to provide the reader some context, the values on the baseline questionnaire were 3.95 and 15 MET-hrs/wk.

Table 5

Risk of incident atrial fibrillation according to baseline frequency of strenuous physical activity, such as swimming, aerobics, cycling, and running.

	Baseline Strenuous Physical Activity Frequency (times per week)				
	Rarely/Never	<1	1 to 3	4+	P-trend
AF events, N	427	172	263	105	
Incidence rate [*]	2.37	1.80	1.72	2.01	0.0001
Model 1 Hazard Ratio (95% CI)	1.0	0.86 (0.72–1.02)	0.78 (0.67–0.91)	0.85 (0.69–1.05)	0.006
P-value		0.09	0.002	0.14	
Model 2 Hazard Ratio (95% CI)	1.0	0.87 (0.73–1.04)	0.80 (0.69–0.94)	0.88 (0.71–1.09)	0.02
P-value		0.13	0.006	0.25	
Model 3 Hazard Ratio (95% CI)	1.0	0.88 (0.73–1.05)	0.85 (0.73–1.00)	0.98 (0.78–1.21)	0.19
P-value		0.15	0.04	0.82	
Model 4 Hazard Ratio (95% CI)	1.0	0.88 (0.74–1.06)	0.86 (0.73–1.01)	0.98 (0.79–1.22)	0.23
P-value		0.18	0.06	0.86	

[*] Incidence rate is presented in events per 1,000person-years of observation

Model 1: Age, randomized treatment, cholesterol, current smoking, past smoking, alcohol, diabetes, and race adjusted

Model 2: Model 1plus hypertension

Model 3: Model 1 plus body mass index (kg/m2)

Model 4: Model 1 plus hypertension and body mass index.