

EDITORIAL COMMENT

Physical Fitness, Physical Activity, Exercise Training, and Atrial Fibrillation



First the Good News, Then the Bad*

Paul D. Thompson, MD

Atrial fibrillation (AF) is the most commonly treated arrhythmia in clinical practice (1), accounting for approximately one-third of U.S. hospital admissions for arrhythmia (1) and affecting an estimated 1% of the U.S. population (1) and >33 million individuals worldwide (2). The list of risk factors for AF is long and includes the usual suspects of structural heart disease, age, hypertension, increasing body mass index (BMI), and diabetes, but also the less widely appreciated factors of increased height (3) and inflammation (4)—the latter either independently or via its relationship with obesity (5).

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Low physical activity is also a risk factor for AF. Pathak et al. (2), in this issue of the *Journal*, demonstrate that both greater exercise capacity and increases in exercise capacity with exercise training reduce AF recurrence. These authors evaluated 1,415 consecutive clinic patients with AF. The 825 patients with a BMI ≥ 27 kg/m² were offered a physician-led program designed to produce weight loss and increase exercise activity. AF recurrence was determined by clinical review, 12-lead electrocardiogram, and 7-day Holter monitoring. A total of 308 patients

had baseline and follow-up symptom-limited exercise tests plus an AF assessment and were included in the analysis.

Patients were divided into low (n = 95), adequate (n = 134), and high (n = 79) cardiorespiratory fitness groups on the basis of their baseline exercise performance and followed for an average of 4 years. AF freedom over study duration without medical or ablative therapy was 12% in the low, 35% in the adequate, and 66% in the highest fitness groups demonstrating that baseline fitness predicts future AF. Increasing fitness via the study intervention was also associated with reduced AF recurrence. For every increase in metabolic equivalent (MET) of performance (1 MET = 3.5 ml O₂/kg/min), there was a 9% decrease in AF recurrence. The rate of AF recurrence was 89% in those gaining <2 METs of exercise performance, but only 40% in those gaining ≥ 2 METs. This effect of improving fitness reducing AF recurrence persisted even after adjustment for weight changes and baseline exercise performance. To demonstrate this, the authors divided patients into 4 groups: 1) those with both <10% weight loss and <2 MET gain, 2) those with <10% weight loss and ≥ 2 MET gain, 3) those with >10% weight loss and <2 MET gain, and 4) those with >10% weight loss and ≥ 2 MET gain. At final follow-up, freedom from arrhythmia without drug therapy was 13.2, 36.7, 44.8, and 75.6%, respectively, supporting the idea that increased exercise capacity provided benefit beyond that provided by weight loss alone.

This is not the first study to demonstrate that higher fitness, measured indirectly by exercise duration (6) or more directly by maximal oxygen uptake (7), predicts less frequent AF. Cardiorespiratory fitness should not, however, be equated with habitual physical activity. Physical activity and exercise training both increase fitness, but baseline exercise

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From the Department of Cardiology, Hartford Hospital, Hartford, Connecticut. Dr. Thompson has received research support from Genomas, Roche, Sanofi, Regeneron, Esperion, Amarin, and Pfizer; has served as a consultant for Amgen, Regeneron, Merck, Esperion, and Sanofi; has received speaker honoraria from Merck and AstraZeneca; owns stock in Abbvie, Abbott Laboratories, General Electric, Johnson & Johnson, and JA Willey; and has provided expert legal testimony on exercise-related cardiac events and statin myopathy.

capacity is directly affected by cardiac output, making it reasonable that those with the healthiest hearts and associated higher fitness would have lower rates of AF. Nevertheless, increasing levels of physical activity also has been shown to reduce AF incidence, but this relationship of exercise to AF is complex, influenced by both intensity and lifetime exposure to activity, and seems to be a U-shaped relationship with the greatest levels of physical activity possibly increasing AF incidence.

Moderate levels of physical activity reduce AF risk. In the Swedish Mammograph Cohort study (8), physical activity was assessed in 36,513 women at baseline, 2,915 of whom developed AF. The incidence of AF over a median follow-up of 12 years was 15% lower in women exercising ≥ 4 h weekly versus those exercising < 1 h weekly. In the Women's Health Initiative Observational Study (9), physical activity was also assessed at baseline in 81,317 women, 9,792 of whom developed AF. The incidence of AF over an average follow-up of 11.5 years decreased with progressively more physical activity and was 10% lower in women exercising > 9 MET task hours per week versus those with no reported weekly exercise. This effect was independent of BMI. In the Women's Health Study, among 34,759 women, 968 developed AF after a median of 14.4 years (10). Women exercising 7.5 MET hours weekly had a 14% lower risk of AF, but this was not significant after adjusting for BMI. Interestingly, in the Women's Health Initiative Observational Study even the most physically active women, those exercising > 15 MET task hours weekly in strenuous physical activity, had a 9% lower rate of AF (9). Similarly, among 5,445 men and women ≥ 65 years old in the Cardiovascular Health Study (11), 1,061 of whom developed AF over 12 years of follow-up, there was a progressive decline in AF with increasing amounts of leisure time physical activity.

In contrast to this stepwise reduction in AF with total physical activity, the relationship between AF and exercise intensity suggests a curvilinear response with diminishing benefit or even risk with the most intense exercise. AF incidence was 28% lower in the Cardiovascular Health Study with moderate-intensity physical activity (11). Those exercising at the highest intensity, however, had a risk of AF not significantly different from the no-exercise group. Similarly, among the 16,921 male participants in the Physicians' Health Study (12), 1,661 men developed AF over 12 years of follow-up. AF risk increased with the frequency of vigorous exercise, so that men exercising vigorously 7 days per week had a 20% higher risk. Subgroup analyses suggested that this increased risk with vigorous activity only

occurred in men < 50 years old and in men who were joggers.

With some exceptions (11), these studies adjusted for multiple AF risk factors, but such risk adjustment may adjust away the possible benefits of exercise on AF risk. Vigorous exercise training reduces blood pressure (13), C-reactive protein (13,14), and body weight (13), for example, all risk factors for AF, so that adjusting for these factors may mask the benefits of exercise in modifying risk factors, or even suggest harm when there is none. Nevertheless, studies that both adjusted, and did not, for these risk factors still observed an increased AF risk with sustained, vigorous intensity exercise. Furthermore, there are now a systematic review (15) and a meta-analysis (16) suggesting that athletes who engaged in long-term, endurance exercise training have an increased AF incidence.

There are also a series of studies examining former participants in endurance events. Among 52,755 cross-country or Nordic skiers who participated in the 90-km races from 1989 to 1998, 919 developed AF before December 2005 (7). Participants in ≥ 5 races were 30% more likely to develop an arrhythmia than those who participated in only 1 race, largely because of a 29% higher rate of AF. Others also used national health records and self-reported endurance training to examine the incidence of AF in 2,366 men who participated in the 1999 Birkebeiner, a 54-km cross-country ski race. Compared with 1,179 men from the community, participants in the race had a 16% increase in AF incidence for every 10 years of exercise training. Possible mechanisms for an increase in AF in endurance athletes have not been defined but enhanced vagal tone or increased left atrial size, both known effects of exercise training, are possible as is repeated exposure to the acute increase in inflammation after prolonged vigorous exertion and/or the acute increase in catecholamines that occurs with any vigorous exercise session.

There is not universal agreement that vigorous endurance exercise training increases AF risk. As noted, the most active women in the Women's Health Initiative Observational Study had lower rates of AF, but differences between men and women in epidemiological studies of physical activity are not new possibly because of differences in the range of physical activity between the sexes (17). Also, AF is not more frequent among young, elite Italian athletes, and a meta-analysis did not find an association between intense physical activity and AF, but when there is this much research interest in a clinical topic, there is usually some substance to the concern.

But any concern about too much intense exercise is clearly not an issue for most patients. What is most

exciting about this new study by Pathak et al. (2) is that it is the first to demonstrate that increasing exercise capacity reduces AF risk. There are limitations to the report. The major concern is that this is not a randomized controlled clinical trial, but a prospective, observational trial, and those individuals adopting an active lifestyle may be different or have made other changes that affected AF risk.

The results beg for confirmation by clinical trial, but exercise training trials in patients are notoriously difficult because of both low adherence to prolonged exercise training and crossover of sedentary control subjects to the exercise arm because patients join

because they are interested in exercise training. Nevertheless, these new results, and the cumulative data linking moderate physical activity to reduced AF risk, suggest that until definitive trial data are available, clinicians should recommend moderate exercise training to patients with AF, not only to reduce AF, but also for its overall cardiovascular benefits (13).

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Paul Thompson, Department of Cardiology, Hartford Hospital, 80 Seymour Street, Hartford, Connecticut 06102. E-mail: paul.thompson@hhhealth.org.

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