Atrial fibrillation and physical activity

Should we exercise caution?

N. John Bosomworth MD CCFP FCFP

Abstract

Objective  To review the evidence on the effects of various levels of physical activity (PA) on the incidence of atrial fibrillation (AF) in both the general population and in endurance athletes.

Data sources A PubMed search was done initially using the MeSH headings or text words (with the search-field descriptor TIAB [title and abstract]) atrial fibrillation and exercise or physical activity or athlet* or sport*, without additional filters. Conclusions regarding quality and strength of evidence were based on the GRADE (grading of recommendations, assessment, development, and evaluation) system.

Study selection No interventional studies were available. Observational studies were therefore considered acceptable, and, although larger long-term prospective cohort studies were preferred, case-control or cross-sectional trials were also included in this review.

Synthesis Available evidence suggests a dose-response association linking increased exercise levels with reduced incident AF in women. The same is true in men at low and moderate levels of exertional activity. In men only, high levels of PA are associated with increased risk of AF in most, but not all, studies. This risk is moderate, with a hazard ratio of 1.29 in one of the better studies. The risk of AF for most people who exercise regularly is lower than that of a matched sedentary population.

Conclusion Atrial fibrillation is probably less common as PA increases, with a demonstrable dose-response relationship. Exercise at any level should be promoted for its effect on physical well-being and mortality reduction. In men exercising at high levels, beneficial effects on AF might be lost and risk might exceed that of the sedentary population; however, the evidence is neither robust nor consistent. These men should be made aware of this modest increase in risk should they choose to continue to engage in high levels of PA.

Case description

H.R., a 60-year-old man, visits you in the office. He has been a runner for 20 years and has just completed his 15th marathon. His physical examination findings show no abnormalities and he has an unremarkable medical history. His father had atrial fibrillation (AF) and died following a stroke at the age of 79. Three of his friends in his running club have recently developed AF and have been advised to reduce their levels of exercise. H.R. wants to know whether it is safe to continue his current training schedule of 50 to 60 km per week.

In 1967, Kannel made the following statement: “Prospective epidemiologic studies are hampered by inadequate methods for assessing physical activity, and by a paucity of really physically active adults in the populations under study.” In the span of more
than 4 decades since Kannel’s observation, a paradox has arisen in the manifestation of physical activity (PA) in North America. Data from the Canadian Health Measures Survey using accelerometry, rather than self-reported estimations, suggest that 69% of adult activity is sedentary. Only 15% of Canadian adults in that survey met or exceeded the World Health Organization’s recommendation for leisure-time PA. In contrast, increasing numbers of people are participating in endurance sports and extreme sports.

A recent survey in the United States (US) comparing cohorts from 1988 to 2010 shows the sedentary population to have increased from 19.0% to 51.7% in women and from 11.4% to 43.5% in men. On the other hand, marathon participation has increased 140% since 1990 in the US, and the numbers of 24-hour ultramarathon participants have increased, with more female representation and the fastest times being posted by older runners in the 40-to-49 age group. There is a trend to steadily increasing incidence and prevalence.

Exercise has total prevalence in that even sedentary people exhibit some PA. This confounder, along with compliance and blinding issues, makes controlled studies difficult. Exercise with high intensity or frequency of PA on AF. The Cardiovascular Health Study showed a graded reduction in AF progression from light to moderate PA, but this benefit disappeared with high-intensity exercise; 58% of participants were women. The large Danish Diet, Exercise has total prevalence in that even sedentary people exhibit some PA. This confounder, along with compliance and blinding issues, makes controlled studies difficult.

Study selection
A PubMed search was done initially using the MeSH headings or text words (with the search-field descriptor "tiab", "TIAB") atrial fibrillation and exercise or physical activity or athlet* or sport*, without additional filters. Recent available reviews and meta-analyses were searched for additional trials. Conclusions regarding quality and strength of evidence were based on the GRADE (grading of recommendations, assessment, development, and evaluation) system.

No interventional studies were available. Observational studies were therefore considered acceptable, and, although larger long-term prospective cohort studies were preferred, case-control or cross-sectional trials were also included in this review.

SYNTHESIS

Early studies examining athletes with arrhythmias suggested that most were young, male, and competing at an elite level. Approximately 25% of these arrhythmias were AF. Several case-control studies that examined patients presenting with lone AF in arrhythmia clinics or emergency department settings followed. Odds ratios for AF in patients engaged in vigorous sports ranged from 3.13 to 15.11 in these studies. Again, most patients were male. Most had paroxysmal AF and predominantly vagal triggers, and, in keeping with the lone AF definition, there were no echocardiographic or clinical cardiac abnormalities apart from occasional “mild” hypertension. These studies involved highly selected patients, did not correct for confounding variables, and were at high risk of bias.

Subsequent studies have included the general population and athletes, and have examined patients at all ages, including those with cardiac risk factors and comorbidities.

Cohort studies
In observational literature, cohort studies are the most reliable because they can clarify cause and effect and help determine the incidence and natural history of a condition. Of the available cohort studies listed in Table 1, the studies by Mozaffarian et al (Cardiovascular Health Study), Aizer et al (Physicians’ Health Study), and Andersen et al stand out because of appropriate setting and evaluation. No interventional studies were available. Observational studies were therefore considered acceptable, and, although larger long-term prospective cohort studies were preferred, case-control or cross-sectional trials were also included in this review.

DATA SOURCES

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### Table 1. Cohort studies

<table>
<thead>
<tr>
<th>STUDY</th>
<th>STUDY CHARACTERISTICS</th>
<th>MEAN AGE OF PARTICIPANTS, Y</th>
<th>DEFINITION OF HIGH-INTENSITY EXERCISE AND END POINTS</th>
<th>OUTCOMES</th>
<th>LIMITATIONS</th>
<th>RISK OF BIAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karjalainen et al,31 1998</td>
<td>• Top-level veteran orientees (ie, runners) • 228 in orienteer group vs 212 in control group; 100% men • 10-y follow-up</td>
<td>47.5</td>
<td>• High position in veteran ranking is an indicator of y of intense training • Lone AF</td>
<td>• AF developed in 5.3% of orienteers vs 8.9% of control group (RR = 0.55; P = .012)</td>
<td>• Men only • Cohort information insufficient • No correction for confounding • Unreliable outcome assessment • Potential recall bias</td>
<td>High</td>
</tr>
<tr>
<td>Frost et al,32 2005</td>
<td>• Danish Diet, Cancer, and Health Study data • 19,593 (53%) men and 18,807 women • Mean 5.7-y follow-up</td>
<td>56</td>
<td>• Heavy physical workload (self-report) • AF or atrial flutter</td>
<td>• No differences between the sexes* • No differences overall*</td>
<td>• Few subjects exposed to heavy work or vigorous PA • Relied on registry outcomes • Could not separate AF from atrial flutter • Potential recall bias</td>
<td>Moderate</td>
</tr>
<tr>
<td>Heidbuchel et al,33 2006</td>
<td>• 137 patients after ablation for atrial flutter; 83% men • 31 of the 137 patients regularly engaged in sports before ablation • Mean 2.5-y follow-up</td>
<td>58</td>
<td>• Intense competitive activity ≥ 3 h per wk • Development of AF after ablation for atrial flutter</td>
<td>• AF development in high PA (HR = 1.81; P = .02) • No differences between the sexes</td>
<td>• Status after ablation not comparable • Higher rate of cardiovascular disease • Potential for recall bias • No correction for confounding</td>
<td>Moderate</td>
</tr>
<tr>
<td>Molina et al,34 2008</td>
<td>• 252 Barcelona marathon runners vs 305 sedentary men; 100% men • Retrospective cohort study • Mean 11.6-y follow-up</td>
<td>39</td>
<td>• Marathon running • Lone AF</td>
<td>• Endurance sport practice associated with higher risk of lone AF (HR = 8.80, 95% CI 1.26 to 61.29; P = .028)*</td>
<td>• Men only • Control group recruited from different population • 5-y difference in follow-up duration • Risk of recall bias • All AF events not considered</td>
<td>Moderate</td>
</tr>
<tr>
<td>Mozaffarian et al,35 2008</td>
<td>• Cardiovascular Health Study Medicare eligibility lists in US communities • 54,462 participands; 42% men • Post hoc analysis of RCT • 12-y follow-up</td>
<td>73</td>
<td>• ≥ 6 MET† of intensity • ≥ 1840 kcal/wk (self-report) • AF on annual examination or electrocardiogram</td>
<td>• Graded reduction in AF with light to moderate PA intensity† • No reduction in AF with high PA intensity (RR = 0.87, 95% CI 0.64 to 1.19)*</td>
<td>• With an older cohort, there was less high-intensity PA • No sex differences examined</td>
<td>Low</td>
</tr>
<tr>
<td>Aizer et al,36 2009</td>
<td>• 16,921 men in Physicians’ Health Study • Post hoc analysis of RCT • 12-y follow-up</td>
<td>51</td>
<td>• Sufficient to “work up a sweat” 5-7 d/wk (self-report) • AF</td>
<td>• RR for 0 vs 5-7 d/wk (joggers) of vigorous exercise was 1.20 (95% CI 1.02 to 1.41; P = .04)* • Elevated risk observed if aged &lt; 50 y (RR = 1.74, 95% CI 1.23 to 2.47; P = .01)</td>
<td>• Men only • Some retrospective subgroup analysis • Association seen at 3-y evaluation but not at 9 y</td>
<td>Low</td>
</tr>
<tr>
<td>Pelliccia et al,37 2010</td>
<td>• 114 Olympic athletes vs 97 people in control group; 78% n • 8.6-y follow-up</td>
<td>22</td>
<td>• Participation in Olympic-endurance disciplines and having multiple games experience • Cardiac symptoms or events</td>
<td>• No cardiac events developed for more than 8 y • Reduced incidence compared with general population</td>
<td>• Very young study cohort • Small group and therefore few potential outcomes • Screening of multiple cardiovascular systems before enrolment • Control group was very fit; had participated in 1 Olympic game</td>
<td>High</td>
</tr>
<tr>
<td>Everett et al,38 2011</td>
<td>• 34,759 women who had been part of the Women’s Health Study • 20-y follow-up</td>
<td>57.5</td>
<td>• ≥ 6 MET† of intensity • ≥ 15 MET† h/wk • AF</td>
<td>• No difference in incident of AF among quintiles after adjusting for hypertension and obesity*</td>
<td>• Women only • Very few women underwent strenuous activity • Self-assessment of PA intensity • Self-assessment of outcomes</td>
<td>Low</td>
</tr>
</tbody>
</table>

Continued on page 1064
Cancer, and Health Study database, composed of 49% women, showed no change in AF incidence with exercise; however, very few participants undertook strenuous exercise. Another large study of runners and walkers demonstrated graded reduction in arrhythmias with increasing PA, with younger participants and women showing the most benefit. Other cohorts that included women showed no effects of PA on AF. It is reasonable to conclude that in women, increased PA is associated with neutral or reduced risk of AF. Increasing participation in endurance events by women might provide further information.

Larger cohort trials in the general population provide an opportunity to examine the effects of...
low- and moderate-level exercise. The Cardiovascular Health Study, 35 which combined women and men, suggested incremental reduction in incident AF going from low to moderate PA levels. An increase was seen at high exercise levels, but risk for these participants was no different than that for non-exercisers (Figures 1 and 2). 36,37 With a large cohort of men, Drca et al 43 showed no change in AF among men who continued to exercise for longer intervals; however, for a smaller subset of men who were active more than 5 hours per week at age 30 and subsequently remained active, the relative risk of AF was 1.19. In a study with a very large cohort of men and women, Williams and Franklin 41 suggested a continuous reduction in arrhythmias of 4.8% per metabolic equivalent task hours per day in an aggregate of walkers and runners (Figure 3). 41 Arrhythmias were self-reported and not differentiated, but AF was considered to be the largest contributor to symptoms.

Data that show an increase in the risk of AF at the upper extremes of PA have been derived primarily from men, usually functioning at competition level (Table 2). 31,34,37,39,46-50 A number of studies in men 31,33,34 and some very large cohorts 36,39,40,46 document an increase in incident AF with increasing levels of activity. Some of these studies include only high-level athletes, so do not consider more modest activity levels. 31,34,39,46 Hazard ratios (HRs) for increased AF range from 1.2 in the Physicians’ Health Study 36 to 8.8 among a cohort of marathon runners 34 (Table 1). 31-46 Of particular interest is a study by Andersen et al 39, with a mean follow-up of 9.7 years, this study had 52,755 competitive cross-country skiers who were very fit athletes participating in a 90-km race. Compared with athletes who completed only 1 race, those participants who completed more than 5 races had an increased HR of 1.29 for AF (Figure 4). 39 This is a reliable study examining vigorous activity, and it extends the dose-response curve established by cohorts taken from the general population.

Several trials done in men showed no exercise effect. 32,37,44,45 The larger cohort study by Frost et al 32 considered only work-related PA and might not have been comparable to other studies. Pelliccia et al 37 examined a small population of Olympic athletes with a much lower mean age than in other studies.

Overall, cohort studies of incident AF in men suggest either no effect or a benefit at low and moderate levels of PA. In general population studies (Figures 1 and 2), 35,36 there is a suggestion of increased risk at the upper extremes of intensity or frequency of exercise. Of trials done in competitive athletes, all but 1 small cohort 37 suggest an increasing dose response for AF with increasing intensity, frequency, or duration of PA. However, contributing to uncertainty at this level is the Williams and Franklin study. 41 which examines activity outcomes in excess of 3 times the currently recommended exercise level (1.8 metabolic equivalent task hours per day). In spite of the likelihood that some runners in this study (only 41% men) are approaching activity levels seen in elite athletes, a dose-response relationship is seen for arrhythmia reduction at all levels of exercise intensity (Figure 3). 41

### Studies in competitive athletes

Most available studies evaluating competitive athletes have shown increased risk of AF with higher levels of PA (Table 2), 31,34,37,39,46-50; however, some of these were case-control or cross-sectional studies and had a high risk of bias. The more reliable trials 34,39,49 suggest a HR varying from 1.16 to 8.8 for increased risk of AF, with most of this very heterogeneous group of studies falling closer to the lower end of this range. All but 2 studies 37,39 included only men. The analysis by Andersen et al, noted previously, is likely to be most representative of risk in elite athletes (Figure 4). 39

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**Figure 1.** Cardiovascular Health Study data to determine hazard ratios for AF, by exercise levels: **Circled data point indicates a statistically significant change from baseline.**

![Figure 1](image1)

**Figure 2.** Physicians’ Health Study data to determine hazard ratios for AF, by PA per week: **Circled data point indicates a statistically significant change from baseline.**

![Figure 2](image2)
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Available evidence suggests a dose-response relationship between increased exercise levels with reduced incident AF in women. The same is true in men at low and moderate levels of exertional activity. In men only, high levels of PA are associated with increased risk of AF in most, but not all, studies. This risk is moderate, with an HR of 1.29 in one of the better studies. Men undertaking high levels of endurance activity should be made aware that this is associated with a modest increase in risk of AF (grade 1C: strong recommendation, low-quality evidence). The risk of AF for most people who exercise regularly is lower than that of a matched sedentary population. There is currently no firm threshold or guideline that can be drawn from existing literature.

Table 2. Studies in athletes

<table>
<thead>
<tr>
<th>STUDY</th>
<th>STUDY TYPE</th>
<th>TYPE OF ATHLETES</th>
<th>AF OUTCOMES</th>
<th>RISK OF BIAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andersen et al,</td>
<td>Cohort</td>
<td>Swedish cross-country skiers for 90-km event</td>
<td>• HR = 1.29 (95% CI 1.04 to 1.61) for &gt;5 completed races</td>
<td>Low</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td>• HR = 1.20 (95% CI 0.93 to 1.55) for those with fastest times</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• 87% of study participants were men</td>
<td></td>
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<tr>
<td>Baldesberger et al, 2008</td>
<td>Case control</td>
<td>Former Swiss elite cyclists</td>
<td>• AF developed in 10% of cyclist group and in 0% of control group (BGD P value of .028)</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Study included only men</td>
<td></td>
</tr>
<tr>
<td>Grimsmo et al, 48 2010</td>
<td>Cross sectional</td>
<td>Elite-level Norwegian cross-country skiers</td>
<td>• AF prevalence of 16.7% was found</td>
<td>High</td>
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<td></td>
<td></td>
<td></td>
<td>• Lone AF prevalence of 12.8% was found</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>• Study included only men</td>
<td></td>
</tr>
<tr>
<td>Karjalainen et al, 1998 Cohort</td>
<td>Top-level orienteers (runners)</td>
<td></td>
<td>• AF developed in 5.3% of orienteers vs 8.9% of control group (RR = 5.5; P = .012)</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Study included only men</td>
<td></td>
</tr>
<tr>
<td>Molina et al, 2008 Retrospective cohort</td>
<td>Runners in Barcelona Marathon</td>
<td></td>
<td>• Endurance sport practice associated with higher risk of lone AF (HR = 8.80, 95% CI 1.26 to 61.29; P = .028)</td>
<td>Moderate</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Study included only men</td>
<td></td>
</tr>
<tr>
<td>Myrstad et al, 2014 Cohort</td>
<td>Norwegian cross-country ski racers for 56-km event</td>
<td></td>
<td>• Increased risk of AF for 10 y of vigorous PA (HR = 1.16, 95% CI 0.06 to 1.28)</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Study included only men</td>
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<tr>
<td>Myrstad et al, 2014 Cross sectional</td>
<td>Participants in Birkebinner cross-country ski race—a course of 54 km and 1000 m uphill</td>
<td></td>
<td>• AF in men currently practising endurance sport (OR = 1.81, 95% CI 1.04 to 3.14)</td>
<td>High</td>
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<td></td>
<td></td>
<td></td>
<td>• Study included only men</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• 78% of study participants were men</td>
<td></td>
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<tr>
<td>Pelliccia et al, 2010 Cohort</td>
<td>Olympic athletes</td>
<td></td>
<td>• No cardiac events developed for more than 8 y</td>
<td>High</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Reduced incidence compared with general population</td>
<td></td>
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<tr>
<td>Van Buuren et al, 2012 Cross sectional</td>
<td>Elite German handball players</td>
<td></td>
<td>• AF prevalence of 30.3% in former athletes</td>
<td>High</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Study included men only</td>
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</table>

AF—atrial fibrillation, BGD—between-group difference, HR—hazard ratio, OR—odds ratio, PA—physical activity, RR—risk ratio.
There is controversy as to whether changes seen in the cardiac structure and function of athletes represent benign adaptation to the stress of exercise or pathological change producing increased risk of arrhythmias. It is also unclear whether increased atrial ectopy from the pulmonary veins produced by increased PA is the primary cause of observed arrhythmias or whether other mechanisms are dominant. Baldesberger and colleagues did not document increased ectopy in their survey of elite cyclists. This can lead to bradycardia and reduced atrial refractory period, as well as a trigger or modulator of the less-muscular chambers of the atria and the right ventricle with progressive dilation of right ventricular ejection fraction as duration of intense exercise increases. Dilation of the less-muscular chambers of the atria and the right ventricle might result if exercise stress continues and there is insufficient time for recovery, leading, in some people, to microtrauma, inflammation, fibrosis, and potential substrate for arrhythmias. Some authors argue for the presence of an exercise-induced arrhythmogenic right ventricular cardiomyopathy.

Despite the speculation summarized in Figure 5, no established physiologic mechanism exists to explain any association between high exercise intensity and AF.

**Pathophysiology**

There is controversy as to whether changes seen in the cardiac structure and function of athletes are predominantly due to physiological adaptation to the stress of exercise or pathological change producing increased risk of arrhythmias or whether other mechanisms are dominant. Baldesberger and colleagues did not document increased ectopy in their survey of elite cyclists. This can lead to bradycardia and reduced atrial refractory period, as well as a trigger or modulator of the less-muscular chambers of the atria and the right ventricle with progressive dilation of right ventricular ejection fraction as duration of intense exercise increases.

Increased vagal tone is present in many endurance athletes. This can lead to bradycardia and reduced atrial refractory period, as well as a trigger or modulator of heart rhythm by creating conditions for re-entry. Exercise induces an increase in the pressure of pulmonary arteries, which is especially prominent in athletes. During PA, higher pressure measures are seen in the right atrium and ventricle, with progressive reduction in right ventricular ejection fraction as duration of intense exercise increases.

Dilation of the less-muscular chambers of the atria and the right ventricle might result if exercise stress continues and there is insufficient time for recovery, leading, in some people, to microtrauma, inflammation, fibrosis, and potential substrate for arrhythmias. Some authors argue for the presence of an exercise-induced arrhythmogenic right ventricular cardiomyopathy.

Despite the speculation summarized in Figure 5, no established physiologic mechanism exists to explain any association between high exercise intensity and AF.

**Prognosis**

High-performance athletes with AF are probably unlikely to have comorbidities. The population subset with these findings is generally men who are younger than age 60 with normal findings on physical examinations, chest x-ray scans, electrocardiograms, and echocardiographic investigations—criteria for the condition previously termed lone AF. The effect of exercise on risk factors such as hypertension and glucose intolerance, together with the effect of preselection of healthy people who can better tolerate PA, might predispose athletes to lower cardiovascular risk over time. In one study, paroxysmal AF in the general population progressed to permanent AF in 19% over 10 years. In another study of athletes with AF who were followed for 9 years, paroxysmal AF continued to occur in 56% of them, paroxysmal AF progressed to permanent AF in 18%, and no symptoms were observed in 26%. While there might be some prognostic value, the term lone AF is probably otherwise not useful, as management is mainly focused on thromboembolism prevention and symptom control, as it is for all AF.

The odds ratios for mortality in AF were found in the Framingham study to range between 1.5 and 1.9, with the lowest risk being in men. Available data in athletes with AF show either no change or reduction in cardiovascular and all-cause mortality.

Numerous meta-analyses without exception have demonstrated reduction in mortality from 15% to 50% over various time periods as a result of PA. This reduction is also seen in studies done specifically on athletes. The most marked mortality reduction is seen in progression from sedentary to light activity. At the highest level of exercise intensity there is a suggestion of loss of mortality reduction; however, in no case is this risk higher than that of the sedentary population.

**Case resolution**

H.R. has no identified risk factors for AF or heart disease and, as a runner, has already self-identified as being at lower relative risk of cardiovascular and all-cause mortality. As a 60-year-old man, H.R. has a 5.7% risk of developing AF. His present activity level might be associated with a 30% increased relative risk of developing AF. His 10-year risk of developing AF might therefore approach 7.4%.

As a land surveyor and mountain climber, H.R. requires a high level of fitness to maintain his quality of life. He elects to continue at his present activity level and accept the modest increased risk this might present. You inform him that a reduction in his activity to moderate levels is associated with a lower-than-average risk of AF with preservation of the health benefits of exercise.

**Conclusion**

Atrial fibrillation is probably less common as PA increases,
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Figure 5. Characteristics of endurance exercise speculated to promote AF

Endurance sport

Triggers
- Pulmonary vein ectopy
- Performance-enhancing drugs

Modulators
- Increased vagal tone
- Bradycardia
- Reduced atrial refractory period

Substrate
- Increased volume load
- Increased stretch
- Fibrosis
- Inflammation

AF—atrial fibrillation.

with a demonstrable dose-response association. Exercise at any level should be promoted for its effect on physical well-being and mortality reduction. In men exercising at high levels, beneficial effects on AF might be lost and risk might exceed that of the sedentary population; however, the evidence is neither robust nor consistent. These men should be made aware of this modest increase in risk should they choose to continue to engage in high levels of PA.

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Competing interests
None declared

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References
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