Relation of Vigorous Exercise to Risk of Atrial Fibrillation

Anthony Aizer, MD, MSc[a,b,h,*], J. Michael Gaziano, MD, MPH[b,c,d,e], Nancy R. Cook, ScD[b,g], Joann E. Manson, MD, DrPH[b,g], Julie E. Buring, ScD[b,d,f,g], and Christine M. Albert, MD, MPH[a,b,c,g]

Limited data suggest that athletes may have a higher risk of developing atrial fibrillation (AF); however, there has been no large prospective assessment of the relation between vigorous exercise and AF. Logistic regression analyses stratified by time were used to assess the association between frequency of vigorous exercise and risk of developing AF in 16,921 apparently healthy men in the Physicians' Health Study. During 12 years of follow-up, 1,661 men reported developing AF. With increasing frequency of vigorous exercise (0, 1, 1 to 2, 3 to 4, 5 to 7 days/week), multivariate relative risks for the full cohort were 1.0 (referent), 0.90, 1.09, 1.04, and 1.20 ($p = 0.04$). This risk was not significantly increased when exercise habits were updated or in models excluding variables that may be in the biological pathway through which exercise influences AF risk. In subgroup analyses, this increased risk was observed only in men <50 years of age (1.0, 0.94, 1.20, 1.05, 1.74, $p < 0.01$) and joggers (1.0, 0.91, 1.03, 1.30, 1.53, $p < 0.01$), where risks remained increased in all analyses. In conclusion, frequency of vigorous exercise was associated with an increased risk of developing AF in young men and joggers. This risk decreased as the population aged and was offset by known beneficial effects of vigorous exercise on other AF risk factors. © 2009 Elsevier Inc. (Am J Cardiol 2009;103:1572–1577)

Although vigorous exercise has numerous health benefits, case reports and limited data suggest that elite athletic men engaging in endurance exercise that increases parasympathetic tone, particularly jogging, may be at higher risk for the development of atrial fibrillation (AF).[1–3] There are limited data on the role of vigorous exercise in the development of AF in men participating in exercise at a less competitive level, where the known beneficial effects of exercise may counterbalance this potential risk. We hypothesized that young men in whom parasympathetic tone is most pronounced may be at highest risk of developing AF. To further define the risks and benefits of exercise on AF risk, we prospectively examined the relation between amount and type of vigorous exercise and subsequent development of AF in men in the Physicians' Health Study.

Methods

The methods of the Physicians' Health Study have been described in detail elsewhere.[4] The study complies with the Declaration of Helsinki, was approved by the institutional review board of Brigham and Women's Hospital (Boston, Massachusetts), and participants gave informed consent. Briefly, 22,071 men who were physicians, 40 to 84 years old in 1982, with no history of myocardial infarction, stroke, transient ischemic attacks, or cancer were randomized to aspirin and/or β-carotene using a double-blind, placebo-controlled, 2×2 factorial design. Information on health status, risk factors for cardiovascular disease and AF, and dietary and lifestyle factors was collected by questionnaires. Participants who did not complete the 3-year follow-up questionnaire regarding exercise habits (n = 678) and those who reported a diagnosis of myocardial infarction, angina, percutaneous coronary artery intervention, coronary artery bypass surgery, transient ischemic attack, cerebrovascular disease, claudication, peripheral vascular surgery, congestive heart failure, or cancer before the 3-year questionnaire (n = 1,572) were excluded from the analyses.

Physicians were asked at 15, 17, 18, and 19 years after enrollment if they had ever been diagnosed with AF and the date of diagnosis. In addition, participants were asked annually to report any new medical conditions. Participants were excluded from the analyses if they did not return ≥ 1 questionnaire regarding AF diagnosis (n = 2,352) and had not reported AF on 1 of the annual questionnaires. Because AF onset often precedes diagnosis by months and AF often leads to fatigue and exercise intolerance that might effect exercise habits, participants who reported developing AF before or within 3 years after the 3-year exercise questionnaire were excluded (n = 548).[5] After these exclusions, 16,921 participants were available for this study.

Three and 9 years after enrollment, information on exercise habits was collected. The questionnaires asked, "Do you engage in a regular program of exercise vigorous enough to work up a sweat?—Yes/No." Use of "exercise

[a]Center for Arrhythmia Prevention and Divisions of [b]Preventive Medicine, [c]Cardiovascular Medicine, and [d]Aging, Department of Medicine, Brigham and Women's Hospital, [e]Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), VA Boston Healthcare System, [f]Department of Ambulatory Care and Prevention, Harvard Medical School, and [g]Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts; and [h]Leon H. Charney Division of Cardiology, Department of Medicine, New York University Medical Center, New York, New York. Manuscript received November 24, 2008; revised manuscript received and accepted January 31, 2009.

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*Corresponding author: Tel: 212-263-5656; fax: 212-263-8534.
E-mail address: anthony.aizer@nyumc.org (A. Aizer).

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Table 1
Relation of frequency of vigorous exercise to baseline clinical characteristics and risk factors for atrial fibrillation

Characteristic	Nonexercisers	<1 day/wk	1–2 days/wk	3–4 days/wk	5–7 days/wk	p Value
Total cohort	6,321 (37.4%)	762 (4.5%)	3,215 (19.0%)	4,496 (26.6%)	2,127 (12.6%)	
Mean age (yrs)*	52.6	50.0	51.1	51.1	52.1	<0.01
Mean BMI (kg/m^2)*	25.1	24.8	24.7	24.4	24.0	<0.01
Parental myocardial infarction before age 60 yrs*	8.9%	10.4%	10.2%	9.6%	10.0%	0.10
Smoking status*						
Never	49.0%	55.7%	53.6%	54.8%	51.9%	<0.01
Previous smoker	37.4%	35.4%	37.0%	38.8%	43.1%	<0.01
Current smoker	13.8%	9.1%	9.4%	6.5%	5.0%	<0.01
Medical conditions						
Diabetes mellitus†	3.1%	2.2%	2.5%	1.6%	1.9%	<0.01
High cholesterol level†‡	14.0%	11.5%	14.1%	14.2%	13.3%	0.93
Hypertension†§	29.5%	23.5%	25.1%	23.4%	21.9%	<0.01
Left ventricular hypertrophy‖	0.28%	0.26%	0.16%	0.22%	0.28%	0.62
Episodes of alcohol intake*						
<1 time/wk	28.9%	24.2%	22.7%	23.6%	24.7%	<0.01
1–6 times/wk	46.9%	55.3%	54.1%	54.3%	50.9%	<0.01
≥1 time/day	24.2%	20.5%	23.2%	22.2%	24.4%	0.25
Fish consumption >1 meal/wk¶	89.5%	91.0	92.1%	92.2%	90.9%	<0.01
Multivitamin consumption*	32.1%	32.6%	34.4%	35.7%	39.2%	<0.01
Vitamin C consumption*	19.5%	23.2%	23.3%	24.7%	26.7%	<0.01
Vitamin E consumption*	8.3%	8.4%	9.2%	11.1%	12.6%	<0.01

* Information ascertained on baseline questionnaire.
† Information ascertained on baseline and 24-month questionnaires.
‡ Diagnosis of high cholesterol level was based on self-report, a total cholesterol level ≥260 mg/dl (6.7 mmol/L), or use of cholesterol-lowering medications.
§ Diagnosed based on a self-reported systolic blood pressure ≥160 mm Hg, a diastolic blood pressure ≥90 mm Hg, or use of antihypertensive medications.
‖ Information ascertained on 15-year questionnaire.
¶ Information ascertained on 12-month questionnaire.

vigorous enough to break a sweat" has been validated to correlate with maximal oxygen uptake capacity and maximum exercise capacity on treadmill testing.[6,7] Subjects who responded "yes" were asked questions characterizing their exercise pattern. Exercise frequency was reported with response options of "<1 day/week, 1 to 2 days, 3 to 4 days, 5 to 7 days." Duration of each exercise episode was asked with responses of "≤10 minutes, 11 to 24 minutes, 25 to 40 minutes, 41+ minutes." The 3-year questionnaire asked, "What types of vigorous exercise do you engage in? Racquet sports, swimming, jogging/running, cycling (including indoor), other." This was followed with, "If you jog/run, how long is your usual distance? One mile or less, 1.1 to 2 miles, 2.1 to 3 miles, 3.1 to 4 miles, >4 miles."

AF cases were assessed by self-report. Although physicians have been documented to reliably self-report other cardiovascular end points such as angina and coronary revascularization, we performed a validation study on 400 randomly selected participants who reported AF on the 15-year questionnaire to determine the reliability of a self-reported diagnosis.[8] These men were sent supplementary questionnaires with detailed questions regarding their diagnosis and treatment of AF and a request for permission to review AF documentation.

Of these men, 352 (88%) provided information regarding the previous self-report of AF. Nine of the 48 nonrespondents were deceased. Of these respondents, 39% had paroxysmal, 32% had persistent, and 29% had permanent AF. Medical records were available for 225 men, confirming the self-reported diagnosis of AF in 99% (n = 223). Another

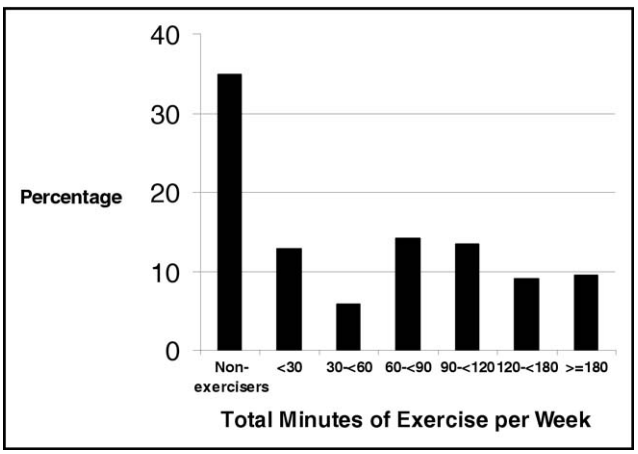

Figure 1. Distribution of total exercise time per week (minutes).

101 men reported that medical record documentation existed but was currently unavailable. In only 26 of respondents (7%) was the diagnosis of AF not further supported. In addition to the 2 cases disconfirmed by medical record review, 12 subjects reported that they had never had a history of AF (misclassification on 15-year survey) and 14 reported that no medical records or electrocardiographic data ever existed to corroborate the diagnosis of AF (self-diagnosis). Although a participant's report of AF was found to be reliable, date of AF diagnosis was not reliably reported. The mean difference between patient-reported diagnosis dates and medical record diagnosis dates was 4.5 ± 7.8 years.

Table 2
Relative risk of atrial fibrillation according to frequency of habitual vigorous exercise

Variable: Frequency of Habitual Vigorous Exercise	Nonexercisers	<1 day/wk	1–2 days/wk	3–4 days/wk	5–7 days/wk	p Value for Trend
Exercise at 3 yrs						
Age-adjusted (model 1)*						
RR (95% CI)	1.0	0.90 (0.69–1.18)	1.04 (0.91–1.20)	0.99 (0.87–1.12)	1.15 (0.98–1.33)	0.17
Multivariable model 2†						
RR (95% CI)	1.0	0.87 (0.66–1.15)	1.05 (0.91–1.22)	1.00 (0.87–1.14)	1.13 (0.97–1.33)	0.19
Multivariable model 3‡						
RR (95% CI)	1.0	0.90 (0.68–1.20)	1.09 (0.95–1.26)	1.04 (0.91–1.19)	1.20 (1.02–1.41)	0.040
Updated exercise						
Age-adjusted (model 1)*						
RR (95% CI)	1.0	1.09 (0.83–1.43)	1.02 (0.88–1.18)	0.96 (0.85–1.09)	1.08 (0.93–1.26)	0.69
Multivariable model 2†						
RR (95% CI)	1.0	1.09 (0.82–1.44)	1.02 (0.88–1.18)	0.96 (0.84–1.09)	1.07 (0.92–1.26)	0.76
Multivariable model 3‡						
RR (95% CI)	1.0	1.14 (0.86–1.51)	1.06 (0.91–1.23)	1.01 (0.89–1.16)	1.16 (0.99–1.36)	0.21

* Model 1 controlled for age and treatment assignment (aspirin or placebo, β-carotene or placebo).

† Model 2 excluded possible physiologic intermediaries between exercise and AF. Model 2 controlled for age, treatment assignment (aspirin or placebo, β-carotene or placebo), parental history of premature myocardial infarction, alcohol intake, smoking habits, fish consumption, multivitamin intake, and vitamin C and E intakes.

‡ Model 3 controlled for age, treatment assignment (aspirin or placebo, β-carotene or placebo), BMI, history of diabetes, history of hypertension, history of hyperlipidemia, parental history of premature myocardial infarction, alcohol intake, smoking habits, fish consumption, multivitamin intake, vitamin C intake, vitamin E intake, left ventricular hypertrophy, congestive heart failure, and evidence of cardiovascular disease.

Means or proportions of baseline risk factors and treatment group assignment were computed for the 5 categories of vigorous exercise reported on the 3-year questionnaire. Significance of associations was tested using Mantel-Haenszel chi-square test for trend for categorical and linear regression for continuous variables. In primary analyses, we examined whether frequency of participation in a regular program of vigorous exercise, as reported on the 3-year questionnaire, was associated with development of AF. Secondary analyses examined the relation between duration and type of vigorous exercise and AF development. To examine associations specific to each type of vigorous exercise, participants who reported engaging in >1 exercise type were excluded from the analyses, and participants who did not exercise regularly and did not engage in any exercise types served as the reference group.

Because exercise habits change over time and because the effects of exercise on development of AF may change as the population ages, our prespecified analysis plan included a secondary analysis using updated exercise data from 9 years for cases of AF that developed 3 years after the 9-year exercise questionnaire (1,059 of 1,661 AF cases). Because date of AF onset was often assessed retrospectively and our validation study suggested that a participant's reported date of diagnosis might be unreliable, it was prespecified to use logistic regression stratified by time based on dates of AF questionnaires, rather than Cox regression, to obtain adjusted estimates of AF risk.

Three separate models were developed. Model 1 controlled for age and treatment assignment (aspirin or placebo, β-carotene or placebo), and models 2 and 3 simultaneously controlled for additional AF risk factors. These 2 multivariable models were constructed to control for confounding while considering the effects of exercise on biological processes within the potential causal pathway for AF development. For example, participants with higher body mass index (BMI) may be less likely to exercise, and because BMI has been previously shown to independently predict the development of AF, it is a possible confounder. However, exercise decreases BMI; thus BMI is possibly part of the means through which exercise may affect AF development. The first multivariable model (model 2) considers all AF risk factors influenced by exercise, such as BMI, as lying completely within the causal pathway. Model 2 therefore excludes these variables. In contrast, to adjust for possible confounding by a variable such as BMI, the variable must be included in the model. Model 3 treats risk factors as being solely confounders.

Because of the long follow-up, these variables were updated at various time points. To test for a trend between exercise frequency or duration and development of AF, frequency and duration were redefined continuously by assigning each participant the midpoint value of the appropriate response category. To test for plausible effect modification by age, cross-product terms between age and exercise frequency at 3 years were added to all 3 models. Analyses were also repeated after stratification by age at the time when exercise habits were reported.

Results

At 3 years, 63% of participants reported engaging in a regular program of vigorous exercise and 13% reported exercising 5 to 7 times/week (Table 1). In regular exercisers, mean total amount of time spent exercising per week was 108 ± 78 minutes (Figure 1). Frequency of vigorous exercise was inversely associated with age, BMI, smoking, diabetes, and hypertension and directly associated with alcohol, fish, multivitamin, and vitamin C and E intakes.

Table 3
Relative risk of atrial fibrillation according to frequency of habitual vigorous exercise at three years, stratified by age group

Variable: Frequency of Habitual Vigorous Exercise	Nonexercisers	<1 day/wk	1–2 days/wk	3–4 days/wk	5–7 days/wk	p Value for Trend
Age <50 yrs						
Age-adjusted (model 1)*						
RR (95% CI)	1.0	0.96 (0.56–1.63)	1.15 (0.84–1.57)	0.95 (0.71–1.28)	1.69 (1.22–2.33)	0.014
Multivariable model 2†						
RR (95% CI)	1.0	0.95 (0.55–1.66)	1.22 (0.88–1.68)	1.00 (0.73–1.36)	1.69 (1.21–2.37)	0.015
Multivariable model 3‡						
RR (95% CI)	1.0	0.94 (0.53–1.67)	1.20 (0.87–1.66)	1.05 (0.76–1.43)	1.74 (1.23–2.47)	<0.01
Age ≥50 yrs but <65 yrs						
Age-adjusted (model 1)*						
RR (95% CI)	1.0	0.87 (0.61–1.24)	1.01 (0.85–1.21)	0.97 (0.82–1.14)	1.09 (0.88–1.34)	0.57
Multivariable model 2†						
RR (95% CI)	1.0	0.88 (0.61–1.27)	1.02 (0.85–1.22)	0.97 (0.82–1.15)	1.07 (0.87–1.33)	0.65
Multivariable model 3‡						
RR (95% CI)	1.0	0.93 (0.65–1.35)	1.07 (0.89–1.29)	1.03 (0.86–1.22)	1.16 (0.93–1.44)	0.25
Age ≥65 yrs						
Age-adjusted (model 1)*						
RR (95% CI)	1.0	1.00 (0.51–1.95)	1.06 (0.77–1.46)	1.15 (0.88–1.49)	0.94 (0.67–1.31)	0.97
Multivariable model 2†						
RR (95% CI)	1.0	0.78 (0.37–1.64)	1.03 (0.75–1.43)	1.12 (0.86–1.47)	0.92 (0.66–1.29)	0.99
Multivariable model 3‡						
RR (95% CI)	1.0	0.81 (0.39–1.71)	1.10 (0.79–1.53)	1.12 (0.85–1.48)	0.97 (0.69–1.37)	0.86

* Model 1 controlled for age and treatment assignment (aspirin or placebo, β-carotene or placebo).
† Model 2 excluded possible physiologic intermediaries between exercise and AF. Model 2 controlled for age, treatment assignment (aspirin or placebo, β-carotene or placebo), parental history of premature myocardial infarction, alcohol intake, smoking habits, fish consumption, multivitamin intake, and vitamin C and E intakes.
‡ Model 3 controlled for age, treatment assignment (aspirin or placebo, β-carotene or placebo), BMI, history of diabetes, history of hypertension, history of hyperlipidemia, parental history of premature myocardial infarction, alcohol intake, smoking habits, fish consumption, multivitamin intake, vitamin C intake, vitamin E intake, left ventricular hypertrophy, congestive heart failure, and evidence of cardiovascular disease.

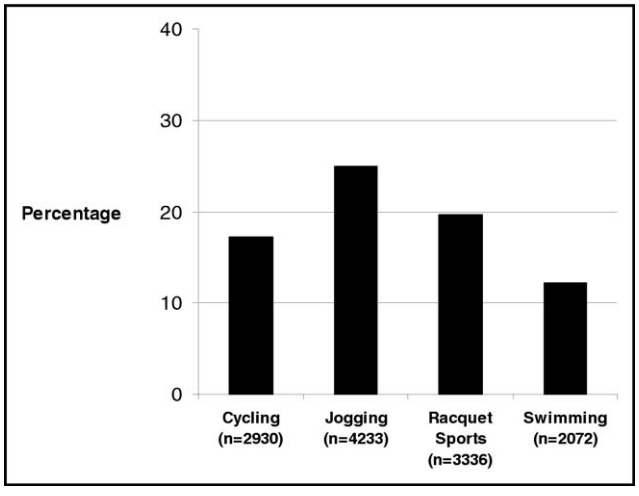

Figure 2. Frequency of participation in different sports activities.

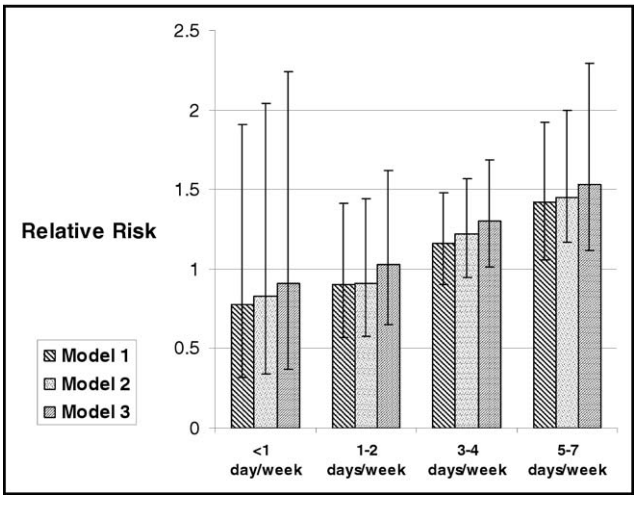

Figure 3. RR of AF according to jogging frequency at 3 years.

Frequency of vigorous exercise at 3 years was not associated with subsequent development of AF in age-adjusted models or in model 2, which excluded covariates that were medical conditions and/or risk factors that could be influenced by exercise. After controlling for all potential confounding variables and medical conditions associated with AF (model 3), increasing frequency of vigorous exercise at 3 years was associated with a small increased risk of developing AF (for variables in each model, see Table 2). Men who exercised 5 to 7 times/week had the greatest risk of developing AF compared with those who did not exercise ($p = 0.025$). These analyses were repeated using exercise habits updated at 9 years. In the maximally adjusted model, the most frequent exercisers still had a marginal, but not significantly increased, risk of developing AF (relative risk [RR] 1.16, 95% confidence interval [CI] 0.99 to 1.36, $p = 0.076$); however, the trend over categories was no longer statistically significant. Duration of exercise was not related to development of AF in any of the 3- or 9-year updated models (data not shown).

Because previous associations between exercise and AF had been reported primarily in young men and the relation observed in the present study decreased over the course of the study, we hypothesized that the effects of vigorous exercise on the incidence of AF may decrease as the population ages. To test this hypothesis, it was prespecified to stratify men by their age (<50, 50 to 65, >65 years) at the time of the 3-year exercise questionnaire. In men <50 years old, increasing frequency of exercise was associated with an increased risk of developing AF across all 3 models (Table 3). The increase in risk appeared limited to those who exercised 5 to 7 times/week. In contrast, there was no association in men >50 years of age, and the test for an interaction between exercising 5 to 7 times/week and age >50 or <50 years was significant in the full multivariate model ($p = 0.02$). When age-stratified analyses were repeated using updated exercise habits at 9 years, exercise frequency across the 5 categories was not significantly associated with AF in any age group; however, risk of AF remained significantly increased in men <50 years old at the time of the 9-year questionnaire who exercised ≥5 times/week (RR 2.08, 95% CI 1.16 to 3.71, $p = 0.014$). The test for interaction between age >50 and <50 years and this category of exercise was not statistically significant in the updated model ($p = 0.12$).

Participants who exercised regularly were then subdivided based on type of vigorous exercise reported at 3 years (Figure 2). In the maximally adjusted model, men who regularly and exclusively jogged (9.6% of cohort) were at increased risk of developing AF ($p < 0.01$), whereas no significant increase in risk was found with regular cycling, swimming, or racquet sports. Increased frequency of jogging was associated with an increased risk of developing AF in all 3 previously defined models (Figure 3). Men who jogged exclusively 5 to 7 times/week had a significantly increased risk of developing AF (RR 1.53, 95% CI 1.12 to 2.09, $p < 0.01$) compared with men who did not exercise vigorously after controlling for multiple cardiovascular risk factors. There was also a direct, statistically significant relation between miles jogged per episode and development of AF across all 3 models. In the maximally adjusted model, men who jogged >4 miles were at the highest risk (RR 1.38, 95% CI 1.06 to 1.79, $p = 0.016$). When primary analyses were repeated in the subgroup of participants who did not jog regularly ($n = 12{,}721$), no association between frequency of vigorous exercise and development of AF was found in the age-adjusted or multivariate models (data not shown).

Discussion

In this large prospective cohort study of apparently healthy men, a complex association between exercise and development of AF was observed. After adjustment for multiple potentially confounding lifestyle factors and health conditions, higher frequency of participation in a regular program of vigorous exercise at 3 years was associated with a modestly increased risk of developing AF. This increased risk was primarily in those who exercised 5 to 7 times/week. These men had a 20% increased risk of developing AF compared with those who did not exercise. The relation between vigorous exercise and AF was no longer significant when exercise habits were updated at 9 years or in models excluding possible biological intermediaries. The increase in risk decreased with increasing age. In men ≥50 years of age, no significant association was found; in men <50 years of age who exercised 5 to 7 times/week, the association was statistically significant in all analyses.

Secondary analyses found that frequency of jogging was most strongly associated with development of AF. Men who jogged ≥5 days/week had a 53% increased risk of developing AF compared with men who did not exercise, after controlling for multiple risk factors. When joggers were excluded, the relation between frequency of vigorous exercise and AF was no longer present, suggesting that jogging may account for much of the association.

These results expand on previous epidemiologic data regarding the relation between exercise and AF, which is limited to case series and small case–control studies. Case series have suggested that the incidence of AF may be higher in athletes.[1,2,9] A retrospective case–control study found a higher incidence of long-term sport activity in men with lone AF compared with controls.[10–13] In a small prospective study, the 10-year cumulative incidence of lone AF in 300 top-ranked runners was 5.3% compared with 0.9% in 495 healthy controls.[3] Although limited, these data are consistent with our findings that frequent endurance exercise, particularly jogging, may increase the risk of developing AF. In addition, the mean age of exercisers in all studies was <60 years, consistent with our finding that the association is strongest in younger populations.[13]

There are several mechanisms through which frequent exercise might influence risk of AF, including left atrial enlargement, left ventricular hypertrophy, left ventricular dilation, and the most commonly cited mechanism, an increase in parasympathetic tone.[2,14,15] Left atrial size is significantly increased in competitive athletes, and left atrial size is a strong and independent risk factor for AF.[16,17] However, left atrial size does not appear to explain the entire association between exercise and AF. In a case–control study including 107 patients with lone AF, greater participation in cumulative moderate and heavy physical activity was significantly associated with development of AF even after controlling for left atrial size.[11] Part of this unexplained risk may be due to an increase in parasympathetic activity in habitual exercisers. Jogging in particular results in greater enhancement of the parasympathetic nervous system compared with other exercise types.[18,19] Heightened parasympathetic tone has been associated with AF onset in patients with structurally normal hearts; and in animal and human studies, parasympathetic stimulation frequently induces and maintains AF, whereas vagal denervation prevents AF.[20–22]

Aging results in decreased parasympathetic activity.[23] Therefore, habitual exercise in older subjects may lead to a less significant increase of parasympathetic activity. Also, lone AF comprises a smaller proportion of AF cases in older patients in whom underlying structural heart disease is more common. This may explain why no association between exercise and AF in older men was found. Alternatively, men susceptible to AF because of exercise may have developed AF at a younger age and therefore would be excluded from

analyses of older populations. It is also possible that participants exercised less vigorously as they aged, decreasing the power to detect an association between exercise and AF.

In addition to the profibrillatory effects, exercise has multiple beneficial effects on cardiovascular health that may lower AF risk. Exercise lowers blood pressure, improves lipid profile and glucose control, and decreases risk of cardiovascular disease. Removal of the potentially inappropriate control of these intermediaries (model 2) eliminated or significantly attenuated the association between exercise and AF compared with maximally adjusted analyses (model 3). This suggests that any profibrillatory effect of exercise is counterbalanced by additional antifibrillatory effects in most of but not the entire population.

Some limitations warrant discussion. First, our measurement of physical activity, although correlated with maximal oxygen uptake capacity, is limited compared with more objective measurements of physical fitness. Although we assessed exercise habits at 2 time points, physicians' habits may have further changed over time. If such misclassification of exercise habits were random, this may have decreased our ability to detect associations between exercise habits and AF. AF can be occult and serial electrocardiograms were not available for the entire cohort; thus underdetection may exist in these analyses, although it is less likely in a cohort of physicians. Because AF was self-reported, men who exercise may be more likely to notice they are in AF and seek medical attention. Perhaps participants who exercised frequently developed undiagnosed AF resulting in decreased exercise tolerance that could have influenced exercise habits leading to an underestimation of the association between exercise and AF. The limited number of men <50 years of age at the time of the 9-year exercise questionnaire (n = 949, 6.3%) may have limited our power to detect an association in the updated analysis.

With respect to generalizability, our findings are limited by the selective nature of the cohort, namely healthy men physicians free of known cardiovascular disease at baseline. It is unclear if this same relation between exercise and AF extends to women or less healthy populations. Any participant who died before 1997 (n = 1,713) did not complete 1 of the AF questionnaires. As a result, participants with healthy lifestyle habits, such as exercise, may have been over-represented.

Although the primary, secondary, and subgroup analyses were prespecified, concern for multiple comparisons is warranted. However, the consistency and strength of the association of exercise with development of AF in men <50 of age and joggers and previous epidemiologic and physiologic studies supporting these findings support the validity of these results. As with any observational study, our study cannot prove causality and the present observed associations could be due, at least in part, to residual confounding. However, vigorous exercise was directly associated with several AF risk factors, and, therefore, it is also possible that more complete control for risk factors would have strengthened the inverse associations observed.

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