

Exercise Training and Atrial Fibrillation Further Evidence for the Importance of Lifestyle Change

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Atrial fibrillation (AF) is the most common clinical arrhythmia with a global burden that has increased progressively, contributing to rising hospitalizations and substantial healthcare demands.¹⁻³ Although aging is an important contributor to the rising AF prevalence, key mechanistic promoters of AF include modifiable risk factors such as obesity, hypertension, diabetes mellitus, and obstructive sleep apnea.

Article see p 466

Exercise training and physical activity improve the management of hypertension and diabetes mellitus,⁴ assist in weight management,⁵ and improve cardiac structure and function.⁶ Surprisingly, despite these favorable modifications of arrhythmogenic risk factors, greater physical activity only modestly reduces incident AF rates.^{7,8} At the extreme end of the exercise spectrum, endurance athletes, who engage in the greatest volume of exercise training, encounter a risk of AF that rises significantly. Cohort studies provide estimates of AF risk in the endurance athlete population that range from a 2-⁹ to 7-fold¹⁰ elevation in incident AF risk. Until recently, the AF and exercise story has stopped here: that physically active individuals experience a small reduction in risk, but doing too much increases arrhythmia risk considerably, consistent with a classic J-shaped phenomenon. Perhaps, in part because of these findings and a misguided fear of promoting arrhythmias, there is a scarcity of data regarding the effects of exercise training in patients with nonpermanent AF.

In the current issue of *Circulation*, Malmo et al¹¹ provide the results of their randomized, controlled trial, in which they compared a popular form of high-intensity exercise, aerobic interval training, with a control group who were not prescribed exercise. The authors randomly assigned 51 AF patients referred for catheter ablation to exercise or no exercise over 12 weeks, and recorded AF burden from implantable loop recorders as the primary study outcome. Notably, the authors demonstrate a significant reduction in AF burden in the exercise group, where the mean time in AF declined from 8.1% to 4.8%,

with no significant change in the control group. Of the exercise group, 38% of patients experienced a decline in their arrhythmia burden in comparison with only 20% of the control group. Increased AF burden was more common in the control patients (64%) than in the exercise group (12%). Importantly, patients in the exercise group experienced fewer and less severe symptoms following the intervention, with no concomitant change in the control group. In comparison with controls, patients randomly assigned to exercise also increased their peak oxygen consumption ($\text{Vo}_{2\text{peak}}$), cardiac function, and quality of life, while improving body mass index and blood lipids.

These are important and timely findings that are consistent with data from our group showing that gains in cardiorespiratory fitness are associated with significant abatement of arrhythmia burden both with and without rhythm control strategies.¹² In our cohort of >300 symptomatic, overweight, and obese AF patients, each 1-metabolic equivalent incremental gain in fitness corresponded to a 9% reduction in AF recurrence over a 4-year follow-up. Taken together, these 2 studies provide empirical support for exercise training and physical activity as a key element in the treatment of patients with AF. Importantly, for those who remain concerned about potential arrhythmogenic effects of exercise, there is no evidence to suggest that exercise training within current guidelines exacerbates AF. This should not be surprising given the large differences in the dose of exercise engaged in by an AF patient in comparison with that practiced by the endurance athletes in which AF risk appears to be higher.

We commend the authors on their study, although there are several subtle points that should be raised to place these findings into context. First, as highlighted in their discussion, patients randomly assigned in this study were typically healthy with mild risk factor prevalence. As such, exercise training only modestly reduced body mass index and had no significant impact on blood pressure, MRI-derived left atrial size, or inflammation, all of which are independent arrhythmogenic risk factors. In comparison, we showed that long-term improvements in fitness resulted in significantly reduced blood pressure, inflammation, and left atrial size, while also improving blood lipid status and glycemic control. The majority of these risk factors were higher at baseline in our patients in comparison with those enrolled in the Malmo et al study. On the one hand, it is likely that the benefits of exercise may be understated within this reasonably healthy cohort, given its positive effect on risk factor profile. On the other hand, it is encouraging that exercise exerts antiarrhythmic benefits in the absence of large changes in other risk factors, thus suggesting an independent effect. Second, this study included only a 12-week intervention with 4-week follow-up period. Despite

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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(*Circulation*. 2016;133:457-459.)

DOI: 10.1161/CIRCULATIONAHA.115.020800.)

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Circulation is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIRCULATIONAHA.115.020800

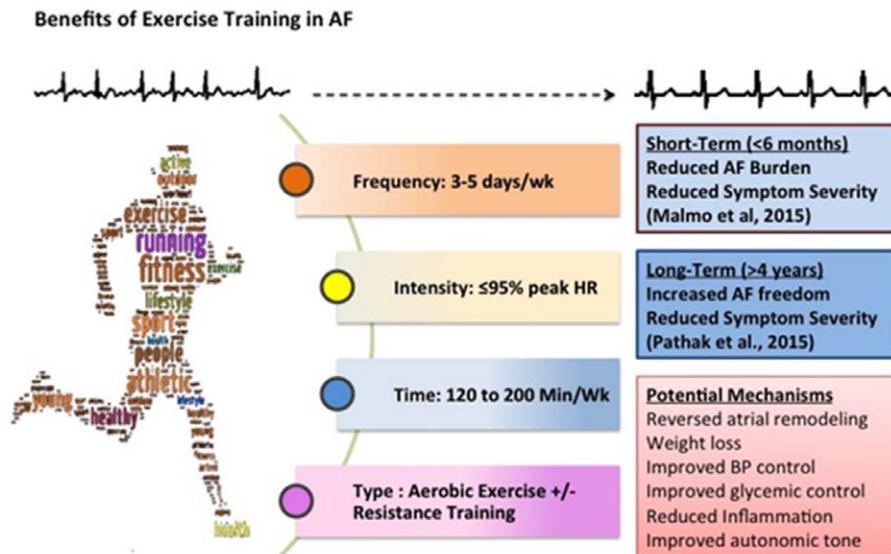


Figure. Overview of existing knowledge regarding exercise training and atrial fibrillation. AF indicates atrial fibrillation; BP, blood pressure; and HR, heart rate.

the favorable findings over this duration, it cannot be ascertained whether prescribing exercise training presents an effective long-term strategy in the treatment of AF.

Previous studies including lifestyle interventions with weight loss have shown clinically significant benefits in AF patients over a longer-term follow-up.^{13,14} This leaves open the question of whether supervised exercise training and its benefits can be maintained similarly beyond the 16-week period. In the post HF-ACTION¹⁵ era, there has been increasing skepticism regarding the efficacy of supervised exercise training as an achievable long-term strategy for the management of cardiovascular disease. In the HF-ACTION trial, initial gains from supervised exercise training over 3 months were diluted by a lack of adherence following the supervised intervention, thus resulting in only modest benefits at final follow-up. Future studies in patients with AF require longer-term interventions and follow-up, and alternative strategies for maintaining appropriate activity levels and exercise habits outside the clinic, as well.

The study of Malmo et al¹¹ also provides some mechanistic insight into the benefit of exercise training for patients with AF. These findings show that exercise reduces AF burden in the absence of significant changes in left atrial size, blood pressure, and inflammation. Although body mass index and blood lipids were modestly improved, the primary mechanism(s) driving the benefit of exercise may not be apparent from these measures alone and instead may come from the direct effects on autonomic factors and intrinsic electrophysiological measures that require invasive procedures for assessment. In animal and human studies, AF risk factors such as hypertension¹⁶ and obesity¹⁷ are associated with atrial remodeling, characterized by conduction slowing, low atrial voltages, and increased interstitial fibrosis. A key question that remains to be answered is whether exercise training can independently reverse atrial remodeling or whether its effects are mediated via other pathways.

If exercise is to be accepted into the management strategy for patients with symptomatic AF, can we optimize the prescription? In this study, patients underwent aerobic interval training, in which they engage in four 4-minute bouts

of high-intensity (commonly 85% to 95% peak heart rate) aerobic exercise, each interspersed by 3 minutes of active recovery. Previous studies from this center have shown the benefits of this form of exercise for heart failure¹⁸ and metabolic syndrome.¹⁹ In our clinic, we prescribe exercise up to 85% of peak heart rate for a total duration of 200 minutes per week, a strategy that leads to greater AF freedom in those who make significant gains in cardiorespiratory fitness.¹² In the absence of comparative data of training modalities for AF patients, current recommendations should focus on prescribing forms of aerobic exercise that patients enjoy and are most likely to adhere to, rather than being overly specific. However, the current evidence supports the efficacy of aerobic exercise activities up to, or close to, peak heart rate if appropriate and achievable to the patient (Figure). Further studies will hopefully contribute to defining the optimal aerobic exercise dose for patients with AF and also establishing the role of resistance training within the exercise prescription.

Although the current study contributes long overdue data regarding exercise training in patients with AF, we should also be mindful of the patients who did not meet the enrolment criteria in this study. Malmo et al enrolled 51 patients from 313 screened for inclusion. Approximately 40% met the inclusion criteria of symptomatic, nonpermanent AF referred for first AF ablation, thus leaving 188 patients (60%) excluded. Previous studies have shown the benefits of exercise training on cardiorespiratory fitness and quality of life for those patients with permanent AF.²⁰ However, we are left to postulate on whether exercise can provide specific benefits to the patients who are not candidates for AF ablation or who are undergoing repeat AF ablation. These patients likely include those with a more advanced atrial substrate, adding complexity to the arrhythmia management.

For those undergoing initial catheter ablation, we have also shown that weight loss and aggressive risk factor management before initial catheter ablation leads to a significant reduction in AF recurrences over a 3- to 4-year follow-up period, in comparison with usual care controls.¹³ This raises the prospect

that exercise training prescribed within the periablation period may offer similar benefits by reducing long-term postablation arrhythmia recurrences, thus improving patient outcomes while simultaneously reducing healthcare demands and exposure to multiple procedures. Although this question is not addressed in the current study, future randomized, controlled trials are warranted to provide data regarding how exercise training may modulate ablation outcomes.

The results from this study require confirmation by larger trials with longer follow-up. However, this study presents an exciting development for the treatment of AF and adds to the rising wave of evidence showing that, in many patients, lifestyle change, including weight management and exercise alongside risk factor management, provides an effective front-line strategy to reduce AF symptoms and provide a potent antiarrhythmic benefit. We encourage clinicians to promote exercise, among other lifestyle modifications, to their patients in a bid (1) to dampen the burden of AF and its associated symptoms and (2) to decrease the heavy reliance on pharmaceutical and interventional strategies for arrhythmia management.

Sources of Funding

Dr Mahajan is supported by the Leo J. Mahar Lectureship from the University of Adelaide and by an Early Career Fellowship jointly funded by the National Health and Medical Research Council of Australia and the National Heart Foundation of Australia. Dr Pathak is supported by an Early Career Fellowship funded by the National Health and Medical Research Council of Australia. Dr Lau is supported by a Robert J. Craig Lectureship from the University of Adelaide. Dr Sanders is supported by a Practitioner Fellowship from the National Health and Medical Research Council of Australia and by the National Heart Foundation of Australia.

Disclosures

Dr Sanders reports having served on the advisory board of Biosense-Webster, Medtronic, CathRx, and St Jude Medical. Dr Sanders reports having received lecture and consulting fees from Biosense-Webster, Medtronic, St Jude Medical, and Boston Scientific. Dr Sanders reports having received research funding from Medtronic, St Jude Medical, Boston Scientific, Biotronik, and Sorin. The other authors report no conflicts.

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KEY WORDS: Editorials ■ atrial fibrillation ■ exercise physiology ■ exercise training

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Circulation. 2016;133:457-459; originally published online January 5, 2016;
doi: 10.1161/CIRCULATIONAHA.115.020800

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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