The role of aerobic exercise in the prevention and management of atrial fibrillation. Friend or foe?

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Summary

Atrial fibrillation is the arrhythmia with the highest prevalence world-wide. In fact, scientific literature seems to show a high prevalence of atrial fibrillation in endurance athletes too. However, currently the relationship between atrial fibrillation and aerobic exercise is controversial. On the one hand, aerobic exercise could be defined as a useful tool to be used as primary prevention strategy for the development of cardiovascular diseases, including arrhythmias. On the other hand, some authors identify it as a risk factor, specifically if it is performed at high intensity with large regular volumes. But the exact mechanism by which aerobic exercise might increase the risk of atrial fibrillation is unknown, although it could be related to anatomical and functional changes at the cardiac level. This review aims to update the knowledge about the effect of aerobic exercise on atrial fibrillation to establish a prescription pattern. The results of the present work, according to the current evidence, show the aerobic exercise as a non-pharmacological strategy, both for the primary and secondary prevention of atrial fibrillation. The preventive effect of aerobic exercise on atrial fibrillation seems to be related to the reduction of associated risks. Although there is no consensus on the exercise load, it is considered that aerobic exercise should be practiced often and at a moderate-vigorous intensity to get the greatest benefits. More research is required to determine the best parameters of aerobic exercise in atrial fibrillation.

Key words:
Cardiac arrhythmia.
Primary prevention.
Secondary prevention.
Risk factor.

El papel del ejercicio aeróbico en la prevención y manejo de la fibrilación auricular. ¿Amigo o enemigo?

Resumen

La fibrilación auricular es la arritmia que presenta mayor prevalencia en la población a nivel mundial. De hecho, la bibliografía científica existente parece mostrar también una elevada prevalencia en deportistas de resistencia. Sin embargo, actualmente la relación entre la fibrilación auricular y el ejercicio aeróbico resulta controvertida. Por un lado, el ejercicio aeróbico puede considerarse una herramienta de prevención primaria para el desarrollo de enfermedades cardiovasculares, incluidas las arritmias. Por otro, realizar actividades de alta intensidad de manera regular con grandes volúmenes, ha sido identificada por algunos autores como un factor de riesgo. Actualmente, se desconoce el mecanismo exacto por el cual el ejercicio aérobico podría incrementar el riesgo de fibrilación auricular, pero podría estar relacionado con cambios anatómicos y funcionales a nivel cardíaco. Esta revisión pretende realizar una actualización del efecto que presenta el ejercicio aérobico sobre la fibrilación auricular para establecer una pauta de prescripción. Los resultados del presente trabajo, según la evidencia actual, parecen mostrar al ejercicio aérobico como una estrategia no farmacológica útil tanto para la prevención, como para el tratamiento de la fibrilación auricular. El efecto preventivo del ejercicio aeróbico en la fibrilación auricular parece estar relacionado con la disminución de factores de riesgo asociados. Aunque no existe consenso sobre la carga de ejercicio, se considera que el ejercicio aeróbico debería practicarse regularmente y a una intensidad moderada-vigorosa para alcanzar los mayores beneficios. Se requieren más investigaciones para determinar los mejores parámetros de ejercicio aeróbico en la fibrilación auricular.

Palabras clave:
Arritmia cardíaca.
Prevención primaria.
Prevención secundaria.
Factor de riesgo.

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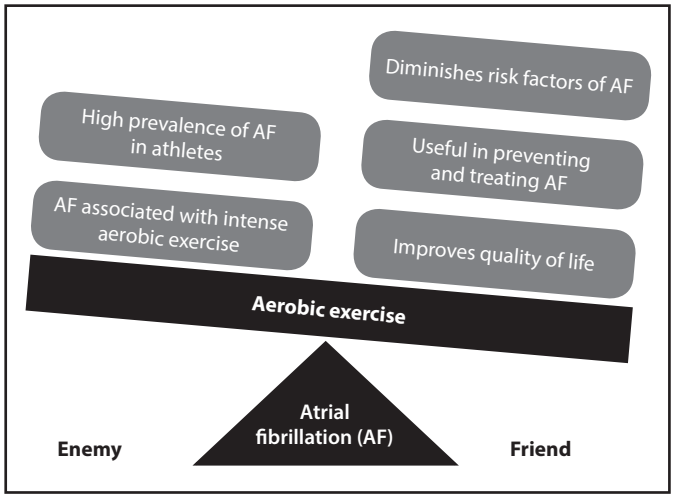
Introduction

A series of complications exist that can alter a normal heart rate, making it quicker, slower or more irregular[1]. Atrial flutter, ventricular tachycardia, supraventricular tachycardia, ventricular fibrillation and atrial fibrillation (AF) are the most common arrhythmias. Among them, AF is most prevalent – 1-2% of the general population[2,3] – and is associated with a high mortality rate and associated cardiovascular mortality[1,4].

Age has been determined as the main risk factor for developing AF[5,6]. However, other conditions such as hypertension, obesity, chronic kidney disease or diabetes mellitus are also considered to be predisposing factors[7,8]. It has been demonstrated that regular aerobic exercise (AE) has positive effects on controlling blood pressure[9], body weight index[10], kidney function[11] and insulin sensitivity[12]. Therefore, AE can positively influence a number of predisposing factors and should be considered as a possible prophylactic to AF[13]. Maximum AE has also been successfully applied as a non-pharmacological treatment in AF patients, showing reversion rates of up to 27% in patients with scheduled electrical cardioversion[14]. Furthermore, AE positively affects well-being and quality of life of such patients independently of its efficacy on AF's symptomatology[15]. However, there is a certain controversy regarding the relationship between AE and AF (Figure 1). While moderate AE appears to be an adequate tool for FA prophylaxis and treatment, some research demonstrates that high doses of AE increase the probabilities of developing lone AF; in other words, without other associated heart diseases[16]. For example, the prevalence of AF in cross-country skiers has been registered at 12.8% compared to 1-2% within the general population[17]. An association, marked by the characteristics of the AE training load, appears to exist in the apparently paradoxical relationship between AE and AF. The volume, frequency and intensity of AE can determine its positive or negative influence, although the exact limits of this relationship are still unknown. Performing exercise of moderate intensity, volume and frequency appear to have a preventive effect, while vigorous exercise practised over a long time increases the risk of developing AF[14].

Figure 1. Controversy in the relationship between aerobic exercise and atrial fibrillation.



This paradox beckons a two-directional consideration regarding physical exercise. On the one hand, it concerns the perspective of training professionals and, on the other, that of clinicians. This work aims to review of the state of the art on AF – including its links to AE – and to establish a prescription framework for AE based on scientific evidence for the prevention and treatment of AF.

Atrial fibrillation

Heart contractions are produced through electrical signals that originate in the right atrium, concretely in the sinoatrial node (SA node). These signals make the atria contract and pump blood to the ventricles. Blood flows from the SA node through the muscular fibres to the atrioventricular node (AV node), which gives the signal to the ventricles to contract and pump blood to the lungs and the rest of the body[18]. In AF, electrical signals do not begin in the SA node but instead come from several different locations. Consequently, the heart's contractions are not synchronized and the atria and ventricles contract independently of one another[18]. This misalignment entails a loss of function in the atrium which, in turn, leads to blood stasis predisposing to blood clot formation[19].

Such an alteration in the heart's electrical system makes it beat quickly and irregularly[19]. In normal conditions, the heart beats regularly at a rate of between 60-100 beats per minute (bpm). In AF, this rate is higher—ventricular frequency between 90-170 bpm—and is accompanied by a high rate of atrial contraction (>300 bpm)[18,20]. An analysis of the heart rate via electrocardiogram (ECG) can allow an irregular heart rate that is characteristic of AF to be observed. Other defining aspects can also be observed, such as the absence of P waves, which sometimes appear as visible electrical activity in V1 derivations and irregular RR intervals[19,20].

Types of atrial fibrillation

Symptoms of AF include palpitations, angina pectoris, fainting—including syncope—, dyspnea, chronic fatigue and limited exercise tolerance; patients with AF can also, in some cases, be asymptomatic[1,21]. But regardless of its clinical pattern, AF negatively affects patients' quality of life[22]. *The European Heart Rhythm Association*[19-21] proposes a classification of AF based on its clinical presentation and its impact on patient quality of life (Table 1). Other possible references to classify AF are based on its form of presentation (i.e. acute or chronic) and duration of the arrhythmia (i.e. more or less than 48 hours). According to this classification, three types of AF are defined (Table 2): paroxysmal, persistent and permanent or chronic[20,23].

It is common for AF to co-exist with other cardiovascular diseases[24,25]. However, the type of AF most frequently associated with the

Table 1. Classification of atrial fibrillation types of the European Hearth Rhythm Association (EHRA).

Score	Characteristics
EHRA I	No symptoms.
EHRA II	Light symptoms that do not impede normal daily activity.
EHRAIII	Strong symptoms that affect normal daily activity.
EHRA IV	Incapacitating symptoms that impede normal daily activity.

Table 2. Classification of atrial fibrillation types based on their presentation and duration.

Type	Characteristics
Paroxysmal	Characterized by short-lasting episodes recurring within 48h, capable of evolving up to 7 days. This type of AF is spontaneously interrupted.
Persistent	Lasts 7 days or more Interruption of the arrhythmia is not spontaneous and must be induced by medication or electrical cardioversion.
Chronic	AF is classified as chronic when it is impossible to re-establish the heart's rhythm after one year of treatment or several recurrences. In this case, treatment must be interrupted and the arrhythmia should be accepted by the doctor and patient as chronic.

intense practice of AE is diagnosed with an absence of other symptoms after a physical examination, a thyroid function test, an electrocardiogram test and a stress test. This lone AF is usually diagnosed in young adult males (i.e. <60 years) with a prevalence oscillating between 2 and 50%, depending on the population of the study[16].

AF epidemiology

AF affects between 1-2% of the general population[26], with increases in those rates affecting as much as 0.5% more youths and adults younger than 40[13] and up to 8% in adults older than 80[27]. Regardless of age, the incidence of AF is 1.5 times greater in men than in women[23]. Despite a clearly established difference regarding the sexes and AF, the exact mechanisms of those differences are unknown; the influence of hormonal, structural and electro-physiological factors have been suggested in this respect[28]. In Spain, the total prevalence of AF is 4.4%[4] while in the USA it affects between 2.7-6.1 million people, with an estimated increase of 15.9 million people expected in 2050[7].

In contrast to what is observed in other cardiovascular diseases, AF has a higher prevalence among the physically active and athletic population, with a prevalence between 0.2% and 60%[3]. AF has been particularly linked to endurance sports and has proven to depend not only on the intensity of the activity but also the accumulated number of hours that the patient has practised the activity throughout his/her life[19]. It is remarkable that an inverse association has also been observed. Mont *et al.* (2002) recorded a greater rate of sports practise (62.7%) among lone AF patients in comparison with the general population (15.4%)[29]. The type of sport practised also appears to influence the probability of developing AF as it is more common in marathon runners, cyclists and cross-country skiers than those who practise other types of sports[7].

Participation in long-duration endurance sports has increased in recent years, which entails an increased incidence risk of AF associated with exercise in the forthcoming decades[30].

Risk factors

Based on the data related to prevalence, age appears to be the main risk factor in developing AF. Indeed, 70% of AF patients are within an age range between 65 and 85 years. AF is also commonly associated with other cardiovascular diseases. Hypertension is experienced by 70-80% of patients diagnosed with AF in the sedentary population[31]. Variations in blood pressure observed during episodes of hypoxemia and hypercapnia[5,8] in patients with sleep apnoea also appear to be responsible for predisposition in developing AF in this population (i.e. 4 times more probable)[5]. Finally, patients with cardiac insufficiency (CI) are 5 times more at risk of developing AF[5]. It is a two-way relationship between CI and AF inasmuch as patients with AF are also 2 to 3 times more at risk of developing CI[7]. The development of AF in CI patients can also predispose to an increased risk of thromboembolism and a symptomatic deterioration of CI[20].

Obesity is also considered a predisposing factor to developing AF. Concretely, it has been determined that there is a 49% probability of developing AF in obese patients in comparison with patients of normal weight[32]. This is likely due to alterations in the cardiac structure that can lead to increased intra-atrial pressure. Moreover, obese patients can be resistant to treatment with antiarrhythmics and radiofrequency ablation[7,8]. Other factors such as cigarette smoking, chronic kidney disease, diabetes mellitus, excessive alcohol consumption, thyroid disorders and family history are accepted as risk factors[5,6].

The high prevalence of AF among those who practise endurance sports indicates that AE could be a significant predisposing factor to developing AF[2]. Such an association with endurance sports suggests that AF could be more linked to the duration and frequency of the exercise performed than with its intensity. In this spirit, accumulated years of practising endurance activities has been associated with a gradually increased risk of AF (i.e. 1.16 OR for every 10 years practised)[13]. The same conclusion has been reached in other research. For example, Molina *et al.* (2008) reported an annual incidence rate of lone AF in marathon runners of 0.43/100 while the rate for sedentary men was 0.11/100[33]. Similarly, very frequent exercise (i.e. 5-7 sessions per week) increases the risk of developing AF in comparison with the sedentary population[34]. The same findings have been replicated upon comparing the incidence of AF in individuals that practise more than 5 hours of exercise per week with

that of individuals who practise less than 1 hour per week[35]. Furthermore, recent meta-analyses have observed a significant association between age and the practise of sport. The risk of suffering from AF in adults aged under 54 years is almost twice as great as the general population; this association has not been observed in regards to older athletes. However, publication bias cannot be ruled out[36].

The mechanism behind high frequency, long-duration AE-induced AF could be related to the heart's ability to adapt to this type of stimulus, which induces a remodelling of the general cardiac structure[37] and, in particular, of the atria[2,38]. Recent research carried out with rodent models demonstrated how frequent AE (i.e. 1 hour per day for 8 to 16 weeks) increased susceptibility to develop AF. Subsequent analysis of heart structure and functioning pointed to atrial enlargement, fibrosis and changes in autonomous regulation as potential factors responsible for the development of AF[39]. In line with these findings, it has been shown that approximately 20 % of competitive athletes have a left atrial (LA) diameter of more than 40 mm[2].

Such findings are opposed to those published by Brugger *et al.* (2014). In this retrospective study, the structure and function of the heart were analysed in three groups of amateur runners with different accumulated doses of exercise throughout their lives: less than 1,500 hours, between 1,500-4,500 hours and more than 4,500 hours. The findings indicate that the structural and electrical remodelling of the heart does not influence mechanical atrial function and, thus, could not be considered responsible for the possible development of AF[40]. The incidence of AF in the runners that participated in this study was 6.6%, which is less than the average given their condition. Nevertheless, these findings provide an opportunity for future studies to clarify the physiological mechanisms behind exercise-induced AF.

Furthermore, the literature indicates that the relationship between physical exercise and AF is dependent upon the patient's sex. Intense physical exercise has been associated with lesser risk of AF among women and higher risk among men[41,42]. Mohanty *et al.* (2016) hypothesize that a "threshold effect" must exist in physical exercise which, once passed, makes risk of AF greater; this threshold would seemingly be different between men and women[41]. Despite that, the physiopathological mechanisms of the sexual differences regarding AF are still hypothetical[43].

Many studies on physical exercise and AF only include male athletes despite women undertaking a considerable proportion of athletic activities[36,42]. Recent research describes specific remodeling associated with the gender of endurance athletes. Apparently, men have a higher risk of AF associated with an enlarged right atrium and of greater remodeling in comparison with women[44].

In addition to the previously discussed aspects, genetic factors must also be considered given their relevance in recent publications[45,46]. Fatkin *et al.* (2018) offer three hypotheses to describe the relationship between genetic variations and AF in athletes caused by physical exercise. Firstly, genetic variations exist that can trigger AF in isolation from physical exercise. Secondly, genetic variations associated with AF could have an additive effect that is independent of physical exercise. Finally, complex synergistic interactions could exist between genetic factors and physical exercise. Moreover, mecanosensitive ion channels are proposed as a nexus between genetics and alterations in the heart's remodeling[45].

Atrial fibrillation treatment

Treatment of AF can be divided into two types of therapy: pharmacological and non-pharmacological. Pharmacological therapy attempts to restore sinus rhythm and to avoid thromboembolic complications[47,48], while non-pharmacological therapy is used when success is not reached through the former approach or as another option to improve the patient's symptoms and quality of life[49]. Antiarrhythmics and anticoagulants are two types of drugs prescribed in pharmacological therapy. Antiarrhythmic drugs can be used with the aim of controlling the heart rate or heart rhythm. This type of drug is used not only to improve the symptomatology of AF and reduce the possibility of a cardiovascular event from occurring, it is also used as secondary treatment to improve tolerance to AE[47]. On the other hand, anticoagulant drugs aim to reduce the probability of clot formation and emboligenic events, which is especially high for patients with AF[49].

Pharmacological therapy

Some of the drugs used to control the heart rate include digoxin, calcium channel blockers (CCB) – such as Verapamil or Diltiazem – and β-blockers. These drugs stall blood flow through the AV node, making ventricular contractions slower[47]. Each patient's characteristics should be taken into consideration when choosing the proper drug. For example, since β-blockers and CCBs reduce blood pressure this should be particularly taken into consideration if prescribed to patients with hypotension. Digoxin is recommended for patients with arterial hypotension or sedentary lifestyles. It is used as a complement to other drugs when ineffective alone[48,49]. According to a study by AFFIRM[47] on the efficacy of such drugs, when used as a first line of treatment they attained success rates of 70% for patients treated with β-blockers, 54% for CCB treatment–with or without digoxin–and 58% for digoxin treatment[47].

When patients did not apply pharmacological treatment to control their heart rhythm, the recurrence rate of AF was 71-84% in the first year. This rate can be reduced to 44-67% by applying pharmacological therapy[47]. Amiodarona is one of the drugs used to control the heart rhythm. Alternative drugs include Droneradona, Sotalol and Dofetidila[48]. Electrical cardioversion can also be used to control the heart rhythm. This method has 90% efficacy compared to pharmacological cardioversion (40% success rate), but it cannot be carried out on patients that are ineligible for sedation[47,48]. The risks associated with electrical cardioversion are thromboembolic processes, which entail a risk of 1-2% and can lead to a cerebrovascular accident (CVA). This risk can be mitigated with anticoagulants[20,47]. In any case, the use of antiarrhythmics after electrical cardioversion is necessary as the probability of recurrence remains high otherwise[48].

It has been demonstrated that drugs aimed at controlling heart rate and heart rhythm improve tolerance to exercise in patients with AF[50]. However, there are not enough studies to determine which strategy could be considered best to achieve improvements regarding risk of CVA or death[50]. Thus, choosing any of these strategies depends on each patient's circumstances[49].

One of the complications associated with AF is blood clot formation. This risk increases with age, from 1.5% in patients younger than 60 to 24% in patients older than 80, independently of the type of AF[49].

The European Society of Cardiology indicates that the CHA_2DS_2-VAS_c scale be used to determine the risk of CVA in patients with AF. In patients with CVA risk factors (CHA_2DS_2-VAS_c score of 1 or more in men and 2 or more in women) oral anticoagulants are recommended. Warfarin and other vitamin K antagonists were the first anticoagulants used with AF patients. However, the use of direct thrombin inhibitors (dabigatran) and activated factor X inhibitors (apixaban, edoxaban and rivaroxaban) has increased rapidly as they can be administered in fixed doses and do not require regular monitoring[51,52].

Non-pharmacological therapy

Non-pharmacological therapy for treatment of AF includes an invasive procedure, catheter ablation, and AE. Catheter ablation is an invasive procedure used when patients with resistance or intolerance to antiarrhythmic drugs in order to re-establish and maintain the sinus rhythm[52,53]. This procedure consists in placing catheters in the pulmonary veins to isolate electrical signals, making circular lesions that remodel the electrical system. The success rate of catheter ablation does not appear to depend on the patient as much as it does the type of AF[54]. In this regard, efficacy of the procedure for paroxysmal AF is >70% in a single attempt and can reach up to 80-90% recovery[49]. Conversely, several attempts are required to obtain reasonable results for persistent AF[53]. Moreover, a "hybrid" treatment is currently being proposed to patients that incorporates antiarrhythmic drugs after catheter ablation, but solid evidence does not exist supporting this procedure[52].

Similarly to the case of pharmacological therapy, the effects of therapy via AE depends on the dose administered. AE prevents the development of AF, most likely due to its beneficial effect on associated risk factors, such as heart disease, diabetes mellitus or obesity[13].

In a study performed by LEGACY, it was observed that weight loss in obese individuals with AF was responsible for reducing AF symptomatology, as per assessments via an AF Severity Scale and Holter monitor. This study included a total 355 individuals that were monitored over a period of 5 years. The group of participants who lost most weight (≥10%) presented better results in comparison with those who lost less weight. It, thus, appears possible that several mechanisms exist connecting weight loss with the reduction of AF, since being overweight is associated with several cardiovascular risk factors that are, in turn, associated with increased risk of AF. For this group of participants, in addition to following certain dietary recommendations, low-intensity physical exercise was practised initially three times a week, reaching up to 200 minutes of moderate-intensity physical activity per week[55].

But AE can also prove to be efficient as a treatment for patients with AF. Hegbom *et al.* (2007) administered a program consisting in 24 AE sessions over 8 weeks with a group of patients under 70 years of age with permanent AF. The sessions included exercises to strengthen the core interspersed with moderate-vigorous periods of AE (i.e. 70-90% maximum heart rate). The exercise regiment significantly improved the patients' quality of life, their tolerance to AE and their ability to perform basic everyday activities[56]. Moderate aerobic exercise (i.e. up to 70% maximum heart rate) also appears to be sufficient to generate improvements in patients' quality of life as well as their resting heart rate. Patients' high acceptance of this treatment is notable; adherence to the treatment was registered at 96%. It should be highlighted that the aforementioned AE interventions were brief in duration (i.e. 8 and 12 weeks, respectively), although quite frequent (i.e. 3 sessions per week) and ranging from moderate to vigorous intensity. The findings of this work should be interpreted with caution, as each patient's participation was subject to eligibility criteria and not all patients with AF would be capable of performing exercise programs of this sort. Finally, it is worth highlighting that AE at maximum intensity can be used as shock treatment for AF reversion. Gates *et al.* (2010) applied an incremental maximal exercise treadmill test (i.e. Bruce protocol) with a group of 18 patients aged 36 to 74 on scheduled electrical cardioversion. In five of the participants (i.e. 27%), their AF was reverted after 5.5-18.2 minutes of exercise in heart rate ranges of 164-203 bpm, probably owing to the abrupt change followed by a readjustment of the sympathetic/parasympathetic balance[14].

Conclusion

Scientific evidence demonstrates the efficacy of numerous options to treat AF. Among them, AE appears to be an adequate strategy not only for treatment but also to prevent AF. The findings indicate that performing moderate AE reduces the risk of developing AF and in some cases is efficient to improve the symptomatology of existing AF. It is still unknown how the intensity, volume and frequency of such activity influence efficiency in this regard. In fact, the long-term practise of intense AE is associated with a higher probability of developing AF. Considered as a whole, these findings suggest that AE can be a contrastive prevention strategy and potentially an alternative form of treatment in lieu of other therapies. While the recommended intensity of such exercise must depend on the patient's characteristics, the exercise should be performed frequently. However, there is a lack of scientific evidence establishing the combination of the safest and most efficient AE training load parameters and the possible interactions between AE and other treatments or associated diseases.

Conflicts of interest

The authors do not declare a conflict of interest.

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