CorSalud 2020 Jul-Sep;12(3):327-335

Cuban Society of Cardiology

Review Article

Physical exercise and atrial fibrillation in athletes and heart failure patients: Is it favorable or harmful?

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Este artículo también está disponible en español

ARTICLE INFORMATION

Recibido: 18 de diciembre de 2019
Aceptado: 30 de enero de 2020

Competing interests
The author declares no competing interests

Abbreviations
AF: atrial fibrillation
CHF: chronic heart failure
PE: physical exercise
VO_2: oxygen consumption

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ABSTRACT

Atrial fibrillation (AF), an expected epidemic in the coming decades, is commonly caused by ischemic heart disease and high blood pressure, and it is also associated with overweight and obesity. Physical exercise (PE) is considered a way to correct cardiovascular risk factors and it is therefore recommended in the prevention of cardiovascular diseases. It is also an integral part of cardiac rehabilitation. Although it has been noted that PE can increase the risk of AF, the cardiovascular benefits of regular physical activity are unquestionable. An improved health status and a longer life expectancy have been proven in endurance athletes. Mild or moderate PE protects against AF, which may be associated with an improved left ventricular systolic and diastolic function, as well as with a decreased arterial stiffness. Cardiac rehabilitation with PE is a currently approved indication in patients with chronic heart failure, with or without AF, which is shown to increase functional capacity and life quality, as well as to reduce overall mortality and hospitalizations.

Keywords: Physical exercise, Atrial fibrillation, Cardiac rehabilitation, Physical education and training, Heart failure, Functional capacity

Ejercicio físico y fibrilación auricular en atletas y en pacientes con insuficiencia cardíaca: ¿Favorable o perjudicial?

RESUMEN

La fibrilación auricular (FA), epidemia esperada en las próximas décadas, es comúnmente causada por la cardiopatía isquémica y la hipertensión arterial, también se asocia con el sobrepeso y la obesidad. El ejercicio físico (EF) se considera una medida que corrige los factores de riesgo cardiovascular y, por tanto, se recomienda en la prevención de las enfermedades cardiovasculares, y forma parte integral de la rehabilitación cardíaca. Aunque se ha señalado que el EF puede incrementar el riesgo de FA, los beneficios cardiovasculares de la actividad física regular son incuestionables. Se ha comprobado un mejor estado de salud y una mayor expectativa de vida en atletas de resistencia. El EF ligero o moderado protege contra la FA, lo que puede estar asociado a un mejoramiento de las funciones sistólica y diastólica del ventrículo izquierdo, así como a una disminución de la rigidez arterial. La rehabilitación cardíaca con EF, es una indicación aprobada actualmente en pacientes con insuficiencia cardíaca crónica, con FA o sin ella, la cual está demostrado que incrementa la capacidad funcional y la calidad de vida,

así como que reduce la mortalidad general y las hospitalizaciones.
Palabras clave: Ejercicio físico, Fibrilación auricular, Rehabilitación cardíaca, Educación y entrenamiento físico, Insuficiencia cardíaca, Capacidad funcional

INTRODUCTION

The prevalence of atrial fibrillation (AF) is estimated to be between 1-2% in general population, and more than 15% in people over 80 years old[1,2], however, taking into account that this cardiac arrhythmia can often be asymptomatic, such figures may be underestimated. Its prevalence increases with age, it increases markedly after 65 years old and it is very low, almost non-existent, before 25 years old[3].

Due to the expected population aging in the upcoming decades at a global level, an epidemic of AF can be expected, which becomes increasingly evident nowadays; therefore, there is an urgent need to study and to precise the underlying mechanisms of this arrhythmia and to implement and apply the appropriate prevention programs.

Regarding generic issues, AF is classified as: paroxysmal, recent-onset, and persistent or permanent. In addition, clinical subtypes of the arrhythmia have been suggested, including the secondary to underlying structural heart disease and AF in athletes.

Atrial fibrillation is commonly caused by ischemic heart disease and high blood pressure, and it is also often associated with overweight and obesity[4]. Physical exercise (PE), which prevents the increase of body weight as well as the development of high blood pressure, is considered a measure that corrects cardiovascular risk factors and, it is therefore, frequently recommended as a preventive measure in healthy individuals, as well as in hypertensive and obese patients; it is also an integral part of rehabilitation and secondary prevention in patients with ischemic heart disease, even after a myocardial infarction and the onset of heart failure[5-7].

Physical exercise and atrial fibrillation

Although there is evidence on PE increasing the risk of AF[3,8,9], the cardiovascular benefits of regular physical activity are unquestionable. For more than 25 years, Sarna *et al*[10] have shown an improved health status and longer life expectancy in endurance athletes compared to a similar group of non-athletes. However, extreme or intensively prolonged PE, as well as physical inactivity, may favor the development of AF, indicating an "ambiguous" effect of physical exercise that protects the heart at low loads but which can cause it damage at high loads, due to the activation of specific biochemical and neurohormonal mechanisms[2,9].

The debate about PE as a risk factor for AF has existed for more than two decades, nevertheless, in 2016, two independent groups of researchers described a "U-shaped" association between physical activity and AF[8]. Morseth *et al* [11] described a "U-shaped" phenomenon in the relationship between physical activity performed during leisure time and AF in 20,484 adults who were followed-up and examined prospectively during 20 years. The risk of AF was higher, but not significant, in individuals who practiced intense physical exercise than in those who had little activity; while a significantly higher risk was found only when the onset of permanent AF was considered.

Calvo *et al*[12] also found a "U-shaped" relationship between the duration of high-intensity PE and AF in a case-control study. The lowest risk of AF corresponded to the lowest point of the "U-shaped" curve and it was found in individuals engaged in regular, time-limited physical training; while the highest risk was observed in those performing vigorous PE as a sport practice with more than 2 000 hours accumulated in a lifetime. Inactive individuals showed an intermediate risk of AF. Thus, vigorous or high-intensity physical activity, performed over a long period of time throughout life, was noted as the strongest predictor of AF, suggesting that repeated atrial injuries or stimuli during a long period of time correlated with an arrhythmic substrate that could develop AF[12].

Since then, several studies have researched the complex relationship between physical exercise and AF, and many of them have confirmed the link between vigorous PE and AF[8]. Abdulla and Nielsen[13], in a meta-analysis study, showed that intense physical exercise in athletes was 5.3 times more likely to develop AF than case-control studies. However, high blood pressure, which is the most common risk factor for AF, only showed an increased frequency of association of 1.42 times, demonstrating the relevance of the association between vigorous physical exercise and this arrhythmia. Hence, the term lone AF should be used with caution when dealing with individuals who have been intensively active for a

long time.

However, the relationship between PE and AF is less evident in non-athletes, due to the heterogeneity of methods used to assess the physical exercise intensity, as well as the calculation to determine the number of hours of intense physical exercise performed over a long period of time.

Triggering mechanisms of atrial fibrillation related with extreme physical exercise in athletes

The so-called "athlete's heart" is the heart that efficiently pumps blood to the powerful muscles of athletes who practice strong competitions for a long time with high oxygen demands. We can observe in them functional and structural changes of the mentioned organ that can predispose to cardiac arrhythmias[9].

As a consequence of meeting the fundamental principles of physical training and its physiological effects[14], the heart of a trained individual is able to decrease its rate of contractions at rest, while it increases it during maximum physical exercise, in order to supply the increased oxygen demands. There is evidence that athletes under extreme conditions can exaggeratedly increase the vagal tone and reduce the atrial refractory period, which facilitates the re-entrant mechanism, by also activating the adrenergic tone, which –consequently– facilitates the onset of atrial or ventricular arrhythmias[15].

Large volumes of PE performed during many years, even in trained endurance athletes, can lead to pathophysiological disorders, damaging the autonomic nervous system as well as to develop cardiac remodeling[9].

The anatomical substrate can be the atrial growth and remodeling, which includes anomalous collagen deposition and inflammation. From this we derive the recent concept that the athlete's heart can be proarrhythmic, regardless the existence of structural or electrical genetic abnormalities[15]. Recently, a new syndrome called PAFIYAMA –acronym for Paroxysmal Atrial Fibrillation in Young and Middle-aged Athletes– has been described, that includes events of paroxysmal AF in young or middle-aged athletes, which considers the athlete's heart prone to AF[16].

Other underlying mechanisms in the development of AF in athletes include[9,16]:

- Changes in ion channels in pacemaker cells.
- Disorders in calcium binding proteins.
- Loss of cell junctions and collagen deposition, presumably triggered by the atrial wall thickening[2]

Aldosterone is a mediator of fibrosis and AF that increases in plasma after physical exercise in endurance runners[17,18], even when trained, with the aim of maintaining the ionic and fluid balance necessary for the competition. However, it is not yet known whether aldosterone contributes to create the proarrhythmic substrate in endurance athletes[19].

The mechanism by which mild or moderate PE protects against AF also remains unclear[9]. However, reduced risk of AF may be associated with an improved systolic and diastolic function, as well as to a decreased arterial stiffness, which, over the years, often takes place in athletes and other individuals.

It has been proven that PE improves the cardiorespiratory function in young adults and in the general population[20,21], including patients with ischemic heart disease and myocardial infarction[6,7]; in addition, it improves the profile of cardio-metabolic risk factors, decreases sympathetic tone and produces favorable changes in cardiac structure and function. All this can contribute to the protective mechanisms against the appearance of AF in individuals who regularly follow mild or moderate intensity PE programs, although further studies are needed to define these mechanisms.

Physical exercise and atrial fibrillation in heart failure

Atrial fibrillation and chronic heart failure (CHF) are closely related to age; both increase their prevalence in relation to some risk factors, such as high blood pressure, elderly and obesity[22]. More than 50% of patients with CHF present AF, and more than a third part of those with AF develop CHF; moreover, cases that combine both conditions have a higher risk of mortality than those with only one of them[23].

Physical activity and PE can, in addition to improving symptoms, have antiarrhythmic effects, especially on individuals with paroxysmal AF, as well as protecting against the development of this arrhythmia[24-26].

The HF-ACTION study[27,28], the largest research carried out up to date, which analyzed the effects of aerobic physical training in stable patients with CHF and reduced ejection fraction, showed that PE was associated with increased physical capacity, improved life quality, and decreased new hospitalizations and overall mortality. In the primary analyses of these research outcomes, the AF was highly predictive of overall mortality and hospitalization. By

making a cut of this study, Luo *et al*[29] analyzed the relationship between basal AF and its evolution with physical training (**Figure 1**), described the future events of these patients and found the important findings described in the **box**.

Previous studies have shown that CHF and AF show a worse prognosis when they take place combined in the same patient. In the Framingham study's population, two adjusted analyses showed up to twice the risk of death in those cases suffering from CHF with reduced ejection fraction together with AF[23,30]. Also, in the primary analysis of the aforementioned HF-ACTION study, O'Connor *et al*[27] found AF combined with CHF as a strong predictor of mortality and hospitalization. In this same study, it was pointed out that PE produced an improvement, although modest, in parameters related to physical exercise, for example a 4% increase in the mean peak oxygen consumption (VO_2).

It should be noted that even modest increases in peak VO_2 should be important, since they express an objective measurement of the cardiorespiratory function, even more than other simple variables related to physical activity[31]. The VO_2 peak can predict, with a high degree of reliability, the presence and prognosis of future cardiovascular diseases; it is particularly interesting in determining the prognosis of patients with CHD[32].

It should be noted that previous studies, where physical training programs in patients with AF have been assessed, have also shown a large increase in physical exercise capacity, although they have included series with not many cases and few of them with CHD[33,34]. However, in other recent prospective studies, PE has been associated with positive effects in patients with AF[11,24,25,35]. Proietti *et al*[35] , for example, in a study including 20000 adult patients, observed a lower overall mortality in those cases with AF who reported individual practice of PE on regular basis.

Researchers from the Mayo Clinic in Rochester[36], in a study published in 2018, including 12,043 non-cardiovascular patients referred for exercise stress test, found −after a mean clinical follow-up of 14 years− that 1,222 (10.1%) of them developed AF. They also pointed out that in those who presented the arrhythmia and had a basal aerobic functional capacity of less than 75%, the risk of dying or having a stroke was significantly higher compared to those who had 105% or more. They concluded then, that an improved cardiorespiratory condition is associated with a lower risk of AF, stroke, or death. They pointed out as well that the risk of stroke and death in patients with AF is inversely associated with the cardiorespiratory capacity, thus demonstrating, as the main finding of this study, that the risk of incidental AF, stroke, and mortality has an inverse relationship with the cardiorespiratory aptitude or capacity[36].

Figure 1. High performance athlete during an exercise stress test.

Cardiac rehabilitation programs for patients with atrial fibrillation

Although Myrstad *et al*[37] have recently stated that there are no guidelines for physical activity and physical exercise for patients with AF, several protocols have been published and used in these cases, many of them included in the study by Risom *et al*[38]. In addition, in the case of CHF patients with reduced ejection fraction and AF, the American College of Cardiology together with the American Heart Association has recommended, in their corresponding clinical practice guidelines, physical training in these cases[39].

Although several studies have shown benefits in terms of improving cardiovascular functional capacity with the practice of PE in patients with AF, as well as the consequent decrease in the incidence and recurrence of this arrhythmia events[35,40,41], only a few have examined the impact of cardiac rehabilitation with physical training on this type of patient,

Box. Summary of the HF-ACTION study outcomes[27,28] regarding the benefits of physical exercise in heart failure patients with reduced ejection fraction and atrial fibrillation[29].

Characteristics of the patients
- Elderly: patients were generally older and presented more comorbidities, as well as less physical exercise capacity under basal conditions
- Males: most frequent
- Black race: less frequent
- Worst functional class: (New York Heart Association)
- Worst renal and cardiac function
- Six min shorter test
- Less maximum oxygen consumption
Clinical evolution
- Higher events' frequency: patients with AF had significantly worse evolution in all the assessed aspects, compared to those without the arrhythmia
- Mitigation of association after risk adjustment
Physical exercise
- Similar benefits: patients with AF, despite of having a more severe heart failure, achieved similar benefits with PE, after completing a monitored and structured program, compared to those without AF
- Similar benefits in functional class and life quality: there was no significant difference between the groups (with or without physical exercise and selected at random), between the state of the initial AF and its clinical or functional evolution
- Physical exercise did not increase the appearance of AF's adverse events

AF, atrial fibrillation; PE, physical exercise

without having assessed its true impact on mortality and adverse cardiovascular events[42].

With the aim of evaluating the significance of AF in patients with cardiovascular disease enrolled in cardiac rehabilitation, Younis *et al*[42] assessed 304 patients with AF and 1,873 case-control studies without this arrhythmia who took place in a rehabilitation program, all of them had a confirmed cardiovascular disease, mainly after acute myocardial infarction, angioplasty or coronary surgery, decompensated heart failure, and valve replacement or plasty. Patients took place in a structured six-month cardiac rehabilitation program consisting on 60-minute PE sessions twice a week and an individualized protocol was used according to the consensus document developed by the European Society of Cardiology[43]. A maximum exercise stress test was performed, using the Bruce protocol at the beginning of the program, which was repeated 8±5 months later[44].

Patients with atrial fibrillation showed lower levels of initial physical aptitude compared to their non-AF peers; nonetheless, these patients had greater increases in functional capacity during the rehabilitation program than those without the arrhythmia, which had been previously reported by Vanhees *et al*[45]. Therefore, according to the outcomes of Younis *et al*[42], basal functional capacity is the most important predictor of cardiovascular complications or overall mortality in patients with a history of AF who took place in cardiac rehabilitation programs. Survival analysis (Kaplan-Mayer) showed a significant decrease ($p<0.001$) in the occurrence of events at five years in patients where improvement of their physical condition was demonstrated. In addition, cardiac rehabilitation may decrease the risk of morbidity and mortality in patients with AF, although this effect may be relatively modest. Patients at high risk can be easily identified by performing an exercise stress test prior to the start of the rehabilitation (**Figure 2**). In their case, it might be useful to prescribe a program of intensive supervised cardiac rehabilitation in order to increase their functional capacity and, consequently, to improve their future evolution.

As a conclusion, it is reaffirmed that in patients with AF taking place in cardiac rehabilitation programs with PE, the resulting increase in cardiovascular function, assessed by a conventional exercise stress test or by analysis of exhaled gas, is associated with a decrease in the risk of mortality or new hospitalizations during their clinical follow-up.

Life quality related to health

Other outcomes from the HF-ACTION study also showed that physical training provided a modest, though significant, increase in health status determined by the Kansas City Cardiomyopathy Questionnaire[28,29]. In this analysis, patients with AF had a significantly lower functional and physical exercise capacity, but presented a similar health status related to their disease, compared to patients in sinus rhythm in basal conditions. Although patients with

AF achieved similar short-term gain of cardiopulmonary reserve and functional status with PE, they reported only minimal improvements in health status with physical exercise.

Physical exercise has previously shown to mildly increase the life quality and symptoms in patients with permanent AF, but this has been verified with the use of other health status's assessment instruments, for example, the well-known SF-36 in its short form[29,46].

In many studies, it is difficult to assess and to compare the health status of this type of population incorporated to physical training due to the use of different scales and instruments, as well as several intervention programs with PE, which often prevents reaching definitive conclusions in this regard.

CONCLUSIONS

Atrial fibrillation in patients with chronic heart failure is associated with elderly, reduced physical exercise capacity under basal conditions, as well as with an increased frequency of complications in form of new clinical events; however, in cases with chronic heart failure without atrial fibrillation, there is no difference in the response to physical exercise related to a satisfactory clinical evolution or favorable changes in physical exercise capacity.

There is evidence that functional capacity is inversely proportional to atrial fibrillation and its recurrence. In the HF-ACTION[27-29] study, the physical exercise volume had a range in time from three to seven METs (metabolic equivalents) or hours per week, which was associated with a reduction in cardiovascular mortality and new hospitalizations due to chronic heart failure in a 30%. This is not exactly the 36 sessions of physical exercise to be performed in 12 weeks that is proposed as a method to obtain long-term benefits.

PERSPECTIVES

Cardiac rehabilitation is a currently approved indication in patients with chronic heart failure, with or

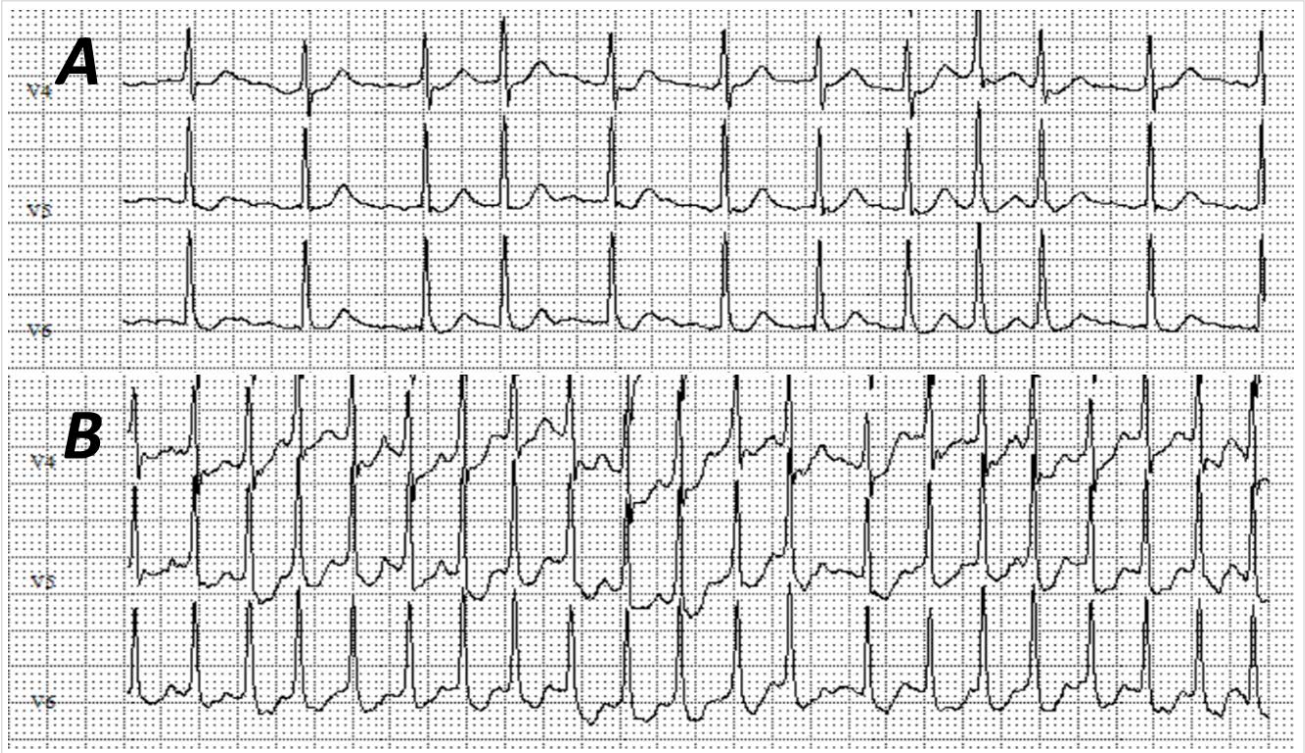

Figure 2. Electrocardiographic trace of an evaluative exercise stress test carried out in a treadmill (Ergocid- AT Plus, Combiomed [Cuba]), in a 49-year-old woman with a mitral prosthesis that was surgically placed three months before (due to a mitral disease of rheumatic origin), with the aim of putting her into a rehabilitation program with supervised physical exercises. She had a heart rate of 120 beats per minute in basal conditions (**A**) and reached 204 beats per minute in maximum physical exercise (**B**).

without AF, which is shown to increase functional capacity and life quality, as well as to reduce overall mortality and hospitalizations. In order to meet this purposes 36 PE sessions should be recommended, as part of rehabilitation, during 12 weeks, with indication of being continued at the hospitals or at home, with the aim of reaching 90 minutes of physical exercise per week in the first three months, followed by 120 minutes later indefinitely.

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