Atrial Fibrillation in Endurance Athletes
From Mechanism to Management

Adrian D. Elliott, PhD*, Rajiv Mahajan, MD, PhD,
Dennis H. Lau, MBBS, PhD, Prashanthan Sanders, MBBS, PhD

KEYWORDS

• Atrial fibrillation • Athlete • Arrhythmia • Exercise • Cardiac

KEY POINTS

- Atrial fibrillation (AF) risk is elevated by endurance sports participation. Risk estimates range from a 3-fold to 9-fold increase, based on smaller case-control studies, to a 30% increase, based on larger cohort studies.
- Atrial remodeling seems to be a primary mechanistic promoter of AF in athletes, likely accompanied by autonomic alterations favoring re-entry.
- Despite limited data in athletes, treatment options include radiofrequency catheter ablation, which has been shown to have similar efficacy to that in nonathletic control patients. Rate control may be poorly tolerated, whereas anticoagulation should be guided by recommended guidelines using the CHA_2DS_2-VASc score.

INTRODUCTION

Exercise training exerts considerable health benefits, contributing to a substantial decline in cardiac and all-cause mortality in those who engage in regular physical activity.[1] Both measured physical activity[2] and cardiorespiratory fitness[3] strongly predict long-term health outcomes. In those who engage in more extensive endurance training, the benefits on mortality are profound,[4] although not necessarily over and above those observed with more modest exercise habits.

Despite the stream of empirical evidence supporting the benefits of exercise, the concept of exercise producing adverse effects on the heart draws considerable interest from both the medical research environment and the wider population. Traditional and social media are drawn to the stories in which an athlete experiences a cardiac disorder or worse, sudden cardiac death.

Although these events are infrequent and isolated,[5,6] there is mounting evidence to suggest that prolonged exercise training over many years

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Centre for Heart Rhythm Disorders, South Australian Health and Medical Research Institute, Royal Adelaide Hospital, University of Adelaide, Adelaide, South Australia, Australia
* Corresponding author. Centre for Heart Rhythm Disorders, Level 8, South Australian Health and Medical Research Institute, Royal Adelaide Hospital, University of Adelaide, Adelaide, South Australia 5000, Australia.
E-mail address: adrian.elliott@adelaide.edu.au

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may result in ventricular arrhythmias for a small minority of athletes.[7] Yet, more common within the endurance athlete population, with consistent data from both Europe and the United States, is the relative increase in atrial arrhythmia risk in endurance athletes compared with nonathletes.

PREVALENCE OF ATRIAL ARRHYTHMIAS IN ENDURANCE ATHLETES

Atrial fibrillation (AF) is the most common clinical arrhythmia with a growing global burden[8] leading to rising hospitalizations and health care demands.[9–11] Risk factors for AF include hypertension, obesity, and diabetes mellitus, as well as obstructive sleep apnea and alcohol intake. Recent evidence strongly supports risk factor modification, including increasing cardiorespiratory fitness, for the management of AF.[12–14] However, in the past 20 years, there has been a swell of evidence confirming that endurance sports practice also presents an independent risk factor for AF.

Based on the clinical observation that AF appeared more frequently in endurance athletes, Karjalainen and colleagues[15] compared AF prevalence in highly ranked orienteers versus age-matched healthy control participants from an earlier study. Using self-report to identify participants with AF before confirmation by medical records, AF was found to be more prevalent in athletes versus nonathletes (5.3% vs 0.9%, relative risk 5.5, 95% CI 1.3–24.4), despite lower mortality and vascular events in the athletes. In a case analysis, Mont and colleagues[16] later revealed that among lone AF patients seen in an outpatient arrhythmia clinic, the proportion of athletes among the AF group was substantially greater than that in the general population (63% v 15%, respectively). The same center subsequently published the findings of an age-matched case-control study,[17] in which 51 men with lone AF were compared against controls selected from the general population. The proportion of lone AF subjects reporting current sports practice was higher than in controls (31% v 14%; odds ratio [OR] 3.1, 95% CI 1.4–7.1). Interestingly, this study also attempted to determine a dose-risk assessment using sporting history questionnaires. Current sporting practice with greater than 1500 lifetime exercise hours increased AF risk (OR 2.9, 95% CI 1.2–6.9) compared with those who did not engage in sports. More recently, a similar case control study of subjects with lone AF has revealed a threshold of 2000 lifetime training hours, above which AF risk increases (OR 3.88, 95% CI: 1.55–9.73).[18]

Similar conclusions have been drawn from studies comparing AF prevalence within an athletic population compared with sedentary controls. Molina and colleagues[19] compared 183 amateur marathon runners with a population-based sample of 290 sedentary controls. The annual incidence rate of AF was significantly higher in athletes versus sedentary controls (0.43/100 persons vs 0.11/100 persons, adjusted hazard ratio 8.8, 95% CI: 1.3–61.3). Also in runners, Wilhelm and colleagues[20] noted an AF prevalence of 6.7% for athletes with a mean age of 42 years, considerably higher than recent estimates that suggest the prevalence for 40 to 44 year old men in Western Europe is approximately 0.2%.[8] In a comparison of former professional cyclists versus age and gender-matched golfers, Baldesberger and colleagues[21] identified 6 cases (10%) of AF or atrial flutter in the 62 cyclists, compared with 0 cases from the 62 participant control group.

One of the primary limitations with these studies is the relatively small sample size. This has been addressed recently by a series of studies from Scandinavia in which larger cohorts have been assessed to address the AF risk associated with endurance exercise. In more than 52,000 participants of the Vasaloppet 90 km cross-country ski race between 1989 and 1998, AF occurred more frequently in those who had completed greater than 5 races compared with those who had completed only 1 race, albeit with a lower risk estimate than shown previously (hazard ratio 1.29).[22] In this population, the number of completed races was taken as a surrogate measure of total training dose, although the reference group included participants who had completed 1 race, rather than a true sedentary group. This subtlety likely dampens the true risk estimate drawn from this study, although it does confirm the increased frequency of arrhythmias in athletes. Additionally, Myrstad and colleagues[23] compared a sample of cross-country skiers to a group recruited from a large population survey study. This study of more than 3500 participants (mean age ~ 65 y) found that participants with greater than 30 years of endurance training practice were at a greater risk of both atrial flutter and AF. The prevalence of self-report AF was 12.5% in athletes, with an adjusted risk increase of 26% (OR 1.26) for lone AF per each 10-year increase in training history.

Taken together, these studies provide convincing evidence that endurance exercise training leads to an elevated risk of AF that may be more pronounced in those athletes with more extensive exercise training history.

Searching for a Common Definition

Establishing a link between exercise training and AF depends strongly on the definition of what is

considered as training rather than general physical activity. Similarly, classifying an individual as an athlete may be subjective. Studies have addressed the relationship by classifying athletes using methods such as those who participate in endurance competition,[19,22] former professional athletes,[21] current sports ranking,[15] and self-reported lifetime training hours assessed by questionnaire.[18,24] Between-study methodological differences present an important confounder, particularly when trying to elucidate a threshold above which AF risk is exaggerated. Recent trends in exercise monitoring using mobile devices and wearable technologies will enable prospective studies to provide more objective measures of training status and a more precise description of the association between exercise and AF.

MECHANISMS IN THE PATHOGENESIS OF ATRIAL FIBRILLATION IN ATHLETES

The pathophysiological mechanisms leading to the development of AF are complex and vary between individuals but commonly involve structural, electrical, and autonomic remodeling of the atria, predisposing to re-entry or triggered activity (**Fig. 1**).[25]

In animal models of hypertension,[26] obstructive sleep apnea,[27] and obesity,[28] extensive electrophysiological and structural remodeling, including decreased conduction velocity and atrial voltages, increased conduction heterogeneity, fractionated electrograms, and fibrosis, leads to heightened AF susceptibility. Although traditional risk factors such as obesity and hypertension are strong predictors of AF within the general population, the burden of these risk factors in an athlete population is low. The mechanisms of AF promotion in endurance athletes is not well understood but potentially includes atrial enlargement, vagal enhancement, and increased inflammation as primary mediators.

Atrial Structural Remodeling

Biatrial dilation is a common, well-described adaptation within the athlete's heart.[20,29] Left and right atria undergo enlargement as a result of exercise training, although the clinical significance of such changes is to be determined. In 1777 competitive athletes, left atrial dilation occurred in 20% of athletes but was not associated with increased arrhythmia prevalence.[30] This was a cross-sectional analysis of a young athletic cohort (mean age 24 ± 6 y) that identified arrhythmia by symptoms and routine electrocardiogram, thus raising the possibility that asymptomatic episodes

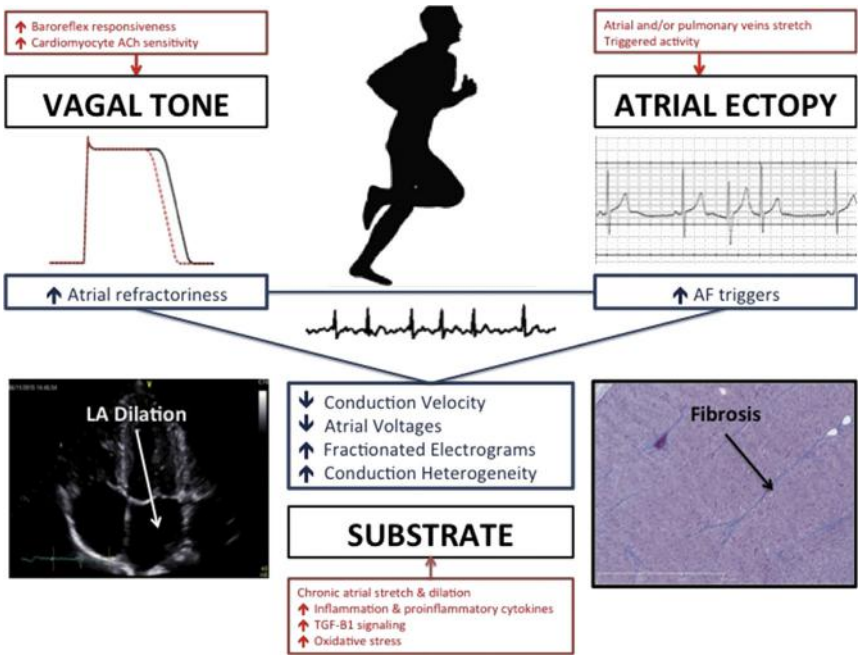

Fig. 1. The mechanisms contributing to AF in athletes. Atrial dilation is commonly observed in endurance athletes and may accompany atrial fibrosis, contributing to a vulnerable substrate. Vagal tone is elevated following the onset of exercise training and may promote re-entry by shortening of the effective refractory period. Increased atrial ectopy has been reported in some studies and may precede the onset of AF in some athletes. ACh, acetylcholine; LA, left atrium; TGF, transforming growth factor.

may have been overlooked. Case-control and cohort studies with an older population support left atrial size as an independent predictor of AF.[19,31]

Fibrosis is a common feature of atrial remodeling observed with other risk factors, such as hypertension[26] and obesity,[28] and may feature within the atria of well-trained endurance athletes. Fibrosis within the ventricles of endurance athletes has been demonstrated previously,[32,33] although, to the authors' knowledge, there are little data on fibrosis within the atrial walls.

In rat models of marathon running, exercise-induced remodeling, including both atrial and ventricular fibrosis, has been demonstrated, consequently contributing to an increased susceptibility for AF[34] and ventricular tachycardia.[35] The profibrotic process is enhanced by several signaling pathways, including the renin-angiotensin-aldosterone system, transforming growth factor-β_1, connective tissue growth factor, proinflammatory cytokines, and oxidative stress.[36] Endurance exercise is associated with acute postexercise elevations in both inflammation and oxidative stress,[37,38] repeated bouts of which may contribute to collagen deposition within the atrial walls.

Animal studies have confirmed the role of inflammation for exercise-induced atrial fibrosis; pharmacologic inhibition of tumor necrosis factor (TNF)-α abolished the exercise-induced promotion of AF and atrial fibrosis in mice.[39] The role of p38 activity in TNF-α regulated fibrosis and AF promotion was also confirmed by its pharmacologic blockade, which prevented atrial fibrosis and AF.[39] Although it is not immediately clear which mechanisms contribute to upregulation of these pathways, the role of stretch in the activation of TNF-α has been shown previously in cardiac cells.[40] During exercise, atrial pressure is elevated,[41,42] therefore providing a stimulus for TNF-α activation.

Despite a clear association between atrial remodeling and AF as a result of endurance exercise, atrial dilation and fibrosis alone seem to be insufficient to promote AF. Preclinical data in rats[34] show that atrial fibrosis persists into a detraining period despite a regression in AF inducibility. This key finding supports the role for other factors in the promotion of AF following exercise training.

Autonomic Influences

Well-trained athletes exhibit enhanced measures of vagal tone, such as heart rate variability,[43] relative to nonathletes. Vagal tone favors a reduced refractoriness and enhanced excitability of the myocardium.[44] In addition, it potentially creates the milieu for re-entry within the atria, leading to AF.[45] Indeed, Bettoni and Zimmermann[46] reported on autonomic variations, from adrenergic drive through an abrupt shift toward vagal dominance, immediately preceding AF initiation. Enhanced vagal tone reduces effective refractory periods within the atria via acetylcholine-mediated K^+ currents, thus potentially contributing to the increased observation of vagally mediated lone AF in endurance athletes.[17] Furthermore, vagally mediated bradycardia would be expected to aggravate the impact of atrial stretch, structural remodeling, and potentially provides a more vulnerable period during which triggers can capture the atrial myocardium.

Preclinical data support a vagal mechanistic involvement in the AF observed in athletes. Guasch and colleagues[34] demonstrated enhanced vagal tone following 16 weeks of training in rats, despite no alterations in sympathetic drive. Moreover, vagal tone was reversible and was indistinguishable between trained and sedentary rats following detraining. Most notably, vagal enhancement was temporally associated with AF inducibility in the trained group, therefore portraying a central role for autonomic alterations as a mechanistic contributor to the AF promotion by exercise. More recently, conflicting data from further preclinical data suggest a lesser role for autonomic alterations; inhibition of vagal tone reduced but did not eliminate AF susceptibility in a mouse model of exercise training.[39] These data show that parallel atrial remodeling and vagal enhancement promote AF in athletes and that in the presence of both factors AF inducibility is substantially increased. However, whether the normalization of vagal tone suppresses AF susceptibility in humans is still unclear.

Atrial Ectopic Triggers

Seminal work by Haïssaguerre and colleagues[47] revealed that ectopic beats originating from the pulmonary veins commonly leads to the spontaneous initiation of AF. The initiation and maintenance of AF can therefore be attributed to the interaction of a trigger, modulator, and vulnerable substrate.

Atrial ectopic burden is higher in both paroxysmal and persistent AF patients[48] and may play a role in the pathogenesis of AF in endurance athletes. Surprisingly, few studies have characterized atrial ectopic burden in endurance athletes. In former professional cyclists, atrial ectopic burden was not significantly higher than a control group matched by age and gender, despite higher

prevalence of AF.[21] In contrast, male runners with a training history greater than 4500 lifetime hours had significantly higher atrial ectopic burden compared with those with less than 1500 training hours.[20] However, the mean burden of ectopic beats was lower than that reported in subjects with AF.[48] It remains unclear whether exercise training per se results in a clinically significant increase in atrial ectopy that contributes to the development of AF in endurance athletes.

MANAGEMENT OF ATRIAL FIBRILLATION IN ATHLETES

Evaluation of an Athlete with Atrial Fibrillation

The initial evaluation of an athlete with confirmed or suspected AF should seek to exclude structural or electrical abnormalities. Evaluation for coronary artery disease should be considered in the older athlete. In addition, the clinician needs to consider the possibility of inherited channelopathies and the potential existence of conventional cardiovascular risk factors. Dilated cardiomyopathies, hypertrophic cardiomyopathy, and valvular abnormalities should be excluded by echocardiography. An electrocardiogram will permit the assessment of accessory pathways, conduction abnormalities, and channelopathies that may contribute to the onset of AF. The risk of AF is increased in those with channelopathies such as Brugada, short QT, and long QT syndromes; with these conditions conferring additional risks in athletes. In particular, AF may be the first arrhythmogenic presentation of these conditions and therefore requires consideration. Similarly, evaluation for conventional cardiovascular risk factors, such as obstructive sleep apnea, hypertension, type II diabetes mellitus, hyperlipidemia, alcohol intake, and hyperthyroidism, should be undertaken. Many of these risk factors have a low prevalence in an athletic population; however, may be present in some and should be considered in the older athlete. Prolonged or frequent rhythm monitoring may be necessary to evaluate the frequency and burden of AF, as well as characterize any asymptomatic episodes.

Despite an absence of detailed decision-making guidelines for the management of AF in athletes, current American Heart Association and American College of Cardiology (AHA/ACC) guidelines regarding eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities[49] supports continued sports participation in athletes with well-tolerated, self-terminating AF or AF that is appropriately managed (**Table 1**).

Detraining

In animal studies, detraining reverses the AF susceptibility brought about by long-term, intensive exercise training,[34] although fibrosis remains elevated within the atria. There are few data on the role of detraining in human athletes with AF, although there are isolated reports of its efficacy for the management of AF before the return to sports participation.[50] In athletes with confirmed or borderline left ventricular hypertrophy, detraining has been shown to reduce atrial dimensions in some studies[51] but not others,[52] although between-studies differences may be due to different baseline left atrial dimension.[51] How this translates for the athlete with AF is not immediately clear but the rationale for detraining presumably centers on a regression in the underlying proarrhythmogenic substrate or a normalization of autonomic influences. In the presence of marked bradycardia, which in this population most often is related to vagal nerve remodeling and altered sinus node function,[53,54] detraining can be associated with an improvement in heart rates,[52] potentially reducing the period during which the atrial myocardium is vulnerable to triggered activity.

Importantly, the feasibility of detraining depends on the athlete's competitive situation in which a professional athlete is unlikely to favor such an approach in the long-term. Full physical deconditioning should also be considered in the context of potential adverse effects encountered by a long-term decline in physical activity levels. In cases in which a detraining strategy is agreed on following consultation with the athlete, the reduction in training load should be considered relative to the athlete's regular program. For example, in an elite endurance athlete with a training volume of greater than 25 hours per week, as shown previously,[55] a prescribed detraining strategy may target less than 5 hours per week, thus representing an 80% reduction in training load. For an athlete engaging in 5 hours per week of training, less than 2 hours per week may be more appropriate. Despite its logical rationale, there is currently no available evidence regarding the efficacy of detraining for the reduction of AF burden. Further studies are required to characterize the outcomes of detraining in athletes with AF and to define the optimal detraining strategy in which this is considered appropriate for AF management.

Rate Control

Current AHA/ACC and Heart Rhythm Society (HRS) guidelines[56] for the management of patients

Table 1
Studies reporting the outcome of catheter ablation in athletes

Study	Sample (*n*)	Age (y)	AF Type (% Persistent)	Athletes	Procedure	Follow-Up	Outcome (% AF-Freedom)
Furlanello et al,[63] 2008	20 A (no C)	44 ± 13	NR	Regular training + competition; >20 h per wk, mean duration 25.2 y	PVI	36 ± 13 mo	OFF AADs Single procedure: NR multiple procedures: 90% (A)
Calvo et al,[64] 2010	42 Lone AF A; 140 AF C	52 ± 10 (A); 49 ± 11 (C)	26% (A); 36% C)	Regular endurance training >3 h per wk, >10 y	PVI + linear lines	19 ± 12 mo	OFF AADs Single procedure: 59% (A), 48% (C) Multiple procedures: 81% (A), 63% (C)
Koopman et al,[65] 2011	94 A; 41 C	51 ± 8 (A); 52 ± 8 (C)	13% (A); 5% (C)	Regular sports training >3 h per wk, >10 y	PVI + linear lines if required	46 ± 28 mo	With AADs Single procedure: 42% (A), 48% (C) Multiple procedures: 85% (A), 87% (C)

Abbreviations: A, athlete, AADs, antiarrhythmic drugs; C, control; NR, not reported; PVI, pulmonary vein isolation.

with AF recommend ventricular rate control for patients with paroxysmal and persistent AF. For symptomatic patients, stricter rate control (resting heart rate<80 beats per minute [bpm]) is suggested as a reasonable target, although for asymptomatic patients, a more lenient target of less than 110 bpm may be appropriate. There are no studies evaluating the efficacy and performance impact of rate control medication in athletes with atrial arrhythmias. For the athlete, beta-blockade may not be well tolerated and is likely to result in a decline in cardiovascular performance during submaximal and maximal exercise.[57,58] Furthermore, bradycardia with nocturnal pauses is also common in this cohort, which may contraindicate beta-blockade. Additional issues arise for some competitive athletes in whom beta-blockers are banned in competition. Although data are lacking, the exercise performance of athletes may be comparatively less impaired by calcium antagonists,[59] which may be a preferred option in this context.

Rate control in the athlete is notoriously vexed and poorly tolerated, predominantly due to the frequent occurrence of resting bradycardia and the impact of such rate-limiting drugs on exercise performance. Therefore, in the authors' experiences, these factors are common reasons for the early use of rhythm control strategies.

Rhythm Control

Ongoing symptoms and poor tolerability of rate control strategies provide the primary rationale for pursuing a rhythm control strategy. The effect of AF on exercise performance, particularly in young, competitive athletes, provides additional justification for prompt rhythm control, obviating rate control.

To date, there is little available evidence regarding the efficacy of antiarrhythmic drugs (AADs) for athletes with AF. Indeed, these have resulted in a similar experience to what has been observed with rate control medications; that is, they are often poorly tolerated. The most often used strategy has been the use of the class IC agents flecainide or propafenone as a pill in the pocket approach for the management of out-of-hospital, symptomatic episodes,[56,60] although this has not been specifically evaluated in athletes with AF. Caution should be noted regarding the management of AF by class IC agents given that they lower atrial rate activity, potentially organizing AF into atrial tachycardia with 1 to 1 conduction.[61] This may have specific consequences in the athlete whereby the low resting heart rate prohibits the addition of concurrent atrioventricular (AV) nodal blocking agents during exercise, with an increase in circulating catecholamines. There may be further acceleration of AV conduction, which can more frequently result in 1 to 1 conduction of organized rhythms to the ventricle. In our patients using pill in the pocket strategy early on, we specifically instruct cessation of exercise during the period of arrhythmia and use of both an AV nodal blocking agent with a class IC agent. In an interesting subset of patients in whom arrhythmia is triggered only during exercise, we have used premedication 30 to 60 minutes before activity, with some success. In our experience, the chronic use of AADs is poorly tolerated in athletes.

The poor tolerability of pharmaceutical therapies has led to the increasing use of catheter ablation. In recent years, catheter ablation has evolved considerably with subsequent improvements in both safety and efficacy,[56,62] thus potentially reducing the dependence on rate control and antiarrhythmic medication for the management of AF.

In the first of recent studies on the use of catheter ablation in an athletic population (**Table 2**), Furlanello and colleagues[63] reported on a cohort of 20 athletes, predominantly competing in endurance sports (>20 h/wk, mean duration of 25.2 y). Participants in this series were men with a mean age of 44 years (range 22–62 y). The ablation strategy sought pulmonary vein isolation in a first procedure, with conduction recurrence assessed in a prescheduled second procedure 3 months later. Over a 36-month follow-up without AADs, 18 (90%) of athletes remained AF-free. Importantly, both exercise tolerance and quality of life were significantly approved after catheter ablation. In the 2 athletes experiencing recurrent AF, these were short-lasting occasional episodes that were self-terminating and did not limit exercise participation or performance.

In a later series, Calvo and colleagues[64] reported on the outcomes of catheter ablation between lone AF subjects with and without a history of regular endurance sports participation (3 h/wk for at least 10 y before diagnosis). Following a 19-month follow-up, there was no significant difference between athletes and nonathletes for single-procedure arrhythmia recurrence (59% v 48%, respectively). Following multiple procedures, athletes were more likely to maintain arrhythmia-free survival than nonathletes (81 v 63%, respectively).

Similarly, the success rates of single and multiple procedure ablation was similar between athletes and nonathletes in a study by Koopman and colleagues.[65] Following a 3-year follow-up, 85% of athletes remained arrhythmia free after multiple procedures, compared with 87% in the

Table 2
Summary of available guidelines regarding atrial fibrillation in athletes

Guideline Statement	Recommendations
AHA/ACC Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 9: Arrhythmias and Conduction Defects[49]	1. Athletes with AF should undergo a workup that includes thyroid function tests, queries for drug use, electrocardiogram, and echocardiogram (class I; level of evidence B). 2. Athletes with low-risk AF that is well tolerated and self-terminating may participate in all competitive sports without therapy (class I; level of evidence C). 3. In athletes with AF, when antithrombotic therapy, other than aspirin, is indicated, it is reasonable to consider the bleeding risk in the context of the specific sport before clearance (class IIa; level of evidence C). 4. Catheter ablation for AF could obviate rate control or AADs and should be considered (class IIA, level of evidence B)
2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation[56]	No specific recommendations. However, text raises following suggestions: • Rule out hypertension and coronary artery disease in the older athlete • Consider ventricular rate response during AF episode, which may require maximal exercise testing. • Consider pill in the pocket approach or catheter ablation.

control group. Rates of arrhythmia recurrence were also similar between endurance athletes and athletes from nonendurance sports.

Several complications have been recognized with the use of catheter ablation for AF.[62] Some of these may have an impact on the performance of the athlete and may warrant specific discussion. Vascular complications at the site of venous access can limit mobility and, in the rare patient, result in pain at the site for a more prolonged period, which may limit the types of exercise that can be performed, usually limited to the first few weeks or months after ablation. Dyspnea is often observed early after the procedure and in the athlete can be noticeably more profound given the baseline level of functioning. Most often this is due to transient factors related to a fluid overload, atrial mechanical dysfunction, or local trauma to the lung. Persistent dyspnea longer than the first 3 months requires evaluation and may have longer term consequences to the level of performance. Phrenic nerve injury is a recognized complication, occurring more frequently with the use of cryoballoon ablation.[66] Although mostly these recover, the course of recovery can be quite prolonged, in rare cases persisting more than 12 months. Fixed obstructive lesions can result in a more lasting impact on exercise performance. These include pulmonary venous stenosis or rarely the stiff left atrial syndrome.[67]

Although evidence for this is sparse, it may be worth consideration in future trials of catheter ablation within athletic cohorts. Notably, however, a significant improvement in atrial function, determined by speckle-tracking echocardiography, in the 12 months following early ablative treatment has been observed. Those managed without catheter ablation had a progressive worsening of atrial function over the same time period.[68]

Overall, catheter ablation seems to yield similar success rates for athletes compared with nonathletes in the absence of other significant factors such as structural heart disease. However, the data to date have been for a limited number of patients and with modest follow-up. Indeed, emerging data have pointed to the importance of also treating the primary insult in improving the outcomes after ablation.[12,13] Nevertheless, based on current evidence, catheter ablation may be considered an effective treatment option, although current data are limited by small sample sizes and the absence of prospective randomized controlled trials.

Anticoagulation

Given the numerous health benefits of chronic exercise training, athletes typically present with a CHA_2DS_2-VASc less than or equal to 1 and, subsequently, a low risk of systemic thromboembolism.

As such, anticoagulation is seldom necessary in this cohort. A small minority of athletes with a CHA_2DS_2-VASC score greater than or equal to 2, such as female masters athletes older than 65 years or those with hypertension as a comorbidity, may require anticoagulation per recommended guidelines.[56] In such a scenario, it may be necessary to consider the bleeding risk in the setting of contact sports or activities in which there is a higher risk of falls, such as in mountain biking or skiing. Anticoagulation needs to be considered in the older athlete.

FUTURE DIRECTIONS

There remains a distinct absence of prospective, long-term data regarding the effects of exercise training on the heart and the risk of arrhythmias. Future studies that address the potential mechanisms, such as atrial remodeling and autonomic alterations, underlying AF-risk in human athletes will provide significant advancement to the field. This will be difficult given the logistical and financial implications of long-term prospective trials within a large population, yet necessary given the recent surge in endurance sports participation, such as in marathons and long-distance triathlons. Importantly, novel structural and functional cardiac imaging approaches alongside invasive and/or noninvasive electrophysiological mapping techniques are now available to provide a unique insight into the cardiac adaptations that accompany exercise training. Such advances will enable the evaluation of the mechanisms contributing to heightened AF risk in the athletic population. Furthermore, studies that address the treatment options for athletes with arrhythmias will provide the necessary evidence to support decision-making regarding the management of AF in this cohort.

SUMMARY

Extensive endurance training increases the risk of AF mostly due to atrial remodeling, including dilation and fibrosis, alongside autonomic alterations favoring vagal tone and a possible increase in the frequency of atrial ectopic triggers (see

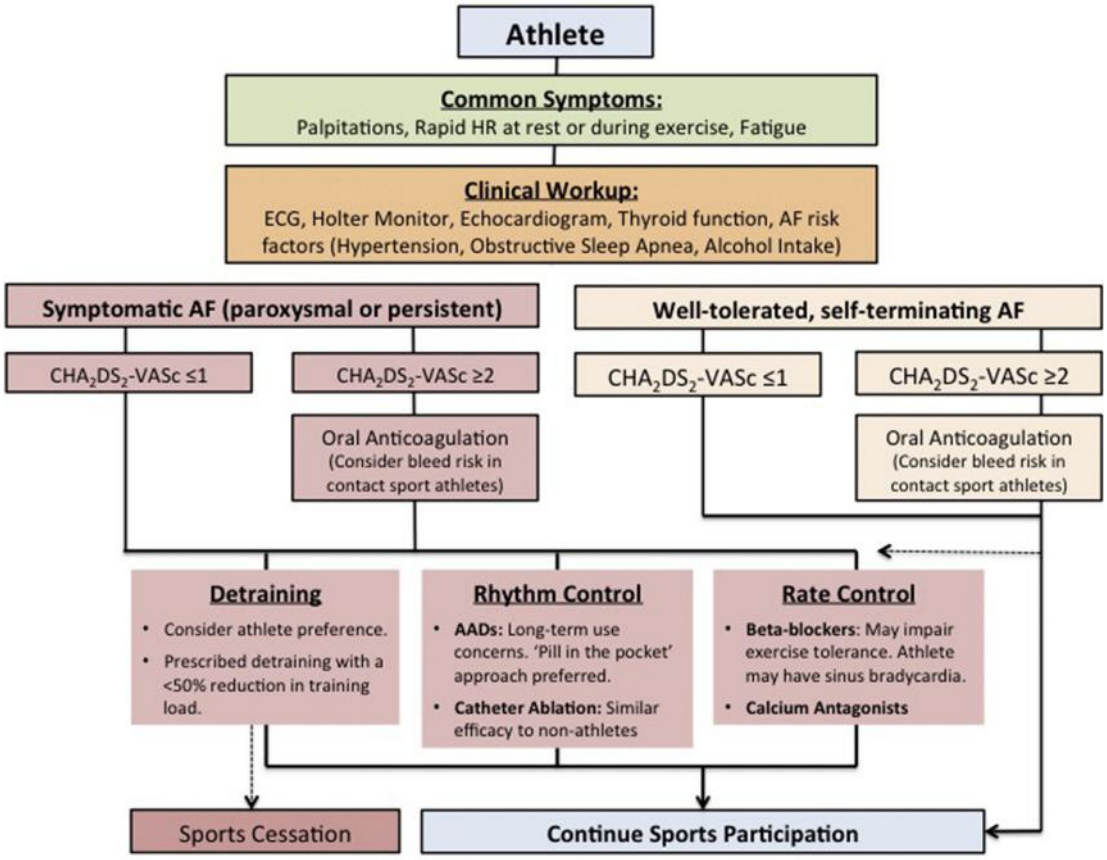

Fig. 2. A schema for the evaluation and treatment of AF in athletes. ECG, electrocardiogram; HR, heart rate.

Fig. 1). Despite the prevalence of AF being well established in human athletes, the mechanistic insights underlying this observation are primarily based on animal studies. Rhythm control using catheter ablation is increasingly used in this cohort due to the poor tolerability of medical therapy. However, data have been limited to single-center studies. Catheter ablation is shown to be equally effective in athletes with AF compared with non-athletes and can thus be considered for the symptomatic athlete seeking rhythm control and a prompt return to sports participation (Fig. 2). Prospective studies are warranted to further evaluate the mechanisms promoting AF in human athletes and to evaluate treatment options in this cohort.

REFERENCES

1. Wen CP, Wai JPM, Tsai MK, et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. Lancet 2011;378:1244–53.
2. Lee D-C, Sui X, Artero EG, et al. Long-term effects of changes in cardiorespiratory fitness and body mass index on all-cause and cardiovascular disease mortality in men: the Aerobics Center Longitudinal Study. Circulation 2011;124:2483–90.
3. Myers J, Prakash M, Froelicher V, et al. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med 2002;346:793–801.
4. Lee D-C, Pate RR, Lavie CJ, et al. Leisure-time running reduces all-cause and cardiovascular mortality risk. J Am Coll Cardiol 2014;64:472–81.
5. Marijon E, Tafflet M, Celermajer DS, et al. Sports-related sudden death in the general population. Circulation 2011;124:672–81.
6. Marijon E, Tafflet M, Antero-Jacquemin J, et al. Mortality of French participants in the Tour de France (1947-2012). Eur Heart J 2013;34:3145–50.
7. Heidbüchel H, Hoogsteen J, Fagard R, et al. High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias. Role of an electrophysiologic study in risk stratification. Eur Heart J 2003;24:1473–80.
8. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. Circulation 2014;129:837–47.
9. Wong CX, Brooks AG, Leong DP, et al. The increasing burden of atrial fibrillation compared with heart failure and myocardial infarction: a 15-year study of all hospitalizations in Australia. Arch Intern Med 2012;172:739–41.
10. Wong CX, Lau DH, Sanders P. Atrial fibrillation epidemic and hospitalizations: how to turn the rising tide? Circulation 2014;129:2361–3.
11. Patel NJ, Deshmukh A, Pant S, et al. Contemporary trends of hospitalization for atrial fibrillation in the United States, 2000 through 2010: implications for healthcare planning. Circulation 2014;129:2371–9.
12. Pathak RK, Middeldorp ME, Lau DH, et al. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the arrest-AF cohort study. J Am Coll Cardiol 2014;64:2222–31.
13. Pathak RK, Middeldorp ME, Meredith M, et al. Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort: a Long-Term Follow-Up Study (LEGACY study). J Am Coll Cardiol 2015;65:2159–69.
14. Pathak RK, Elliott A, Middeldorp ME, et al. Impact of CARDIOrespiratory FITness on arrhythmia recurrence in obese individuals with atrial fibrillation: the CARDIO-FIT Study. J Am Coll Cardiol 2015;66:985–96.
15. Karjalainen J, Kujala UM, Kaprio J, et al. Lone atrial fibrillation in vigorously exercising middle aged men: case-control study. BMJ 1998;316:1784–5.
16. Mont L, Sambola A, Brugada J, et al. Long-lasting sport practice and lone atrial fibrillation. Eur Heart J 2002;23:477–82.
17. Elosua R, Arquer A, Mont L, et al. Sport practice and the risk of lone atrial fibrillation: a case-control study. Int J Cardiol 2006;108:332–7.
18. Calvo N, Ramos P, Montserrat S, et al. Emerging risk factors and the dose-response relationship between physical activity and lone atrial fibrillation: a prospective case-control study. Europace 2015;18(1):57–63.
19. Molina L, Mont L, Marrugat J, et al. Long-term endurance sport practice increases the incidence of lone atrial fibrillation in men: a follow-up study. Europace 2008;10:618–23.
20. Wilhelm M, Roten L, Tanner H, et al. Atrial remodeling, autonomic tone, and lifetime training hours in nonelite athletes. Am J Cardiol 2011;108:580–5.
21. Baldesberger S, Bauersfeld U, Candinas R, et al. Sinus node disease and arrhythmias in the long-term follow-up of former professional cyclists. Eur Heart J 2008;29:71–8.
22. Andersen K, Farahmand B, Ahlbom A, et al. Risk of arrhythmias in 52 755 long-distance cross-country skiers: a cohort study. Eur Heart J 2013;34:3624–31.
23. Myrstad M, Nystad W, Graff-Iversen S, et al. Effect of years of endurance exercise on risk of atrial fibrillation and atrial flutter. Am J Cardiol 2014;114:1229–33.
24. Wilhelm M. Atrial fibrillation in endurance athletes. Eur J Prev Cardiol 2013;21:1040–8.
25. Nattel S, Harada M. Atrial remodeling and atrial fibrillation: recent advances and translational perspectives. J Am Coll Cardiol 2014;63:2335–45.
26. Lau DH, Mackenzie L, Kelly DJ, et al. Hypertension and atrial fibrillation: evidence of progressive atrial

remodeling with electrostructural correlate in a conscious chronically instrumented ovine model. Heart Rhythm 2010;7:1282–90.
27. Dimitri H, Ng M, Brooks AG, et al. Atrial remodeling in obstructive sleep apnea: implications for atrial fibrillation. Heart Rhythm 2012;9:321–7.
28. Mahajan R, Lau DH, Brooks AG, et al. Electrophysiological, electroanatomical, and structural remodeling of the atria as consequences of sustained obesity. J Am Coll Cardiol 2015;66:1–11.
29. Baggish AL. Mechanisms underlying the cardiac benefits of exercise: still running in the dark. Trends Cardiovasc Med 2015;25:537–9.
30. Pelliccia A, Maron BJ, Di Paolo FM, et al. Prevalence and clinical significance of left atrial remodeling in competitive athletes. J Am Coll Cardiol 2005;46:690–6.
31. Mont L, Tamborero D, Elosua R, et al. Physical activity, height, and left atrial size are independent risk factors for lone atrial fibrillation in middle-aged healthy individuals. Europace 2008;10:15–20.
32. Wilson M, O'Hanlon R, Basavarajaiah S, et al. Cardiovascular function and the veteran athlete. Eur J Appl Physiol 2010;110:459–78.
33. La Gerche A, Burns AT, D'Hooge J, et al. Exercise strain rate imaging demonstrates normal right ventricular contractile reserve and clarifies ambiguous resting measures in endurance athletes. J Am Soc Echocardiogr 2012;25:253–62.e1.
34. Guasch E, Benito B, Qi X, et al. Atrial fibrillation promotion by endurance exercise: demonstration and mechanistic exploration in an animal model. J Am Coll Cardiol 2013;62:68–77.
35. Benito B, Gay-Jordi G, Serrano-Mollar A, et al. Cardiac arrhythmogenic remodeling in a rat model of long-term intensive exercise training. Circulation 2011;123:13–22.
36. Schotten U, Verheule S, Kirchhof P, et al. Pathophysiological mechanisms of atrial fibrillation: a translational appraisal. Physiol Rev 2011;91:265–325.
37. La Gerche A, Inder WJ, Roberts TJ, et al. Relationship between inflammatory cytokines and indices of cardiac dysfunction following intense endurance exercise. PLoS One 2015;10:e0130031.
38. Sugama K, Suzuki K, Yoshitani K, et al. Changes of thioredoxin, oxidative stress markers, inflammation and muscle/renal damage following intensive endurance exercise. Exerc Immunol Rev 2015;21:130–42.
39. Aschar-Sobbi R, Izaddoustdar F, Korogyi AS, et al. Increased atrial arrhythmia susceptibility induced by intense endurance exercise in mice requires TNFα. Nat Commun 2015;6:6018.
40. Sun M, Chen M, Dawood F, et al. Tumor necrosis factor-alpha mediates cardiac remodeling and ventricular dysfunction after pressure overload state. Circulation 2007;115:1398–407.
41. Luepker RV, Holmberg S, Varnauskas E. Left atrial pressure during exercise in hemodynamic normals. Am Heart J 1971;81:494–7.
42. Reeves JT, Groves BM, Cymerman A, et al. Operation Everest II: cardiac filling pressures during cycle exercise at sea level. Respir Physiol 1990;80:147–54.
43. Aubert AE, Seps B, Beckers F. Heart rate variability in athletes. Sports Med 2003;33:889–919.
44. Takahashi Y, Jaïs P, Hocini M, et al. Shortening of fibrillatory cycle length in the pulmonary vein during vagal excitation. J Am Coll Cardiol 2006;47:774–80.
45. Coumel P. Paroxysmal atrial fibrillation: a disorder of autonomic tone? Eur Heart J 1994;15(Suppl A):9–16.
46. Bettoni M, Zimmermann M. Autonomic tone variations before the onset of paroxysmal atrial fibrillation. Circulation 2002;105:2753–9.
47. Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339:659–66.
48. Brooks AG, Rangnekar G, Ganesan AN, et al. Characteristics of ectopic triggers associated with paroxysmal and persistent atrial fibrillation: evidence for a changing role. Heart Rhythm 2012;9:1367–74.
49. Zipes DP, Link MS, Ackerman MJ, et al. Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 9: Arrhythmias and Conduction Defects: a Scientific Statement from the American Heart Association and American College of Cardiology. J Am Coll Cardiol 2015;66(21):2412–23.
50. Furlanello F, Bertoldi A, Dallago M, et al. Atrial fibrillation in elite athletes. J Cardiovasc Electrophysiol 1998;9:S63–8.
51. Weiner RB, Wang F, Berkstresser B, et al. Regression of "gray zone" exercise-induced concentric left ventricular hypertrophy during prescribed detraining. J Am Coll Cardiol 2012;59:1992–4.
52. Pelliccia A. Remodeling of left ventricular hypertrophy in elite athletes after long-term deconditioning. Circulation 2002;105:944–9.
53. Stein R, Medeiros CM, Rosito GA, et al. Intrinsic sinus and atrioventricular node electrophysiologic adaptations in endurance athletes. J Am Coll Cardiol 2002;39:1033–8.
54. D'Souza A, Bucchi A, Johnsen AB, et al. Exercise training reduces resting heart rate via downregulation of the funny channel HCN4. Nat Commun 2014;5:3775.
55. Brosnan M, La Gerche A, Kumar S, et al. Modest agreement in ECG interpretation limits the application of ECG screening in young athletes. Heart Rhythm 2015;12:130–6.
56. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation: Executive Summary: A Report

of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation 2014; 130(23):2071–104.
57. Joyner MJ, Freund BJ, Jilka SM, et al. Effects of beta-blockade on exercise capacity of trained and untrained men: a hemodynamic comparison. J Appl Physiol (1985) 1986;60:1429–34.
58. Jilka SM, Joyner MJ, Nittolo JM, et al. Maximal exercise responses to acute and chronic beta-adrenergic blockade in healthy male subjects. Med Sci Sports Exerc 1988;20:570–3.
59. Kindermann W. Calcium antagonists and exercise performance. Sports Med 1987;4:177–93.
60. Alboni P, Botto GL, Baldi N, et al. Outpatient treatment of recent-onset atrial fibrillation with the "pill-in-the-pocket" approach. N Engl J Med 2004; 351:2384–91.
61. Taylor R, Gandhi MM, Lloyd G. Tachycardia due to atrial flutter with rapid 1:1 conduction following treatment of atrial fibrillation with flecainide. BMJ 2010;340:b4684.
62. Gupta A, Perera T, Ganesan A, et al. Complications of catheter ablation of atrial fibrillation: a systematic review. Circ Arrhythm Electrophysiol 2013;6:1082–8.
63. Furlanello F, Lupo P, Pittalis M, et al. Radiofrequency catheter ablation of atrial fibrillation in athletes referred for disabling symptoms preventing usual training schedule and sport competition. J Cardiovasc Electrophysiol 2008;19:457–62.
64. Calvo N, Mont L, Tamborero D, et al. Efficacy of circumferential pulmonary vein ablation of atrial fibrillation in endurance athletes. Europace 2010; 12:30–6.
65. Koopman P, Nuyens D, Garweg C, et al. Efficacy of radiofrequency catheter ablation in athletes with atrial fibrillation. Europace 2011;13:1386–93.
66. Mugnai G, de Asmundis C, Ciconte G, et al. Incidence and characteristics of complications in the setting of second-generation cryoballoon ablation: a large single-center study of 500 consecutive patients. Heart Rhythm 2015;12:1476–82.
67. Wong GR, Lau DH, Baillie TJ, et al. Novel use of sildenafil in the management of pulmonary hypertension due to post-catheter ablation 'stiff left atrial syndrome'. Int J Cardiol 2015;181:55–6.
68. Walters TE, Nisbet A, Morris GM, et al. Progression of atrial remodeling in patients with high burden atrial fibrillation: implications for early ablative intervention. Heart Rhythm 2016;13(2):331–9.