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Exercise and Atrial Fibrillation: Prevention or Causation?

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Regular exercise contributes to improved cardiovascular health and reduced cardiovascular mortality. Previous studies have shown that regular physical activity and high cardiorespiratory fitness both contribute to a reduction in incident atrial fibrillation (AF). However, the risk of AF appears to be paradoxically increased by participation in endurance exercise. Although the mechanisms are not well understood, exercise-induced changes in autonomic tone alongside the development of an arrhythmogenic atrial substrate, appear to contribute to an excess of AF amongst athletes, despite an overall reduction in cardiovascular disease incidence. This review will (i) summarise the evidence showing that regular physical activity and exercise reduces AF incidence, (ii) review the evidence that supports an increase in AF risk by regular endurance exercise, and (iii) discuss the mechanisms and risk factors that may contribute to AF susceptibility amongst otherwise healthy athletes.

Keywords Sport • Arrhythmia • Physical activity • Autonomic • Prevention • Atrial fibrillation

Introduction

Q5 There is an undeniable benefit of physical activity and exercise for the reduction of cardiovascular disease incidence, morbidity and mortality [1,2]. In Australia, over a half of all adults report insufficient levels of physical activity. For those individuals who achieve or exceed guideline recommended levels of physical activity, the health benefits include a 30–
Q6 50% reduction in all-cause mortality [3,4].

However, there are small, yet clinically important caveats to the benefits of exercise. Firstly, although individuals achieving weekly exercise doses that far exceed the recommended guidelines have improved life expectancy and reduced cardiovascular disease [5], the risk of sudden cardiac death may be transiently elevated during and immediately post-exercise [6], particularly in those with unidentified cardiovascular risk factors or so-called 'silent' coronary atherosclerosis. Secondly, a small subset of competitive endurance athletes may experience ventricular arrhythmias potentially as a result of progressive right ventricular remodelling [7,8]. Finally, regular endurance exercise accumulated over many years appears to increase the risk of atrial arrhythmias [9], even despite evidence of reduced mortality within the same cohort (Figure 1).

Atrial fibrillation (AF) is the most common clinical arrhythmia with a growing burden worldwide [10]. In Australia, hospitalisations as a result of AF are rising annually, placing an urgent demand for strategies to reverse these trends [11]. Given the significant contribution of modifiable cardiovascular risk factors to the risk of AF [12], favourable lifestyle behaviours such as physical activity and exercise, that may lower the burden of hypertension, diabetes, and obesity, to name just a few, are also likely to contribute to a reduction in AF risk [13,14]. Indeed, the first section of this review, will briefly identify the key evidence that supports this hypothesis. However, the consistent evidence that shows AF risk to be higher amongst participants of endurance sports subsequently raises the question of how we balance the wide benefits of regular exercise with the potentially negative consequence of AF that may be associated with the accumulation of endurance exercise training over many years. This evidence will be presented alongside the potential mechanistic contributions in the second part of this review.

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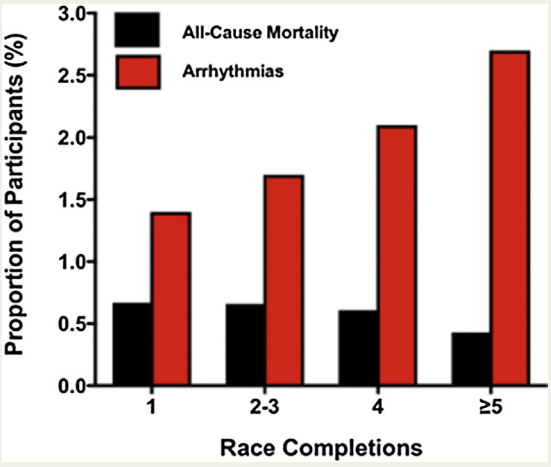

Figure 1 All-cause mortality (black) and AF incidence (red) amongst participants of a long-distance cross-country ski race. Data shows that despite a reduction in mortality for those with the most race participations, AF incidence is significantly higher. Data taken from Farahmand et al. and Andersen et al. [34,61].

Physical Activity, Endurance Exercise and Risk of AF

Physical Activity

A number of studies over the past decade, have sought to determine whether the known benefits of physical activity on heart failure and coronary artery disease, also apply with AF. Indeed, several studies have shown that AF incidence is lowest amongst the most physically active participants. In the Cardiovascular Health Study, participants in the highest quartile of physical activity had a 46% lower incidence of AF, compared to those who were relatively sedentary [15]. The benefits of exercise were reinforced by Swedish data, in which daily walking or cycling blunted the risk of AF by 12 and 19% in men and women, respectively [16,17]. In other studies, the primary benefit of physical activity appeared to be mediated through a blunting of the risk associated with other AF risk factors, such as obesity. For example, in both the Atherosclerosis Risk in Communities [18] and Women's Health Initiative Studies [19], the risk of AF associated with obesity was at least partially dampened by physical activity. However, not all data points to a benefit of physical activity with regards to AF risk; In the Women's Health Study, physical activity did not contribute to a lower risk of AF in adjusted analyses [20]. The contrasting findings regarding physical activity and AF may be due to several factors, including the presence of other risk factors known to promote AF, yet unaccounted for in adjusted analyses. Additionally, the methods for determining AF incidence vary widely, including regular electrocardiographs (ECGs) through to self-reported diagnoses of AF. Finally, physical activity is frequently self-reported from baseline, lending opportunity to subjective bias and time-varying changes in physical activity habits.

Cardiorespiratory Fitness

More recently, efforts to quantify the association between physical activity, exercise and AF have shifted towards evaluating AF risk in participants stratified by cardiorespiratory fitness (CRF), quantified objectively using an exercise stress test. In three separate cohorts, higher CRF was associated with a significantly lower risk of AF. In 1950 middle aged men, from the Kuopio Ischemic Heart Disease Study, patients in the third quartile of CRF (mean CRF: 9.3 METs), exhibited a 30% reduction in risk of AF over a 19-year follow-up [21]. Intriguingly, however, these benefits were blunted for those in the highest quartile (mean CRF: 11.6 METs). Similarly, in a larger cohort >60,000 adults referred for exercise testing and followed for 5 years [22], high CRF was associated with a 56% reduction in AF risk, a finding that was replicated in almost 6000 veterans who underwent exercise testing and were followed for 8 years [23]. Clearly from this data, maintaining high CRF contributes to a lower risk of future AF. However, the range of CRF achieved in most studies (~10-12 METs) is lower than that typically achieved by endurance athletes, thus limiting any conclusions regarding the relationship between more frequent exercise training and AF risk.

Incidence and Mechanisms of AF in Athletes

Endurance Exercise

Based on the evidence presented so far, it is reasonable to conclude that maintaining a fit and active lifestyle reduces the risk of AF. However, these benefits appear not to extend to those who participate in endurance exercise far beyond the volume recommended in current guidelines. The earliest evidence for an excess of AF amongst endurance athletes was from a cohort of orienteers [24], in which the prevalence of AF far exceeded that of a non-athlete control cohort (5.3% v 0.9%). Similar conclusions were drawn from a number of case-control studies, in which endurance sports participants were over-represented amongst patients with lone AF. Mont et al. [25] reported that the proportion of sportsmen amongst patients with lone AF was greater than seen in the general population (63% v 15%). Two further studies from the same centre reinforced these findings. Amongst 51 patients with lone AF [26], the proportion of patients engaged in sports practice was greater than in an age-matched control, free of AF (31% v 15%). In a further comparison of 109 lone AF patients with age-matched controls, >2000 cumulated lifetime hours of moderate or heavy physical activity was a significant predictor of AF incidence [27].

The role of endurance exercise as an arrhythmogenic risk factor has since been strengthened by additional studies documenting a higher risk of AF development amongst athletes versus non-athletes; amongst marathon runners, AF was significantly more prevalent than in an age and gender-matched, non-athletic control group (0.43 v 0.11%) [28]. In a comparison of former, professional cyclists with

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