The beneficial effect of exercise on most aspects of cardiovascular disease is well established with a salutary effect on the incidence of coronary artery disease (CAD), congestive heart failure, and premature death in those who participate in regular physical activity. This effect becomes apparent with moderate increases in activity without a defined upper limit of toxicity. For cardiac arrhythmias, atrial fibrillation (AF) in particular, the story appears more complex. In fact, only limited studies have been published on the beneficial effect of physical activity on AF, whereas a number of case-control studies have emphasized the deleterious effect of exercise when performed at sustained high levels.

1. The role of OSA role in the development of AF is likely related to atrial stretch, autonomic imbalance, oxidative stress, and inflammation. Dimitri et al demonstrated that OSA is associated with volumetric and electric atrial remodeling. OSA has been clinically associated with a 25% greater risk of recurrent AF after catheter ablation. Furthermore, continuous positive airway pressure for OSA is associated with significantly improved AF-free survival after ablation comparable to that of individuals without OSA; ablation in untreated OSA has success rates comparable to that of medical therapy alone.

2. Obesity is similarly associated with atrial stretch, autonomic imbalance, oxidative stress, and inflammation, as well as increased pericardial fat, an emerging marker of cardiovascular risk. The difficulty in evaluating the role of obesity in AF is confounded by the coexistence of other cardiometabolic RFs and OSA. Abed et al demonstrated that in sheep excessive caloric intake leading to weight gain was associated with adverse atrial remodeling marked by increased left atrial mass, fibrosis, inflammation, slower and more heterogeneous atrial conduction, and greater burden of AF. When the sheep were subjected to caloric restriction leading to weight reduction, this resulted in favorable structural and electric atrial changes, that is, reverse remodeling.

3. It is well documented that regular and moderate physical activity improves various parameters of cardiometabolic health and prevents the development of RFs or cardiovascular disease through its beneficial effects on endothelial function, inflammation, and oxidative stress. Several observational studies found that increased physical activity was associated with a reduction in AF. On the other hand, high-level competitive endurance training in marathon runners, cyclists, and elite cross-country skiers has been associated with an increased risk of AF. The mechanisms for this association are related to repetitive and extreme hemodynamic loads, heightened vagal tone, fibrosis, and left atrial enlargement.

The Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation
Intensive RF modification focused on blood pressure and glycemic control, weight management, and OFA was associated with marked improvement in parameters of cardiometabolic health, improvements in cardiac structure, and reductions in burden of AF. RF modification was associated with an ≈5-fold increase in AF-free survival. However, the way in which increased physical activity or cardiorespiratory fitness, in conjunction with RF modification, modulates treatment of AF has not been determined.

In this issue of Circulation, Qureshi et al \(^{18}\) examine the relationship of cardiometabolic RFs and medications. The investigators report the results of a retrospective cohort analysis of the Henry Ford Exercise Testing (FIT) project enrolling 69885 subjects between 1991 and 2009 referred for clinically indicated exercise testing. Individuals with pre-existing AF, atrial flutter, or left ventricular dysfunction were excluded. The final study cohort included 64561 individuals in whom cardiorepiratory fitness, as measured by metabolic equivalents of task (METS), was assessed for development of AF via linkage to International Classification of Disease, Ninth Revision codes in insurance claim files over a mean follow-up of 5.4 years. Cardiorespiratory fitness was stratified into 4 categories of <6, 6 to 9, 10 to 11, and >11 METs. As would be anticipated, there were significant trends toward accumulating cardiometabolic RFs and advancing age as cardiorepiratory fitness declines. A nested Cox proportional hazard model was used to sequentially control for 3 groupings of RFs and medications. The investigators found that the unadjusted 5-year cumulative incidences of AF across the 4 strata of cardiorespiratory fitness were 18.8%, 9.5%, 5.0%, and 3.7%, respectively. For every 1-MET increase, there was an associated 7% decrease in the risk of AF. There was no attenuation of benefit when cardiorespiratory fitness was >10 METs.

The limitations of this study include the retrospective design reliant on coding of clinical characteristics at the time of exercise testing and linkage to billing codes to the subsequent development of AF. An ECG diagnosis of AF would have been more powerful, and the inclusion of atrial flutter as an end point would have been justified given the close pathophysiological underpinnings and clinical relationship.\(^{20}\) A remaining concern is the generalizability of the study. The population is largely a middle-aged cohort referred for stress testing, which presumably has higher prevalence of cardiovascular disease and RFs for AF. Furthermore, the effect of cardiorespiratory fitness on reduction in AF was more pronounced in obese and older individuals, presumed to have higher risk of AF. This limits extrapolation to intermediate- or low-risk groups. It would be reasonable to assume that less fit patients were more likely to be limited by or diagnosed with CAD or heart failure after stress testing. The investigators addressed this concern with adjustment for incident CAD as a time-varying covariate and subgroup analyses of those with incident left ventricular dysfunction or pre-existing CAD; the relationship of cardiorespiratory fitness to AF remained significant. However, incident cardiometabolic RF development over time before the coding of AF was not ascertained and may confound the result.

The fact that blacks are well represented strengthens the conclusion that cardiorespiratory fitness is inversely related to AF for 2 reasons. First, most AF studies enroll a lower proportion of ethnic minorities.\(^{1}\) Second, blacks are known to have a high burden of cardiometabolic RFs but a lower incidence of AF.\(^{1}\) Despite the potential for dilution of the observed effect, the results remain significant.

Overall, this study represents the first cohort to establish a link between cardiorespiratory fitness and incidence of AF, supporting the aforementioned link between physical activity and AF. However, we should recognize that physical activity and cardiometabolic RFs are different physiological markers and that each has a different association with risk of cardiovascular disease.\(^{21}\) It would not be surprising if there were a nonlinear relationship between cardiorespiratory fitness and AF, given this difference and the evident adverse effects in competitive endurance athletes. We should be careful not to overinterpret the results and to intensify the exercise prescription for our patients until several issues are further elucidated: (1) the potential for an upper limit of benefit, given concerns that high-level and sustained exercise training may adversely affect remodeling; (2) the potential benefit of exercise training once AF is established; and (3) the optimal way to improve cardiorespiratory fitness in at-risk populations.

The study is promising in that it suggests further reason to encourage exercise and opens the door to a strategy that complements ARREST-AF and ablation to mitigate the burgeoning epidemic of AF in the future.

Disclosures

None.

References


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Advay G. Bhatt and Kevin M. Monahan

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