Narrative review

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The controversial relationship between exercise and atrial fibrillation: clinical studies and pathophysiological mechanisms

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Atrial fibrillation is the most common clinically significant arrhythmia observed both in the general population and in competitive athletes. The most important risk factors are all preventable by regular physical activity. However, although the benefits of moderate physical activity in controlling cardiovascular risk factors and decreasing the risk of atrial fibrillation have been extensively proved, concerns have arisen about the potential negative effects of vigorous exercise, particularly in endurance athletes. Furthermore, in a subset of patients with atrial fibrillation younger than 60 years, routine evaluation does not reveal any cardiovascular disease or any other known causal factor. This condition is called 'lone atrial fibrillation', and the potential mechanisms underlying this condition are speculative and remain to be clarified. Atrial ectopy, increased vagal tone, changes in electrolytes, left atrial dilatation, and fibrosis have been proposed among others as potential mechanisms. However, no convincing data still exist. Particularly, the increase in left atrial size represents in athletes a physiological adaptation to exercise conditioning and the presence of biatrial fibrosis has not been demonstrated in humans. Thus, contrary to patients with cardiovascular disorders, the atrial substrate seems to play a secondary role in healthy athletes. This review article analyzes the controversial relationship between atrial fibrillation and physical activity, with a particular attention on the pathophysiological mechanisms that could be responsible for atrial fibrillation in the athletic population.

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Introduction

Atrial fibrillation is the most common clinically significant arrhythmia, with an estimated prevalence in the general population of 0.4–1.0%.[1] Atrial fibrillation prevalence increases with advancing age, ranging from 0.5% in young patients (aged <40 years) to more than 5% in patients aged greater than 65 years,[2–4] and this positive association is partly explained by the increasing prevalence of risk factors for atrial fibrillation. The most important risk factors, such as hypertension or diabetes mellitus, are all preventable by regular physical activity.[5] Other cardiac and noncardiac conditions, including structural heart disease, valvular heart disease, alcohol consumption, smoking, and hyperthyroidism, have also been described as risk factors for developing atrial fibrillation.[6–11] However, in a subset of patients with atrial fibrillation younger than 60 years, routine evaluation does not reveal any cardiovascular disease or any other known causal factor. This condition has been termed 'lone atrial fibrillation' (LAF). The prevalence of LAF in the general population ranges from 2–10% to 30% in the studies conducted in patients seeking medical attention.[12]

Atrial fibrillation is also the most common arrhythmia in the athletic population and is more frequently observed in middle-aged than in young athletes.[13] Although the benefits of moderate physical activity in controlling the cardiovascular risk factors and decreasing the risk of atrial fibrillation have been extensively proved,[14–18] concerns have arisen about the potential negative effects of vigorous exercise, particularly in endurance athletes.

Unfortunately, the cause and pathophysiology of atrial fibrillation in athletes are still poorly understood. This article discusses the prevalence of atrial fibrillation in the

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athletic population and explores the pathophysiological mechanisms. Given that the goal of this article is to provide a perspective on how different pathophysiological factors operate to cause atrial fibrillation in athletes, considerations concerning the treatment options for atrial fibrillation in the athletic population go beyond the scope of this review and have not been reported.

Epidemiology

Atrial fibrillation in athletes

Reports from the epidemiological studies demonstrating atrial fibrillation in athletes have been variable on the basis of age, years of training, and type of sport practiced (Table 1). The first article to suggest an increased risk of atrial fibrillation in healthy middle-aged men who practice sport was published by Karjalainen *et al.*[19] in 1998. The authors studied 300 top-ranking orienteering veterans compared to 495 controls. All individuals were enrolled at an age of 35–59 years and retrospectively assessed after 11 years by means of a questionnaire. The incidence of atrial fibrillation was evaluated after excluding from both groups all individuals who had dropped out, died, or had developed during the follow-up risk factors for atrial fibrillation. In this study, atrial fibrillation was observed in 5.3% of athletes vs. 0.9% of controls ($P = 0.012$), with an incidence of atrial fibrillation per year of 0.48 and 0.08%, respectively. Although the authors concluded that sport activity increases the risk of atrial fibrillation in healthy middle-aged men, the study has some limitations. As noted by Delise *et al.*,[20] individuals who had dropped out or died were about twice as many in the control group when compared with athletes (25.5 vs. 13%). Furthermore, the incidence of LAF was very low in the control group (0.9% in 11 years, 0.08% per year), even in a population range at the end of the follow-up from 46 to 72 years. Finally, when analyzing the entire population, the incidence of atrial fibrillation was similar between athletes and controls (6.1 vs. 4.6%; $P = 0.4$).

Despite these limitations, this article was food for thought and stimulated further studies to explore this topic. Indeed, in 2002, Mont *et al.*[21] published a retrospective analysis of LAF patients seen at the outpatient arrhythmia clinic, showing that the proportion of regular sport practice among men with LAF was higher than that from the general population (63 vs. 15%). The same population was analyzed in a case–control study with two age-matched controls for each case from the general population.[22] The analysis showed that sport practice increased the risk of developing LAF more than five times [odds ratio, OR 5.6 (1.35–19)]. The association of current sport practice with LAF was observed at more than 1500 h of sport practice. As noted by Delise,[20] both studies have a selection bias and the results can be at least in part explained by the fact that the Catalonia group of Mont *et al.* is acknowledged to have great expertise in arrhythmias in athletes; consequently, many sportsmen with atrial fibrillation attend their center.

The same research group investigated 183 individuals who ran Barcelona Marathon in 1992 and 290 sedentary healthy individuals included in the REGICOR (Registre Gironí del Cor) study.[23,24] After 10 years of follow-up, the annual incidence rate of LAF among marathon runners and sedentary men was 0.43/100 and 0.11/100, respectively. Although these results were consistent with the previous observations, the study presents the limitation to collect during the follow-up a small number of events ($n = 9$ in marathon runners and $n = 2$ among sedentary individuals). Moreover, 43.6% of runners in this study were smokers and more frequently had a hypertensive response during effort (22 vs. 8%) compared with the sedentary individuals, two conditions related *per se* to atrial fibrillation. Finally, although sport practitioners show a higher relative risk (RR) of LAF when compared with sedentary individuals, the absolute risk of LAF in this active population remains low (<0.5/100 years).

Again in 2006, Heidbuchel *et al.*[25] demonstrated in a group of middle-aged patients undergoing cavo-tricuspid

Table 1 Main studies depicting the risk for atrial fibrillation in athletes

Author, journal, and year of publication	Age (years), mean ± SD (athletes vs. controls)	Number of cases/ number of controls	Type of sport	Cases of atrial fibrillation (athletes vs. controls)
Karjalainen *et al.*, BMJ, 1998[19]	46 ± 7 vs. 50 ± 5	262/273	Orienteering	12/228 (5%) vs. 2/212 (0.9%)
Mont *et al.*, Eur Heart J, 2002[21]	44 ± 13 vs. 49 ± 11	32/19	Endurance sports (>3 h/week)	NR
Elosua *et al.*, Int J Cardiol, 2006[22]	41 ± 13 vs. 44 ± 11	51/109	Endurance sports	16/31 (51%) vs. 35/129 (27%)
Molina *et al.*, Europace, 2008[23]	39 ± 9 vs. 50 ± 13	252/305	Marathon	9/183 (5%) vs. 2/290 (0.7%)
Heidbuchel *et al.*, Int J Cardiol, 2006[25]	53 ± 9 vs. 60 ± 10	31/106	Cycling, running, or swimming >3 h/week	25/31 (81%) vs. 50/106 (48%)
Pelliccia *et al.*, JACC, 2005[26]	24 ± 6 vs. NA	1777/NA	Mixed sports	14/1777 (0.8%) vs. NA
Mont *et al.*, Europace, 2008[30]	48 ± 12 vs. 48 ± 10	107/107	Endurance sports	83/120 (69%) vs. 24/96 (25%)
Myrstad *et al.*, Scand J Med Sci Sports, 2013[31]	69 vs. 72	509/1867	Long-distance cross-country sky	13.2% vs. 11.6%
Baldesberger *et al.*, Eur Heart J, 2008[34]	67 ± 7 vs. 67 ± 6	134/62	Cycling	6/62 (10%) vs. 0/62 (0%)
Grimsmo *et al.*, Eur J Cardiovasc Prev Rehabil, 2010[54]	69 ± 10 vs. NA	78/NA	Cross-country sky	12.8% vs. NA

NA, not available; NR, not reported.

isthmus ablation for common atrial flutter that patients engaged in endurance sport more frequently developed atrial fibrillation during the follow-up compared with the nonendurance population (81 vs. 48%; $P = 0.02$, respectively). Thus, this study suggests that endurance sport may increase the recurrence of atrial fibrillation after ablation for atrial flutter.

Although these previous studies have demonstrated a possible association between exercise and atrial fibrillation, other investigations have not suggested an increased risk of atrial fibrillation in sports practitioners. In 2005, Pelliccia *et al.*[26] found a prevalence of atrial fibrillation of 0.3% among 1777 healthy athletes (age: 24 ± 6 years), thus similar to that observed in the general population, with no difference between those with left atrial diameter less than 40 mm and more than 40 mm. Although this study was conducted in a relatively young population of athletes and left atrial size was assessed only by anteroposterior diameter, the results were obtained in a large population of athletes, engaged in different sporting disciplines, thus the results must be considered with attention.

In a different population, Mozaffarian *et al.*[18] demonstrated that older adults performing moderate physical activity have a lower risk of atrial fibrillation when compared with sedentary individuals.

A recent systematic review and meta-analysis by Abdulla and Nielsen[27] concluded that, even if the risk of atrial fibrillation development in athletes seems to be significantly higher than in nonathletes or in the general population [OR (95% confidence interval, CI) = 5.29 (3.57–7.85); $P = 0.0001$, and Z-score = 8.08], the available sample of the studies was small and controls were not appropriately age-matched in all the studies. Furthermore, the results may also be associated with some bias attributed to the variation in the level of endurance practiced by the different types of athletes across the studies.

A further consideration is that, although a direct relationship between atrial fibrillation and exercise has to be definitively confirmed, LAF in athletes is not necessarily associated with an increased risk of death, maybe because other factors like the lower prevalence of coronary artery disease may reduce the overall risk of mortality and also because persistent atrial fibrillation develops in only a minority of male endurance athletes.[28]

Atrial fibrillation and vigorous exercise: does the degree of intensity play a role?

There are limited data on the role of vigorous exercise in the development of atrial fibrillation in individuals participating in exercise at a less competitive level or even exercising daily.

Aizer *et al.*[29] published in 2009 the results from the Physician's Health Study, which prospectively followed up 16 921 apparently healthy men for 12 years. The authors demonstrated that an increased risk for developing atrial fibrillation at 3-year follow-up compared with controls can be observed only in individuals aged less than 50 years performing highly vigorous exercise, particularly jogging (RR 1.53, 95% CI 1.12–2.09; $P < 0.01$). Conversely, in middle-aged men older than 50 years, exercise, moderate and even vigorous, does not increase the risk of atrial fibrillation.

Vigorous physical exercise associated with occupational activities may theoretically pose a similar risk, and data from the prospective GIRAFA (Grup Integrat de Recerca en Fibril-lació Auricular) study, conducted in 107 consecutive patients with LAF recruited at the emergency room, seem to confirm this theory.[30] Intense physical activity for more than 564 h was associated with a risk for developing atrial fibrillation of 7.31 (95% CI 2.33–22.96; $P = 0.0006$) and 1–563 h was associated with a nonsignificant risk of 1.77 times (95% CI 0.22–14.26; $P = 0.50$).

In a population of 509 elderly Norwegian men with a history of long-term endurance sport practice (cross-country skiers), Myrstad *et al.*[31] demonstrated a higher incidence of atrial fibrillation compared with 1768 elderly men in the general population, with an added risk for atrial fibrillation of 6.0 percentage points. Interestingly, light and moderate leisure-time physical activity during the previous years reduced the risk for atrial fibrillation. The authors hypothesized that exercise intensity was associated with a risk for atrial fibrillation in a U-shaped pattern: whereas moderate intensity was associated with a lower incidence of atrial fibrillation, people reporting the highest intensity had the same incidence as people not exercising.[31] Thus, there could be potential in the cardiovascular adaptations to exercise for a plateau or even a decline in benefits at more extreme levels of endurance exercise.[32] However, data are scant and further prospective studies are essential to investigate whether the degree of intensity of exercise could play a role in the risk for developing atrial fibrillation.

Atrial flutter in athletes

As described by Coumel,[33] high vagal tone in young healthy adults may create a substrate in which LAF and atrial flutter co-exist and they seem to be two expressions of the same underlying condition. Most of the described series included patients suffering concomitant atrial fibrillation and atrial flutter; Hoogsteen *et al.*[28] found that 10% of athletes with atrial fibrillation also suffer from episodes of atrial flutter, suggesting that endurance sports contribute to the development of both arrhythmias. Endurance athletes have a higher risk of suffering from atrial fibrillation after common flutter ablation[25] and Baldesberger *et al.*[34] found a higher incidence of atrial flutter rather than atrial fibrillation in their series of veteran cyclists. Claessens *et al.*[35] found that patients with atrial flutter more frequently performed

regular sports activity, compared with controls ($P < 0.0001$). Endurance was the main sports activity and the proportion of individuals engaged in long-term endurance sports was significantly higher in the lone atrial flutter group vs. the control group (31 vs. 8%; $P = 0.0003$). Thus, chronic sports practice, in particular endurance sports, might play a role in the pathogenesis of atrial flutter in some patients, even if further data are needed.

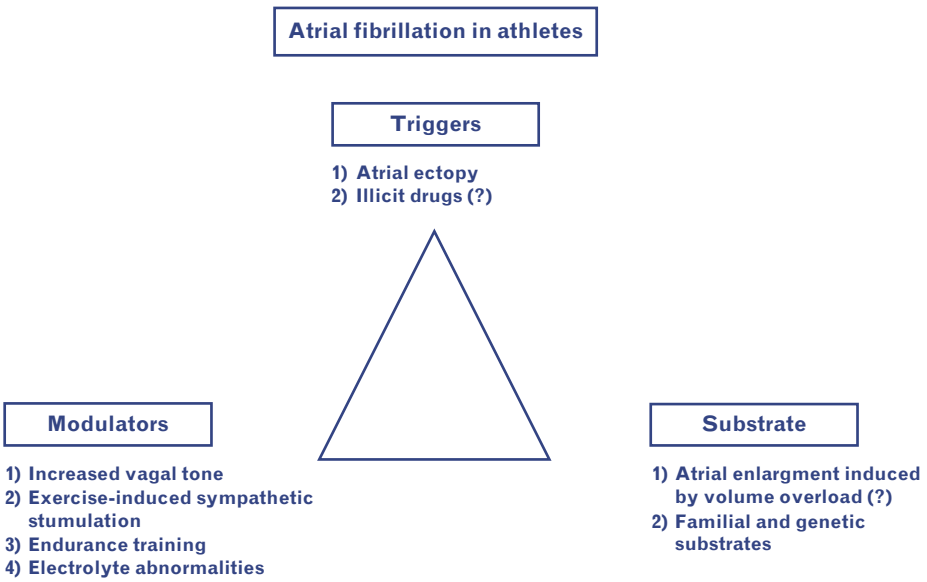
Pathophysiology of atrial fibrillation in athletes

It is well accepted that arrhythmias depend on triggers, substrates, and modulators, and these factors may be present in relation to physical activity.[36,37] Unfortunately, the pathophysiological mechanisms responsible for the development of atrial fibrillation in athletes remain speculative and mostly rely on the experimental data. Atrial enlargement and fibrosis, atrial ectopy, increased vagal tone, changes in electrolytes, among others, have been proposed as the mechanisms. The possible etiopathogenic factors contributing to atrial fibrillation in athletes are reported in Fig. 1.

Biatrial size and function in athletes: adaptive or maladaptive remodeling?

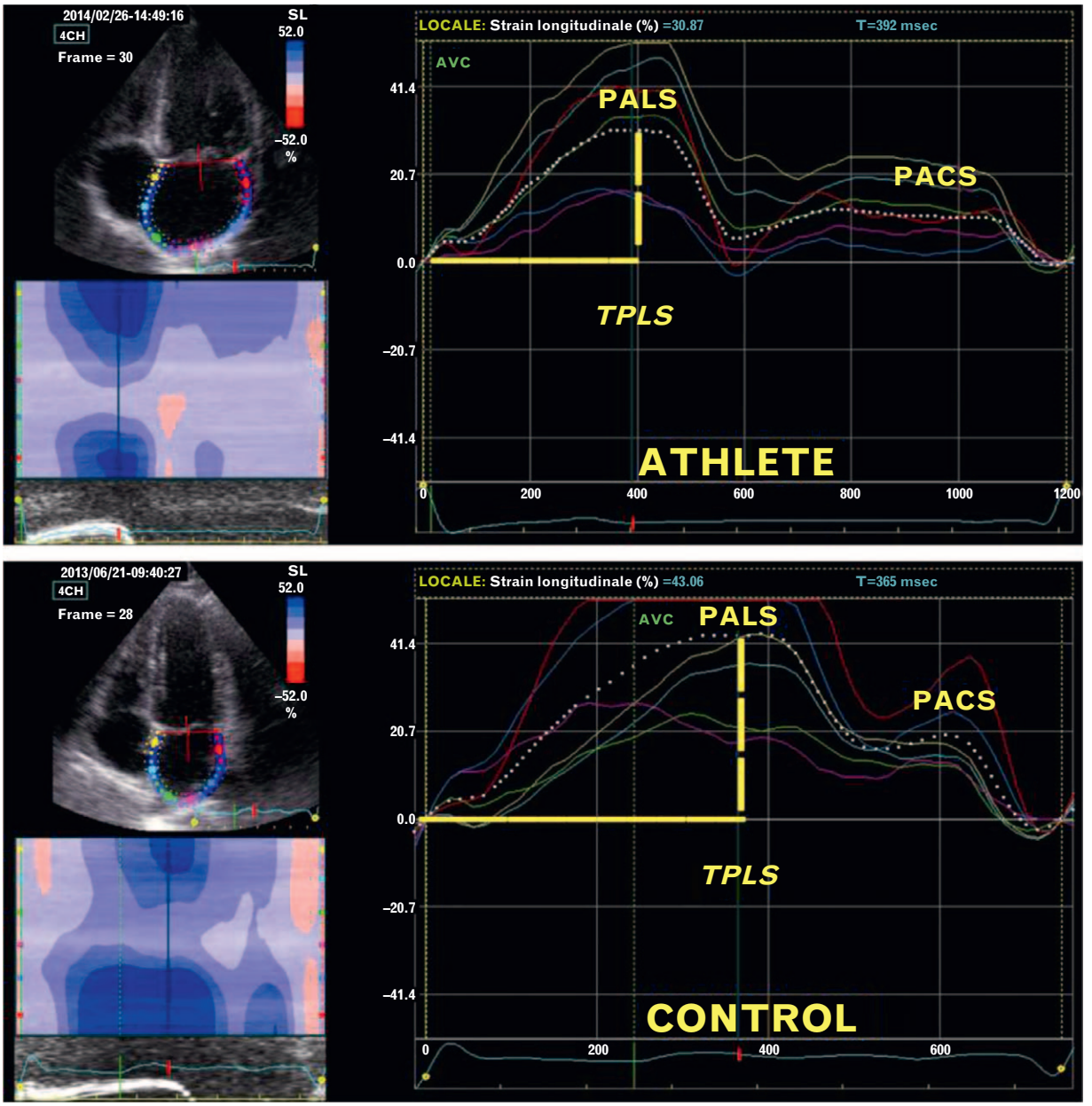
Morphological left atrial remodeling in trained athletes has been recognized as a component of the physiologic cardiac adaptation to exercise conditioning.[38–41] A significant proportion (>20%) of highly trained athletes exhibit an increase in left atrial size,[38,39,41] which in 2% of cases may be so marked[38] that it may mimic the atrial dilatation observed in patients with structural cardiac diseases.[42] In athletes, atrial remodeling occurs in close association with increase in left ventricular cavity size and may be an expression of the global cardiac adaptation induced by intensive athletic conditioning.[38–41] Contrary to the interpretation of atrial remodeling as a benign adaptation, Mont *et al.*[30] demonstrated that left atrial anteroposterior diameter was linearly associated with LAF (OR, 95% CI 1.51 (1.25–1.83, $P = 0.0002$). The authors interpreted the dilatation of the left atrium as a consequence of volume and pressure overload, similar to the data from the hypertensive patients. However, left atrial size is known to be insufficient to provide mechanistic information about the left atrium itself, and, contrary to the previous belief, peculiarities of the left atrial remodeling in the context of athlete's heart go beyond the mere dimensional volumetric increase, including physiological changes in atrial function. In a study conducted on professional soccer players, using two-dimensional (2D) speckle-tracking echocardiography (STE) to characterize myocardial deformation, our group demonstrated that top-level athletes exhibit significant differences in left atrial function, compared with controls, with a normal left atrial reservoir function and a reduced left atrial active contribution to left ventricular diastolic filling at rest[39] (Fig. 2). This phenomenon is associated with a normal and even supernormal diastolic function, and is accompanied by a shift of left ventricular filling period toward early diastole, primarily because of an increase in flexibility, elasticity, and distensibility of left ventricular myocardium.

Fig. 1



Possible etiopathogenic factors contributing to atrial fibrillation in athletes. This figure reports the possible triggers, modulators, and substrates involved in the development of atrial fibrillation in athletes. Note that atrial fibrosis and atrial dilatation induced by pressure overload have not been included, according to the scant data available in humans. The term atrial 'dilatation' has been replaced by atrial 'enlargement' in order to underline the physiological benign meaning of atrial remodeling in athletes.

Fig. 2



Comparison of left atrial myocardial deformation dynamics between athletes and controls. In these representative cases, a reduction in left atrial contractile function (PACS, peak atrial contraction strain) can be observed in the athlete (top) compared with the sedentary control (bottom), because of the physiological shift of left ventricular filling toward early diastole. Furthermore, contrary to the data observed in disease, in which a delay of left atrial time-to-peak longitudinal strain (TPLS) is observed, left atrial TPLS occurs early during the cardiac cycle.

According to the possible increased prevalence of atrial flutter in athletes, particularly typical atrial flutter, a macro reentrant circuit in the right atrium (RA), we characterized right atrial function by 2D STE in 100 top-level athletes and in 70 sedentary controls.[40] Although the right atrial size was increased in athletes, the right atrial function was preserved and a reduction in right atrial active emptying filling was observed in athletes, according to a better diastolic function and a shift in right ventricular filling period toward early diastole, similarly to data observed for the left atrium. Interestingly, despite an increase in atrial size, left atrial and right atrial filling pressures were within the normal range in athletes, suggesting that biatrial enlargement occurs in a model of volume rather than pressure overload.[39,40]

Recently, Brugger *et al.*[43] further supported these data, demonstrating in 95 amateur male runners that left atrial anatomical and electrical remodeling does not have a negative impact on the atrial mechanical function. They

suggested that, given a preserved left ventricular diastolic function, left atrial structural remodeling has little impact on its function, because left atrial emptying is predominantly passive.

Thus, taken together, these studies suggest that biatrial enlargement is a benign adaptation to exercise conditioning and in healthy athletes the atrial substrate seems to play a secondary role, with the triggering activity of pulmonary veins being the predominant mechanisms.[20] Conversely, it seems more plausible in individuals with cardiovascular disorders, in which it has a more important role in the electrogenesis of atrial fibrillation.

Biatrial response to exercise conditioning

Most of the evidence on sports cardiology relies on cross-sectional studies that have the intrinsic limitation to be unable to prove a direct relationship between intensity and duration of exercise training and occurrence of cardiac remodeling. For these reasons, our group conducted in 2012 a prospective, longitudinal study on competitive soccer players, demonstrating that both left atrial morphology and function significantly vary after an 8-month, high-volume training program.[44] These changes are associated with an improvement in left ventricular diastolic function also in individuals already presenting with the features of athlete's heart and have to be interpreted as a benign adaptation to exercise conditioning. These observations have been confirmed also in female competitive athletes,[45] in whom, after 4 months of training, changes in biatrial morphology and function were found. Interestingly, filling pressures were comparable between athletes and controls, and did not vary in response to training either in the left atrium (5.0 ± 1.0 vs. 5.0 ± 0.9; $P = 0.96$) or in the RA (4.0 ± 1.4 vs. 3.7 ± 1.0; $P = 0.39$),[45] confirming that atrial dilatation in athlete's heart occurred as a model of volume rather than pressure overload.

Left atrial fibrosis: a proof or a belief?

Some authors have hypothesized that in athletes both left atrial dilation and left atrial fibrosis might play a relevant role in the determination of supraventricular arrhythmias.[36,46] These observations have been borrowed by pathophysiology and particularly by hypertension and structural heart disease, and, to date, left atrial fibrosis has been observed only in an experimental study in male Wistar rats, conditioned to run vigorously.[47] In humans, only one study found an increase in the humoral markers of fibrosis in 45 elite veteran athletes.[48] However, as *per* design, the study was unable to provide a direct assessment of atrial fibrosis. Recently, magnetic cardiac resonance and echocardiographic imaging have been used to indirectly evaluate left atrial fibrosis. We recently applied the new echocardiographic techniques to demonstrate that myocardial stiffness, known to be directly related to the amount of fibrosis, is normal or even lower in the left atrium and RA of athletes compared with the sedentary individuals and does not vary in response to training.[40,45] Unpublished data from our research group, comparing 150 top-level athletes with 90 controls, demonstrated that left atrial stiffness is lower in athletes compared with controls and is directly correlated with left ventricular stiffness in the athletic population. Individuals in our studies are professional, relatively young athletes engaged in team sports. Left atrial stiffness seems to be particularly low in athletes (0.13 ± 0.04 in our study), whereas left atrial stiffness reported in a study on patients with paroxysmal atrial fibrillation seems to be dramatically higher (0.41 ± 0.24);[49] unfortunately, to date, a direct comparison with age-matched and sex-matched groups has not been performed.

A recent meta-analysis on regular physical activity and risk of atrial fibrillation has demonstrated that the mechanisms of increased left atrial size leading to left atrial fibrosis does not play a role in the development of atrial fibrillation in nonathletes, with physical activity being able on the other hand to positively influence the established risk factors for atrial fibrillation, such as weight, blood pressure, and incident diabetes mellitus.[50] These promising data could reveal new insights into the pathophysiological mechanisms of atrial fibrillation in athletes and need to be confirmed in further large studies and in other cohorts of athletes.

Atrial ectopy

Atrial ectopy, particularly pulmonary vein ectopy, has been shown to be the trigger in most episodes of paroxysmal atrial fibrillation.[51] However, conflicting data exist regarding increased atrial ectopy and physical activity. As it has been demonstrated that atrial ectopy increased with physical exercise,[52,53] it has been proposed that augmented atrial ectopy might also explain the increased risk of atrial fibrillation associated with sport practice, provided that it acts upon an appropriate substrate. However, Baldesberger *et al.*[34] did not find a high incidence of atrial ectopy in former professional cyclists, despite an increase in ventricular ectopy and ventricular tachycardial runs. Therefore, the hypothesis of increased atrial ectopy to explain the association between sports and atrial fibrillation cannot be adequately sustained with the currently available data.

Alterations in autonomic nervous system

Coumel[33] studied the influence of autonomic innervations in the appearance of atrial fibrillation and atrial flutter. According to this study, the vagal influences predominate in normal atria and the formation of macroreentrant circuits might be explained by the shortening of the wavelength of the atrial impulse as a consequence of vagal stimulation. Conversely, diseased atria are more dependent on adrenergic influences, which favor the formation of microreentries and automatic and triggered activities. The essential feature of vagal atrial fibrillation

is its occurrence at night, often ending in the morning. Rest, the postprandial state and alcohol are also precipitating factors.[33]

In the GIRAFA study,[30] vagal atrial fibrillation was the most common form of LAF (70% of patients). Grimsmo *et al.*[54] demonstrated that bradycardia and long PQ time were predictors for the occurrence of LAF, whereas Wilhelm *et al.*[52] found that the athletes practicing endurance sports for more than 4500 h had a significantly greater parasympathetic tone.

Furthermore, experimental data show that increased vagal tone shortens and increases the dispersion of the atrial refractory period, creating the conditions required for reentry.[55] Recently, Grundvold *et al.*[56] demonstrated a relationship between increased vagal tone and incident atrial fibrillation, particularly in physically fit men.

However, the increased vagal tone is not the only modulator to act in LAF patients. Indeed, atrial fibrillation in young healthy athletes can be initiated not only by vagal, but also by adrenergic predominance or by a combined form, and all types can be eventually associated with the overtraining syndrome.[33,57,58] Although vagally induced paroxysmal atrial fibrillation occurred more frequently than adrenergically atrial fibrillation (33 vs. 23%) in a study by Hoogsteen,[28] the authors of this study, in contrast to the literature previously published, reported that athletes with adrenergically induced paroxysmal atrial fibrillation were significantly younger than athletes with the vagal form ($P < 0.05$). Thus, although data seem to suggest a possible influence of autonomic nervous system on atrial fibrillation, further studies are required to determine the effect and interaction of the autonomic system on the atrial substrate in the initiation and maintenance of atrial fibrillation.

Electrolyte abnormalities

Long and vigorous periods of training could generate substantial shifts in the body fluids because of changes in volume regulation and electrolyte levels.[13] Intense training can result in an hourly loss of up to 2 L of body fluids.[59] In this context, inappropriate fluid intake can lead to dehydration and electrolyte depletion, triggering atrial arrhythmias.[60]

Left ventricular remodeling

It has been well established that exercise conditioning is able to markedly influence both morphology and function of the left ventricle (LV).[61–65] The harmonic cardiovascular response to training is able to cause a significant increase in the left ventricular wall thickness and in left ventricular mass, whereas diastolic function remains normal or even supranormal in athletes.[66,67] Although it has been demonstrated that, compared with control individuals, patients with LAF had not only larger atria, but also larger left ventricular mass regardless of the body surface area, the relationship between exercise-induced left ventricular remodeling and the possible occurrence of atrial fibrillation has been poorly investigated in athletes. Future studies are needed to investigate whether the marked remodeling of the LV induced by training, and particularly by endurance training, could be somehow responsible for the development of atrial fibrillation in athletes.

Illicit drugs

Stimulants such as amphetamines, ephedrine, and related substances that are used to enhance sports performance can cause atrial fibrillation. Although some of the studies on athletes include a questionnaire to identify those assuming illicit drugs, most of them do not test directly the presence of these drugs. Thus, because of legal and sports-related consequences, a percentage of athletes experiencing atrial fibrillation in the studies could have assumed stimulants without declaring them, causing a bias that could have markedly affected the relationship between exercise and atrial fibrillation.

Familial and genetic substrates: new frontiers in atrial fibrillation

Genetic contributions are increasingly recognized. A family history of atrial fibrillation in a first-degree relative independently increases atrial fibrillation risk by twofold.[68–70] Although polygenic inheritance is more common, monogenic inheritance has been described for a variety of genes, principally affecting ion channels.[71–73] The athletic population probably does not differ from the general population regarding this aspect. Unfortunately, the genetic characteristics of athletes with atrial fibrillation have not been systematically investigated.

Physical activity in patients with atrial fibrillation: the other side of the coin

Although a controversial relationship exists on exercise-induced LAF, regular physical activity in patients suffering from atrial fibrillation has positive effects. In these patients, exercise intolerance is the major presenting symptom,[74] resulting in an impetus for weight gain and deterioration of the overall health status.[75] Moreover, patients with atrial fibrillation have a higher activity impairment compared with nonatrial fibrillation individuals ($P < 0.001$), primarily responsible for the humanistic burden of atrial fibrillation.[76]

The management of permanent atrial fibrillation is therefore of great importance. A recent meta-analysis suggests that chronic exercise training of low, moderate, and vigorous intensity in adults with permanent atrial fibrillation consistently and significantly improves ventricular rate control, functional capacity, muscular strength and power, activities of daily living, and quality of life.[77] Osbak *et al.*[78] randomized 49 patients with permanent atrial fibrillation to 12-week aerobic exercise training or to

a control group. After 12 weeks of training, an improvement in exercise capacity and in 6-minute walking test ($P = 0.002$), a reduction in resting pulse ($P = 0.049$), and an improvement in the quality of life were observed in the active patients compared with controls.[78] Unfortunately, although chronic exercise might play a fundamental role in managing the symptoms associated with permanent atrial fibrillation, studies examining the effect of short-term chronic exercise training on various outcomes in patients with permanent atrial fibrillation have been limited by small sample size, lack of a control group, and inconsistent outcome measures.[77]

Conclusion

The risk of presenting atrial fibrillation probably depends on the interaction between individual susceptibility (determined by genetic characteristics) and environment, including the potential role of sport practice. However, although most of the available information supports the association between sport practice and LAF, a possible facilitating effect on atrial fibrillation is limited to vigorous endurance exercise, and there are no convincing data demonstrating that the sport itself may be the cause of atrial fibrillation. Thus, prospective studies are warranted to clarify this controversy. These studies should not only investigate the relationship between atrial fibrillation and exercise, but also contribute to establish the mechanisms of atrial fibrillation. Indeed, the identification of left atrial enlargement as a possible substrate for atrial fibrillation in athletes seems to be a weak suggestion, particularly in healthy individuals in whom the triggering from pulmonary veins probably play a primary role. Other mechanisms such as atrial fibrosis have been only hypothesized and not confirmed in humans. The investigation of other triggers and substrates, such as genetic characteristics able to modulate individual susceptibility, will probably clarify the mechanisms underlying the controversial relationship between atrial fibrillation and exercise.

Conversely, chronic exercise training of low, moderate, and vigorous intensity in adults with permanent atrial fibrillation consistently and significantly improves ventricular rate control, functional capacity, muscular strength and power, activities of daily living, and quality of life.

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