Atrial Fibrillation in Athletes - The story behind the running hearts

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Introduction

Atrial fibrillation (AF) is the most commonly encountered arrhythmia in clinical practice but the mechanisms underlying the initiation and maintenance of AF are yet to be clarified. It is wellknown that regular exercise is beneficial to health and reduces the risks of cardiovascular diseases. However, recent studies suggest that long-term endurance exercise, including running, swimming, rowing and cycling, or vigorous competitive sports may increase the incidence of AF in these athletes. 1-3 Since different studies used different criteria to define the intensity of exercise, the association between exercise and AF in people who exercise simply for fitness is not well established. For instance, in the Cardiovascular Health Study, the incidence of AF in older adults (>65 years old) was lower with moderate-intensity but not high-intensity exercise.4 In the Physician Health Study, vigorous exercise, defined as any exercise strenuous enough to break sweat, was associated with an increase in the incidence of AF only in joggers younger than 55 years old.5 However, how much exercise is too much remains debatable. This review article is intended to provide a summary of the possible links between vigorous exercise and AF that occurs in endurance or competitive athletes.

Exercise and AF

It is widely accepted that regular aerobic exercise reduces cardiovascular risks.4-9 For instance, moderate physical activities can reduce the incidence of AF in elderly people.4 However, people who practice competitive sports or endurance sports have a higher incidence of developing AF in the absence of structural heart diseases (lone AF). Elosua et al.9 discovered that if the cumulative hours of life-time sports activities are longer than 1500 hours, there is an increased incidence of lone AF in these subjects. Another study by Mont et al.2 showed an increase in AF incidence if the subjects practiced more than 3 hours of endurance sports weekly for more than two years. A study1 on the incidence of lone AF in marathon runners, in comparison to sedentary men, demonstrated a higher incidence of AF in runners (annual incidence: 0.43/100 for runners, 0.11/100 for sedentary men). Karjalainen et al. [10] followed a group of elite male orienteers (N=300, 35-59 of age) and 495 age and gender matched control for 10 years. They found that although the mortality of the orienteers was much lower than controls (1.7% vs. 8.5%), the incidence of AF was much higher (5.3% vs. 0.9%). All these aforementioned studies suggest that the incidence of AF in male athletes is 1.8-8.8 folds higher than sedentary men.1,2,9,10,11

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Characteristics of AF in Athletes

AF in endurance athletes appears to have the following characteristics. First, they are typically young or middle-aged adults and have practiced endurance sports for several years. Several studies indicate that young or middle-aged athletes who had undergone long-term high-intensity training have the highest incidence of AF. Second, it is more prevalent in male than female athletes. Furlanello et al. followed 146 young elite athletes who had arrhythmia problems (male: 122, female: 24) for a mean of 62 months. In the 13 athletes who developed AF, all of them were male. Third, AF often occurs at night or after meal and less frequently during exercise, which implies that AF in endurance athletes may be related to increased vagal tone. However, AF does occur in endurance athletes during exercise, suggesting that the role of the sympathetic tone cannot be ignored. Fourth, lone, paroxysmal AF in endurance athletes can progress to persistent AF, in contrast to what was originally described. Hoogasteen et al. found that 17% exercise-related paroxysmal AF progressed to persistent AF. This finding was later verified by the GIRAFA study showing that 43% patients with exercise-related AF were in persistent AF.

The Mechanisms Underlying Exerciserelated AF

1. Exercise and the autonomic nervous system

Although high vagal tone manifesting as sinus bradycardia and asymptomatic AV conduction delay in well-trained athletes has been known for decades, clues suggesting the relationship between the autonomic nervous system (ANS) and AF in athletes originally came from the striking resemblance of the typical symptoms of this type of AF and the “vagal AF” originally described by Coumel. The classical symptoms of “vagal AF” described by Coumel include: (1) predominantly male between 30 and 50 of age, (2) usually occurs at night and rarely occurs between breakfast and lunch when the sympathetic tone is high, (3) rarely occurs during exercise or emotional stress, (4) relaxation following stress frequently triggers AF and (5) AF is often preceded by bradycardia lasting from seconds to hours. Since vagal stimulation had been used to induce AF for nearly a century, a logic explanation for AF in athletes is that chronic exercise “tunes” the ANS to be vagally predominant, which in turn triggers paroxysmal AF. However, this hypothesis has not been proven and “vagal AF” continues to be viewed as a rare form of AF that only occurs in a very small population of AF patients, such as endurance athletes.

The heart is richly innervated by the autonomic nervous system (ANS). The cardiac ANS can be divided into the extrinsic and intrinsic components. The former consists of the soma in brain nuclei and chains of ganglia along the spinal cord and the axons that course en route to the heart. The latter is composed of a neural network formed by axons and autonomic ganglia concentrated at the ganglionic plexi (GP) embedded within epicardial fat pads on the heart itself. The intrinsic cardiac ANS functions as the “little brain” on the heart as proposed by Armour et al.

In the past decade, the role of the cardiac ANS in the initiation and maintenance of AF has been actively investigated. Several basic and clinical studies have indicated that the initiation of paroxysmal AF requires the activation of both the sympathetic and parasympathetic components of the cardiac ANS, indicating that perhaps some degree of sympathetic influence may play a cooperative role in the initiation of “vagal AF.” Autonomic denervation has been shown in multiple clinical and experimental studies to suppress AF. Unfortunately, there is no animal model that reproduces the type of cardiac remodeling that is present in endurance athletes. Whether AF in endurance athletes is associated with a hyperactive autonomic state will require further basic and clinical studies.

2. Exercise and Atrial Enlargement (LAE)

Exercise increases the level of circulating catecholamine and leads to a hyperdynamic state of the circulation. In athletes undergoing long-term training, their hearts often develop adaptive changes such as LAE, left ventricular hypertrophy and enlargement. Increased left atrial pressure leads to stretch of the left atrial wall, resulting in shortening of the effective refractory period (ERP) and increasing ERP dispersion, which in turn facilitates the initiation and maintenance of AF. Using echocardiography, Pelliccia et al. studied 1777 athletes...
with structurally normal hearts who participated in 38 types of sport activities. The left atrial dimension was larger than 40 mm in 347 subjects (20%) and larger than 45 mm in 38 subjects (2%). None of the athletes had LV wall motion abnormality or reduced LV ejection fraction. Among the 38 sports, the incidence of LAE was significantly increased in 28 sports, particularly rowing (18%), cycling (10%), ice hockey (10%), rugby (7%) and soccer (7%). Interestingly, athletes with LAE are more likely to win an international competition (40%) than those without LAE (20%). In athletes with LAE, 86% of them had an increased LV end diastolic diameter (>55 mm), in contrast to 34% in athletes without LAE. Although the incidence of AF in athletes was not different from non-athletes, the authors concluded that LAE might be a physiological adaptation to exercise. In contrast, another study by Mont et al. found the LA dimension in former athletes, several years off vigorous training, remained larger than control subjects (38.4±6 mm vs. 34.5±3 mm). Even years after vigorous training had been discontinued, the incidence of AF in these former athletes remained higher than control subjects. Whether LAE is an epiphenomenon of vigorous exercise or is truly a risk factor for AF remains to be investigated.

3. Exercise and Inflammation.

Studies have shown that excessive exercise induced inflammatory responses in the body. For instance, excessive training may lead to tissue injury and subsequently activates circulating monocytes, which in turn produces large quantities of IL-1β, and/or IL-6, and/or TNF-α and systemic inflammation. In patients with lone AF, histological examination of the atrium revealed inflammatory responses compatible with the diagnosis of myocarditis in 66% of the patients. Chung et al. discovered that patients with AF ≤24 hours had higher C-reactive protein (CRP) levels than those in sinus rhythm. Persistent AF patients had a higher CRP level than paroxysmal AF patients and both groups had higher CRP levels than controls. That study is the first to document elevated CRP in non-postoperative arrhythmia patients. These findings were reinforced by a stepwise CRP elevation with higher AF burden. Despite the correlation between inflammation and AF, it remains unclear if inflammation helps initiate or maintain AF or is only a by-product of AF. Moreover, the relationship between exercise, inflammation and AF are yet to be better understood.

4. The Relationship between the Cardiac ANS and AF in Athletes.

The heart is richly innervated by the autonomic nervous system (ANS). The cardiac ANS can be divided into the extrinsic and intrinsic components. The former consists of the soma in brain nuclei and chains of ganglia along the spinal cord and the axons that course en route to the heart. The latter is composed of a neural network formed by axons and autonomic ganglia concentrated at the ganglionated plexi (GP) embedded within epicardial fat pads on the heart itself. The intrinsic cardiac ANS functions as the “little brain” on the heart as proposed by Armour et al. As discussed before, endurance athletes have the propensity for an elevated vagal tone, a higher level of biomarkers for inflammation and dilated atria. The one-million dollar question is: “What is the common trigger and substrate which help initiate and maintain AF in endurance athletes?” Atrial stretch in a dilated atrium is capable of abbreviating the atrial action potential and effective refractory period (ERP) as well as an increasing the ERP dispersion, providing an ideal reentry substrate for AF. However, a timely spontaneous premature beat (trigger) from the PV or non-PV site is still required to initiate AF in atria that have been preconditioned as a reentry substrate. An attractive candidate that provides both the trigger and substrate is a hyperactive state of the cardiac autonomic nervous system. Activation of the parasympathetic elements shortens the action potential and effective refractory period of the atrium and PV whereas activation of the sympathetic elements provides a larger Ca++ transient. A synergistic action of the sympathetic and parasympathetic elements can lead to early after depolarizations and subsequently spontaneous premature depolarizations (triggers). Meanwhile, a hyperactive state of the cardiac ANS may have already prepared a substrate for reentry which is caused by an increased dispersion of the refractoriness as a result of the heterogeneous innervation of the heart by the cardiac ANS. Moreover, cardiac ANS also activates bradykinins and interleukins that can lead to inflammation. In other word, the cardiac ANS...
may serve as the common facilitator for the dynamics of AF initiation and maintenance in athletes. Future studies will be needed to examine the role of the cardiac ANS in AF among athletes to develop a selective therapy to treat them.

5. Treatment for AF in athletes

The first step to treat AF in athletes is to exclude other medical conditions that may predispose endurance athletes to AF, such as hyperthyroidism and pericarditis.31-34 Substances such as cocaine, caffeine, anabolic steroids and sympathomimetics in cold medicines should be discontinued.32,33 In addition, structural heart diseases or other cardiac arrhythmic (e.g. Wolff-Parkinson-White syndrome, hypertrophic cardiomyopathy, long QT syndrome) should be excluded.33,34 As the mechanisms underlying AF in endurance athletes are not well understood, management of this type of AF is mainly based on limited evidence-based studies and therefore remains controversial. The following recommendations are proposed by the Study Group on Sports Cardiology of the European Association for Cardiovascular Prevention and Rehabilitation.33

After all the contributing factors have been eliminated, it is recommended that33 athletes in early stage of paroxysmal AF temporarily discontinue training for two months to stabilize sinus rhythm. The degree of improvement during this resting period determines if athletes can resume their training. In athletes without other cardiac disorders, the recommendation for sports participation also largely depends on the ventricular rate during AF. If history reveals a high ventricular rate or hemodynamic instability during AF, the athletes should be instructed to stop exercising on the emergence of palpitation or related symptoms.33 Such patients may need medications that slow the ventricular rate, ideally at doses that do not cause sinus bradycardia at rest or chronotropic incompetence during exercise.

Of note, the Task Force 7 of the 36th Bethesda Conference recommended that athletes with asymptomatic AF in the absence of structural heart disease who maintain a ventricular rate that increases and slows appropriately and is comparable to that of a normal sinus response in relation to the level of activity, while receiving no therapy or therapy with AV nodal-blocking drugs, can participate in all competitive sports.34 It remains to be determined if athletes with symptomatic AF should discontinue training for two months to stabilize sinus rhythm as recommended by the European task force.33

There is a theoretical risk of using β-block to treat this type of AF as it may further slow the sinus rate and produces an unopposed hyper-cholinergic state, which may indeed facilitate the formation of AF. The use of class Ia or Ic agents to treat AF in athletes remains to be clarified. Of note, AV nodal conduction can be enhanced during atrial tachyarrhythmia. Using class Ia or Ic agents may convert AF to atrial flutter, resulting in 1:1 conduction to the ventricle. Therefore, AV nodal blocking agents such as a β-blocker or Ca++ channel blocker should always be used in conjunction with class Ia or Ic agents.

Since the landmark report by Haissaguerre et al35 indicating that focal AF is often induced by rapid focal discharges originating from the pulmonary veins and/or adjacent atrial tissue, catheter ablation for AF has evolved to be the treatment of choice for drug-refractory AF, particularly for paroxysmal AF. Furlanello et al36 performed catheter ablation (PV isolation ± atrial flutter ablation) on 20 male competitive athletes who had very symptomatic lone AF. Except for one patient whose right inferior pulmonary vein could not be isolated, all other patients had successful PV isolation in the first ablation procedure. Interestingly, when all the patients were restudied, 62 (81%) of the previously isolated PVs have resumed conduction. Most importantly, the incidence of conduction recurrence did not correlated with the recurrence of AF, suggesting that the triggers and/or substrate for AF in these patients are not limited to PVs and adjacent atrial tissue. After 2.3 ± 0.4 ablation procedures, only two athletes continued to have short episodes of AF during 36.1 ± 12.7 months of follow-up. The maximal exercise capacity also significantly improved after ablation. Whether AF in endurance athletes responds differently to ablation than non-athletes remains to be clarified. In addition, AF in athletes may be related to a hyperactive state of the ANS. Ablation targeting the ganglionated plexi along with PV isolation theoretically may yield better results but it remains to be proven.
Conclusions

The association between moderate-intensity exercise and AF remains controversial. But in athletes undergoing high-intensity and long-term exercise, this association appears to be much stronger. A hyperactive state of the cardiac autonomic nervous system may play an important role in the initiation and maintenance of AF in endurance athletes.

References