Regular Physical Activity and Risk of Atrial Fibrillation
A Systematic Review and Meta-analysis

Peter Ofman, MD, MSc; Owais Khawaja, MD; Catherine R. Rahilly-Tierney, MD, MPH; Adelqui Peralta, MD; Peter Hoffmeister, MD; Mathew R. Reynolds, MD, MSc; J. Michael Gaziano, MD, MPH; Luc Djousse, MD, MPH, ScD

Background—Although previous studies have suggested that competitive athletes have a higher risk of atrial fibrillation than the general population, limited and inconsistent data are available on the association between regular physical activity and the risk of atrial fibrillation.

Methods and Results—A systematic, comprehensive literature search was performed using MEDLINE, EMBASE, and COCHRANE until 2011. Extracted data from the eligible studies were meta-analyzed using fixed effects model. Four studies, which included 95,526 subjects, were eligible for meta-analysis. For all of the studies included, the extreme groups (ie, maximum versus minimal amount of physical activity) were used for the current analyses. The total number of participants belonging to the extreme groups was 43,672. The pooled odds ratio (95% confidence interval) for atrial fibrillation among regular exercisers was 1.08 (0.97–1.21).

Conclusions—Our data do not support a statistically significant association between regular physical activity and increased incidence of atrial fibrillation. (Circ Arrhythm Electrophysiol. 2013;6:252-256.)

Key Words: atrial fibrillation ■ epidemiology ■ physical exercise ■ risk factors
Table. Characteristics of the Included Studies

<table>
<thead>
<tr>
<th>Study first author, year</th>
<th>Total No. of Study Participants (% of Men)</th>
<th>No. of Study Participants Used in the Current Meta-analysis</th>
<th>Mean Age, y (SD)</th>
<th>Study Type</th>
<th>Exercise Ascertainment</th>
<th>Follow-up Duration, y</th>
<th>Atrial Fibrillation Ascertainment</th>
<th>Incident Atrial Fibrillation vs None</th>
<th>Variables Adjusted for</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frost et al (2004)</td>
<td>38400 (55%)</td>
<td>20343</td>
<td>56 (4)</td>
<td>Prospective cohort</td>
<td>Work-related physical activity; (1) sedentary (predominantly sitting position)*; (2) sedentary (predominantly standing position); (3) light workload; and (4) heavy workload</td>
<td>Questionnaire</td>
<td>5.7 (mean)</td>
<td>Danish National Registry of Patients validated by manual reviews of the charts and ECGs</td>
<td>240/20343</td>
<td>Age, body height, BMI, smoking, consumption of alcohol, SBP, treatment for HTN, total serum cholesterol, duration of sporting activities, and level of education</td>
</tr>
<tr>
<td>Mozaffarian et al (2008)</td>
<td>5446 (42%)</td>
<td>982</td>
<td>73 (6)</td>
<td>Prospective cohort</td>
<td>(1) no leisure-type physical activity*; (2) leisure-time activity (low intensity); (3) leisure-time activity (medium intensity); and (4) leisure-time activity (high intensity)</td>
<td>Leisure-time activity and exercise at baseline, and at the end of third and seventh annual visits using questionnaire. Walking habits: by self-report at baseline and annually</td>
<td>12 (mean)</td>
<td>Annual resting 12-lead ECG Hospital records discharge diagnosis for all hospitalizations</td>
<td>192/982</td>
<td>Age, sex, race, enrollment site, education, smoking status, pack-year of smoking, coronary heart disease, chronic pulmonary disease, DM, alcohol use, and β-blocker use</td>
</tr>
<tr>
<td>Aizer et al (2010)</td>
<td>16921 (100%)</td>
<td>8448</td>
<td>51 (n/a)</td>
<td>Prospective cohort</td>
<td>(1) no exercise*; (2) exercise to break sweat &lt;1 d/wk; (3) exercise to break sweat 1–2 d/wk; (4) exercise to break sweat 3–4 d/wk; and (5) exercise to break sweat 5–7 d/wk</td>
<td>Questionnaires 3 and 9 y after enrollment</td>
<td>12 (mean)</td>
<td>Data not provided</td>
<td>Age, treatment assignment (aspirin or placebo, beta carotene or placebo), BMI, h/o: DM, HTN, hyperlipidemia; parental h/o premature MI, alcohol intake, smoking habits, fish consumption, multivitamin intake, vitamin C intake, vitamin E intake, LVH, CHF, and evidence of OVD</td>
<td>US</td>
</tr>
<tr>
<td>Everett et al (2011)</td>
<td>34759 (0%)</td>
<td>13899</td>
<td>54.6 (7)</td>
<td>Prospective cohort</td>
<td>Cumulative average physical activity: (1) &lt;2 METS-h/wk*; (2) 2 to &lt;5.9 METS-h/wk; (3) 5.9 to &lt;12 METS-h/wk; (4) 12 to &lt;23 METS-h/wk; and (5) ≥23 METS-h/wk</td>
<td>Questionnaires at baseline, at 36, 72, and 96 mo, at the end of randomized portion of the study and at the end of the 2 y of the observational study</td>
<td>14.4 (median)</td>
<td>Questionnaire at the time of enrollment, at 48 mo and then annually thereafter Medical charts and ECG reviews of those who self-reported AF to confirm the diagnosis</td>
<td>411/13899</td>
<td>Age, randomized treatment, cholesterol, current smoking, past smoking, alcohol, diabetes, race, HTN, and BMI</td>
</tr>
</tbody>
</table>

*BMI indicates body mass index; CVD, cardiovascular disease; CHF, congestive heart failure; DM, diabetes mellitus; ECG, electrocardiogram; h/o, history of; HTN, hypertension; LVH, left ventricular hypertrophy; MET, metabolic equivalent task; MI, myocardial infarction; No, number; SBP, systolic blood pressure; and y, years.

*Reference group.
Data Extraction
Demographic data and the number of patients with AF in regular exercisers and controls were extracted from each study. Two authors (P.O. and O.K.) performed the searching, study evaluation, and data extraction independently, and any disagreement was resolved by a senior author (L.D.)

Exposure Assessment
All of the studies used for the meta-analysis,12-13 divided subjects into 4 or 5 groups on the basis of cumulative PA per week,13 amount and intensity of work-related PA,14 leisure-type PA,15 or amount of exercise per week.12 For all of the studies included, the extreme groups (ie, maximum versus minimal amount of PA) were used for the current analyses. The total number of participants belonging to the extreme groups was 43,672.

Exclusion criteria for each individual study used in the meta-analysis were not uniform. Some studies, such as the study of Frost at al,14 excluded subjects with ischemic heart disease, stroke, and diabetes at baseline, whereas others13 did not. Each study, however, excluded subjects with AF at baseline and incomplete information about PA or AF. All the studies adjusted for incident comorbidities during follow-up (Table).

Regular PA was defined differently at each study (Table). Aizer et al12 divided the patients into several groups on the basis of frequency of sweat-breaking exercise per week. The study of Everett et al13 used metabolic equivalent task for each PA performed and divided the patient into several groups on the basis of metabolic equivalent task range. The study of Frost et al14 evaluated the amount of PA performed at work and divided the patients into several groups. The study of Mozaffarian et al15 categorized patients into several groups on the basis of amount and intensity of leisure-time activity (walking).

Data Synthesis
The meta-analysis was performed by computing unadjusted OR using fixed effects model. OR for new onset incident AF was calculated by comparing the most physically active groups to those in the least active groups along with the 95% confidence intervals. For studies that included men and women and provided sex-specific relative risks, we treated relative risk for each sex as an independent study. Heterogeneity was tested using $I^2$ statistics. The $I^2$ (measured as 0%–100%) indicates the percentage of variation in the study results attributed to between-study heterogeneity rather than sampling error. All analyses were performed with RevMan Analyses Version 5.0.20 (Nordic Cochrane Center, Ringshojaptalet 2008).

Results
Figure 1 illustrates our review and exclusion/inclusion process. Ultimately, 4 longitudinal prospective cohort studies12-15 with follow-up periods of 5.7, 14.4, 12, and 12 years, respectively, published in peer-review journals were eligible for meta-analysis (N=95,526). Of these, we used 43,672 subjects belonging to extreme exercise categories for current analysis. All of the selected studies were graded as good by the criteria developed by the United States Preventive Services Task Force.16 Studies and subject’s characteristics are reported in Table. Three of the studies12,13,15 were conducted in the United States and 1 in Europe.14

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[OR]</th>
<th>SE</th>
<th>Weight</th>
<th>IV, Fixed, 95% CI</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aizer et al.</td>
<td>0.182</td>
<td>0.083</td>
<td>49.7%</td>
<td>1.20 [1.02, 1.41]</td>
<td></td>
</tr>
<tr>
<td>Everett et al.</td>
<td></td>
<td>0.111</td>
<td>27.8%</td>
<td>1.00 [0.80, 1.24]</td>
<td></td>
</tr>
<tr>
<td>Frost et al. (men)</td>
<td>0.086</td>
<td>0.21</td>
<td>7.8%</td>
<td>1.09 [0.72, 1.64]</td>
<td></td>
</tr>
<tr>
<td>Frost et al. (women)</td>
<td>0.14</td>
<td>0.594</td>
<td>1.0%</td>
<td>1.15 [0.36, 3.68]</td>
<td></td>
</tr>
<tr>
<td>Mozaffarian et al.</td>
<td>-0.139</td>
<td>0.188</td>
<td>13.7%</td>
<td>0.87 [0.64, 1.19]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>1.08 [0.97, 1.21]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 3.96, df = 4 (P = 0.41); I² = 0%

Test for overall effect: Z = 1.36 (P = 0.17)

Discussion
Overall, we found that the regular PA is not associated with significantly higher risk of AF compared with sedentary lifestyle. To the best of our knowledge, this is the first meta-analysis to
evaluate the relation between regular PA and AF among non-athletes. The results are important because they demonstrate that regular exercise, which has been long established to have beneficial effects on cardiovascular risks, at the same time does not seem to increase the risk of AF. PA guidelines recommend 150 minutes of moderate PA per week or 75 minutes of vigorous exercise per week. Many physiological mechanisms by which PA may influence AF risk have been suggested, albeit speculative for the most of them.

The potential mechanisms, by which PA may be associated with a higher risk of AF, are those that are thought to be responsible for a higher risk of AF among elite endurance athletes. They include altering the balance between sympathetic and parasympathetic nervous systems, which results in increased vagal tone (vagal AF, initially described in 1994 by Cournel), leading to shortening of the effective refractory period in the atria and increased effective refractory period dispersion, resulting in AF. The second potential mechanism is increase in the left atrial size leading to atrial fibrosis. Our data suggest that in nonathletes such mechanisms may not play a major role for the development of AF. Alternatively, PA in nonathletes might reduce weight, blood pressure, and incident diabetes mellitus, all of which are established risk factors for AF.

Strengths and Limitations

Our study has several limitations. Each of the studies used for the meta-analysis subcategorized the amount of PA differently. Even the type of PA differed across studies, with 3 studies comparing the amount of exercise, whereas 1 compared those the amount of PA at work. However, the study evaluating work-related PA also evaluated for the amount of exercise of the subjects, which was used in statistical analysis (see page 50 of reference 14). The study evaluating occupational activity was the only non-US study in our meta-analysis, which could have created confounding errors. There was also a difference in sample sizes. Because of a small number of studies included to the meta-analysis, we were limited in conducting subanalyses, such as stratification by sex or type of exercise. The ascertainment of AF differed from study to study (Table). In one of the studies, the participants were physicians, who were more likely to recognize AF. Incidence of the outcome may have been under-reported in all of the studies because of asymptomatic or undiagnosed AF. Despite these differences, there was little heterogeneity between studies (P of 0). Lastly, we were not able to examine the effect of cause-specific mortality on our findings because we did not have study-specific points for analysis.

Our systematic review has several strengths, including the novelty of examining regular PA in nonathletes. The studies include both men and women of a wide age range and from different geographic regions. We have large sample size, which improves the statistical power to detect smaller effects.

Conclusions

Overall, our data do not support a statistically significant association between regular PA and higher incidence of AF in nonathletes.

Disclosures

None.

References

CLINICAL PERSPECTIVE

Although previous studies have suggested that competitive athletes have a higher risk of atrial fibrillation (AF) than the general population, limited and inconsistent data are available on the association between regular physical activity and the risk of AF. To investigate whether regular physical activity is associated with an increased risk of AF, we analyzed data published between 1948 and 2011 and found that regular physical activity was not associated with increased risk of AF. These findings suggest that exercise recommendations from the Institute of Medicine should be followed for heart health benefits without concern about elevated risk of AF.
Regular Physical Activity and Risk of Atrial Fibrillation: A Systematic Review and Meta-analysis

Peter Ofman, Owais Khawaja, Catherine R. Rahilly-Tierney, Adelqui Peralta, Peter Hoffmeister, Mathew R. Reynolds, J. Michael Gaziano and Luc Djousse

Circ Arrhythm Electrophysiol. 2013;6:252-256; originally published online March 20, 2013; doi: 10.1161/CIRCEP.113.000147

Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/6/2/252

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Arrhythmia and Electrophysiology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Arrhythmia and Electrophysiology is online at:
http://circep.ahajournals.org/subscriptions/