



Review Article

# The Application of High Intensity Interval Training in Atrial Fibrillation: A Literature Review

**Themistocleous Irene-Chrysovalanto\***, Hadjisavvas Stelios, Efstathiou Michalis A, Stefanakis Manos

School of Life and Health Sciences, Department of Health Science, Program of Physiotherapy, University of Nicosia, Cyprus

**\*Corresponding author:** Themistocleous Irene-Chrysovalanto, School of Life and Health Sciences, Department of Health Science, Program of Physiotherapy, University of Nicosia, Cyprus

**Citation:** Themistocleous I-C, Hadjisavvas S, Efstathiou M A., Stefanakis M (2024) The Application of High Intensity Interval Training in Atrial Fibrillation: A Literature Review. Int J Cerebrovasc Dis Stroke 7: 175. DOI: <https://doi.org/10.29011/2688-8734.100175>

**Received Date:** 26 January, 2024; **Accepted Date:** 02 February, 2024; **Published Date:** 05 February, 2024

## Abstract

Atrial fibrillation (AF) is a significant challenge for cardiovascular health, and exercise interventions have gained attention as potential therapeutic approaches. This literature review aims to provide a comprehensive overview of studies investigating the effects of high intensity interval training (HIIT) on individuals with AF. The limited studies, ranging from randomized controlled trials to case series, have been analysed in order to evaluate the impact of HIIT on several health parameters such as quality of life, aerobic capacity, physiological and cardiovascular parameters in individuals with AF. Emphasis was placed on understanding the safety of these programs, especially considering adverse events and limitations associated with small number of participants and the differences in study design. The findings of these studies reveal promising outcomes related to reduced AF symptoms severity, improved aerobic capacity, quality of life and positive effects on physiological and cardiovascular parameters. The review underscores the need for well-designed studies with larger sample sizes to improve the generalizability of results and address adequately safety concerns. Moreover, it highlights the current research gaps, including a standardized HIIT protocol for individuals with AF and the absence of long-term follow ups data. In conclusion, this review synthesizes existing knowledge on HIIT in AF population, offering insights into its potential benefits, safety considerations and other aspects for future research.

**Keywords:** High intensity interval training; Atrial fibrillation; High intensity training; Interval training; Cardiovascular health

## Introduction

Atrial fibrillation (AF) stands as the prevalent long-lasting cardiac rhythm disorder, characterized by irregular heartbeats [1]. It is estimated that a minimum of 33.5 million people globally is affected by this condition, with its prevalence to vary across different countries [1]. In 2016, the European Society of Cardiology reported that around 20.9 million men and 12.6 million women had received diagnoses of AF and due to changing demographics, longer life expectancies, an incidence of cardiac (hypertension, diabetes, valvular diseases) and non-cardiac (thyroid disorders) risk factors and improved survival rates for chronic illnesses there is an increase in AF prevalence [2-4]. Predictions suggest

that by 2060, European countries will experience a prevalence of 17.9 million AF cases [4], which is a major health concern as AF is linked to elevated mortality rates, heart failure, strokes, and various thromboembolic events [5-7].

Patients diagnosed with AF may experience symptoms like palpitations, dyspnoea, fatigue, dizziness, and fainting [6,8]. It is stated that there is an adverse relationship between the presence of symptoms related to AF and the physical capacity of patients [9]. It's worth emphasizing that the symptoms and duration of AF episodes can differ not only from one individual to another but also within the same person [6,8]. The treatment of AF has two primary objectives: first, to restore and maintain normal sinus rhythm and second, to prevent the patient from experiencing thromboembolic complications [6,8]. In cases where AF persists for an extended period (such as in persistent AF, long-standing persistent AF, and

permanent AF), an additional therapeutic goal is to manage the heart rate within the range of 60-80 beats per minute at rest and 90-115 beats per minute during physical activity. To achieve this heart rate, antiarrhythmic medications are administered, which work by suppressing the function of the atrioventricular node [6,8,10]. Furthermore, treatment should also focus on reducing AF-related symptoms and discomfort [11].

An integrated approach to caring for patients with AF necessitates a well-coordinated and personalised patient care pathway. Despite the improvements in comprehensive care for individuals with AF, exercise rehabilitation is not commonly included in standard care protocols [12]. Nevertheless, the latest report from the European Society of Cardiology on AF management highlights the importance of encouraging patients with AF to engage in moderate-intensity exercise and maintain physical activity levels to reduce the risk of AF [8]. Data from systematic reviews and meta-analyses have reported substantial improvements in cardiovascular capacity and quality of life for individuals with AF who underwent cardiac rehabilitation [13-16]. However, the research on exercise training for AF patients has employed diverse protocols, underscoring the lack of clear consensus regarding the exact exercise recommendations for individuals with AF, in contrast to other cardiovascular diagnosis.

In individuals with non-permanent AF, engaging in aerobic exercise training may contribute to a reduction in AF burden and further improve sinus rhythm [17]. As mentioned before, exercise training for individuals with AF is recommended to be moderate to vigorous intensity in aerobic form with a duration of 210 minutes per week [18]. Moreover, exercise should be adjusted based on any additional comorbidities that the individual may have [17]. Interventions involving aerobic exercise have demonstrated a reduction in the severity of the symptoms, improvement in functional capacity and quality of life both in patients with permanent and non-permanent AF [17-20]. Exercise rehabilitation is a significant and potentially a beneficial intervention for individuals with AF and other health care conditions. Nevertheless, research on exercise training for AF has employed various protocols, highlighting the lack of specific exercise recommendations for patients with AF [13]. Currently, there is limited evidence suggesting that high intensity aerobic training might not yield to an additional benefit, compared to moderate intensity activities. Moreover, individuals engaging to higher demands of exercise reported to have a higher risk of developing AF [21]. On the other hand, there is a growing-evidence in various cardiovascular diseases about the application of high intensity interval training (HIIT), which is superior to moderate intensity continuous training (MICT) in several health parameters [22-24]. Thus, this literature review was conducted to give a comprehensive overview of studies investigating the effects of HIIT on individuals with AF.

### **Atrial Fibrillation**

The established definition of an AF episode is a period of AF lasting a minimum of 30 seconds [4,25]. AF is marked by a rapid and irregular activation of the atria, resulting in both out-

of-sync atrial contractions and irregular ventricular excitation [26]. Confirming the presence of AF necessitates verifying the rhythm through an electrocardiogram (ECG) that displays signs of AF [8]. The electrocardiographic features of AF include: 1) irregularly irregular R-R intervals (when atrioventricular conduction is not compromised), 2) lack of clear and recurring P waves and 3) Irregular atrial activations [8]. More over the development in first-degree relatives [27]. Fibrillation can result from a range of pathophysiological changes, encompassing factors related to hemodynamics, electrophysiology, structural aspects, and autonomic regulation, as well as triggering factors like extrasystoles and atrial tachycardias [28]. These factors can range from genetic variations to visible alterations in atrial structure, all of which can disrupt the electrical function of atrial cells, leading to chaotic atrial electrical activity [28].

Myocardial electrical characteristics are regulated by ionic channels situated on the cell membrane. Cellular activation primarily hinges on sodium, calcium, and potassium channels. The refractory period of cells is primarily determined by the duration between cell activation and the restoration of the action potential to its original state [29]. An increase in the influx of ions, specifically calcium and sodium, leads to an extension of the refractory period, while an increase in the efflux of potassium results in a reduction of this period. Moreover, the proteins found in the connections between cardiomyocytes are responsible for the flow of ions between cells, enabling the normal transmission of electrical signals [28,29]. In the context of AF, there are changes in these components of typical cell electrophysiology, which are referred to as electrical remodelling [29]. The most common type of electrical remodelling occurs due to a sudden influx of calcium into the cells, causing them to depolarize at a higher frequency [26]. This, in turn, leads to the deactivation of calcium currents and an increase in potassium currents, resulting in a shorter action potential duration and an elevated susceptibility to AF [29]. It also contributes to the likelihood of early recurrence after cardioversion and the progression of paroxysmal forms of arrhythmia into more persistent forms [29].

### **Risk Factors of Atrial Fibrillation**

Advancing in age is a significant risk factor for AF. However, the heightened prevalence of other comorbid conditions, as witnessed in clinical settings, cannot solely be attributed to patients' age; there are other factors which also play a role in this pattern [28]. Age-related alterations in atrial electrophysiology and electro-anatomy, such as prolonged conduction time and the development of widespread low-voltage areas, have been documented [30]. These modifications, when combined with age-associated risk factors, collectively contribute to the promotion of AF [30]. Discrepancies in the occurrence of AF among various racial and ethnic groups may arise from variations in healthcare accessibility or the underreporting of AF symptoms, potentially resulting in underdiagnoses in specific populations [31]. Multiple studies examining racially diverse groups have found that Black, Hispanic, Asian, and Native American individuals exhibit the

lowest incidence of AF, even though they have a higher occurrence of cardiometabolic risk factors compared to individuals of European ancestry [32-34]. Following population-based research, it has been demonstrated that having a family history of AF is linked to a 40% higher risk of AF. Up to this point, researchers have identified at least 15 mutations in genes associated with the K<sup>+</sup> channel or its auxiliary subunits that are responsible for causing AF [27]. These mutations involve genes such as ABCB9 (IKATP), HCN4 (If), KCNA5 (IKur), KCND3 (IKs), KCNE1 (IKs), KCNE2 (IKs), KCNE3 (IKs), KCNE4 (IKs), KCNE5 (IKs), KCNH2 (IKr), KCNJ2 (Ik1), KCNJ5 (IKAch), KCNJ8 (IKATP), KCNN3, and KCNH1 [27]. Moreover, mutations that enhance function led to an increase in the repolarizing K<sup>+</sup> current, resulting in a shorter action potential duration (APD) and atrial refractoriness. On the other hand, mutations that reduce function delay repolarization and play a role in Ca<sup>2+</sup>-mediated post-depolarization, which is a contributing factor to AF. Mutations that enhance function can heighten the susceptibility to AF by elevating cellular hyperexcitability, whereas mutations that lead to a loss of function decrease effective refractory period (ERP) and decelerate conduction [27].

On the other hand, a wide array of risk factors and clinical comorbidities, which can be modified through lifestyle changes, are linked to the onset, persistence, and advancement of AF. Patients with long-term hypertension exhibited conduction deficiencies and increased areas of low voltage, indicating atrial-specific alterations that make them more susceptible to developing AF [35]. Left atrial enlargement is a recognized predictor of AF, and in cases of chronic hypertension, various pathological characteristics such as left ventricular hypertrophy and impaired diastolic function are linked to AF. An elevation in left ventricular end-diastolic pressure, which consequently raises left atrial pressure and volume, is a common factor [27]. This leads to atrial remodelling characterized by slower and irregular atrial conduction and heightened pulmonary vein (PV) excitation. Furthermore, the increased mass of the left atrium provides support for multiple re-entry circuits [27].

Glucose intolerance and insulin resistance seem to play a role in the formation of an AF substrate. The intricate molecular process through which insulin resistance influences the heart's structure involves mitochondrial dysfunction and oxidative stress. These factors affect the transcription and translation processes necessary for the heart's adaptation [36].

Indirectly, smoking can elevate the likelihood of myocardial ischemia by increasing systemic catecholamine levels and impacting myocardial function [27]. It can also reduce the oxygen-carrying capacity and promote coronary vasoconstriction [27]. Furthermore, smoking accelerates the progression of atherosclerosis by affecting factors such as lipid profiles, endothelial function, oxidative stress, inflammation, and the potential for blood clot formation [27]. These effects can indirectly raise the susceptibility

to AF by predisposing individuals to atrial ischemia, heart attacks, and heart failure [27].

There are diverse pathophysiological mechanisms contributing to the onset of AF, encompassing structural and electrical abnormalities, remodelling of the tissues and inflammation [37,38]. When there are electrical and structural abnormalities in the tissue of atria, it results in irregular contractions of the atria and uncoordinated blood flow into the ventricles. This in turn can lead to significant fluctuations in cardiac output and blood pressure due to AF [39].

AF particularly in persistent and permanent forms, occurs in a minimum of 20% of individuals with congestive heart failure and its prevalence rises with the severity of the syndrome [40,41]. Heart failure and AF have shared pathophysiology and can mutually worsen each other through mechanisms such as cardiac remodelling, activation of neurohormonal mechanisms and rate-related impairment of left ventricular function [42,43]. Given these frequent co-existences of both conditions, the occurrence of AF is expected in most patients with heart failure [44].

### Management of Atrial Fibrillation

A crucial aspect of AF management involves oral anticoagulation due to the risk of stroke in individuals with AF [8]. The arrhythmia can be managed through controlling the heart rate by slowing down or through controlling the rhythm by re-establishing and maintaining a sinus rhythm [8]. This management via medication, cardioversion and ablation therapy [8].

Studies have shown that maintaining the optimal risk factors and achieving ideal cardiovascular health is strongly linked to a significant reduction in the risk of developing AF and complications [45,46]. In order to reduce the risk of developing AF, those at higher AF risk should undergo a comprehensive targeted lifestyle related risk factor management. This type of management involves a weight loss if it is necessary, more physically active lifestyle, smoking cessation interventions/medication, moderation of alcohol consumption, blood pressure and diabetes monitoring [21,47,48].

Consistent physical activity and exercise training in structured program are crucial for the prevention of cardiovascular health and this statement is supported by evidence both from studies and real-world clinical settings [49,50]. Nevertheless, there is high percentage of physical inactivity; thus, the recommendations are not met. Irrespective of whatever exercise directly benefits AF, individuals engaging in physical activity and exercise may improve their aerobic capacity, muscular strength and flexibility. These outcomes in turn contribute to a better quality of life as they ease in performing daily activities [51,52]. In the following tables (Table 1-3) are demonstrated the exercise training recommendations for individuals with AF.

**Table 1:** Aerobic training recommendations.

Aerobic Training Parameter (FITT)	Recommendation
Frequency	3-5days per week
Intensity	50%-80%HRR (RPE 11-14)
Type	Walking, jogging, stationary cycling, elliptical stepping, rowing, or swimming
Time	30-60 minutes per day
Progression	Initiate exercise at 30%-59% of HRR (RPE 11-14); increase time gradually by 5-10 minutes as tolerated. Gradually increase the frequency to 4-7 days per week
<b>Abbreviations: HRR:</b> Heart Rate Reserve; <b>RPE:</b> Rating of Perceived Exertion Adapted from [53,54]	

**Table 2:** Resistance training recommendations.

Resistance Training Parameter (FITT)	Recommendation
Frequency	1-2 days per week (>60 years old); 2-3 days per week (≤60 years old)
Intensity	40%-50% 1RM, RPE=11-12 (>60 years old); 60%-70% 1RM, RPE = 13-14 (<60 years old)
Repetitions	10-15 (>60 years old); 8-12 (≤60 years old)
Sets	1-2 per muscle group (>60 years old); 2-4 per muscle group (<60 years old)
Rest Period	30-60 seconds between sets
Type	8-10 multi-joint exercises using bodyweight movements, free weights, machines, elastic resistance, and medicine balls
Progression	Increase load intensity when 1-2 reps can be performed properly beyond the prescribed number during 2 consecutive sessions
<b>Abbreviations: 1RM:</b> 1 Repetition Maximum; <b>RPE:</b> Rating of Perceived Exertion Adapted from [53,54].	

**Table 3:** Flexibility training recommendations.

Flexibility Training Parameter (FITT)	Recommendation
Frequency	2-3 days per week
Intensity	Stretch to the point of feeling tightness or slight discomfort
Time	10-30 seconds hold for static stretching; 2-4 repetitions of each exercise
Type	Static, dynamic, and/or PNF stretching
Progression	Gradually increase frequency to 4-7 days per week
<b>Abbreviations: PNF:</b> Proprioceptive Neuromuscular Facilitation Adapted from [53,54].	



Previous randomized controlled trial (RCT) studies have investigated the effects of exercise in individuals with paroxysmal or permanent AF. These RCT highlights the improvements in symptoms, cardiovascular-function and exercise capacity [13,55,56]. From the findings it was suggested that when exercise training it is supervised it is safe, with a low incidence of serious adverse events. Nevertheless, continuously monitoring and special consideration of patients' characteristics are important in order to keep a balance between exercise benefits and potential adverse events associated with exercise. Moreover, other RCTs investigating exercise in patients with permanent AF, presented encouraging findings. Despite the small size of participants Osbak et al. (2012), showed improvements in muscle strength, quality of life and exercise capacity and no adverse events were observed [57]. The HF-Action study (2017) involving patients with AF and heart failure, revealed mixed results [58]. More specifically, it was reported no significant difference in mortality, rates of hospitalization, AF events between exercise group and control group [58]. On the other hand, while the RACE 3-Trial (2018) indicated a higher sinus rhythm in the exercise group, the lack of information regarding physical activity levels in the control group and the heterogeneity in the exercise interventions across studies bring challenges into reaching to conclusive findings [59].

Previous information suggests that regular exercise training could be linked to lower mortality rates of cardiovascular health issues, even in individuals with AF [60]. However, there is limited data regarding how cardiac rehabilitation programs impact serious adverse events and the specific exercise recommendations for this clinical population is also not very strong. On the other hand, there is increasing evidence in other cardiovascular diseases suggesting that HIIT is better or/ and similar than MICT for improving several health parameters [61-63].

It is reported that MICT may enhance the creation of inflammatory cytokines, increase the presence of anti-inflammatory agents, improve the ability of the body to fight oxidative stress and improve the breakdown of blood clots [64,65]. In addition, MICT could improve the functioning of endothelial cells by increasing the production of and availability of nitric oxide (NO), potentially lowering the risk of developing AF and any other cardiovascular health issues in patients with AF [66]. On the other hand, HIIT has unique potentials in improving various physiological aspects [67], as it was demonstrated to enhance exercise capacity and exercise adherence in patients with various cardiovascular conditions. In addition, it has been shown to positively impact quality of life, the cardiac structure and myocardium contraction and mitochondrial function in skeletal muscles [67,68]. These results, suggest that using HIIT as an alternative exercise regimen could be a practical and an effective method to prevent and manage AF, possibly offering outcomes similar to or better than other approaches.

Although there are a lot of data regarding the impact of exercise in AF and various exercise modalities were applied, there is a limited amount of data related to the therapeutic impact of HIIT in individuals with AF.

### **High Intensity Interval Training in AF**

The very first study by Malmo et al. (2016) [55] examined the impact of high intensity in patients with non-permanent AF. More specifically, 51 patients with non-permanent AF were randomized to a group of aerobic interval training (AIT) (n=26) on a treadmill or to a control group (n=25) with-out exercise. Exercise session started with a 10-minute warm up reaching 60-70% of heart rate maximum (HRmax), followed by a 4x4-minute interval at 85%-95% of HRmax, with 3-minutes of active recovery (AR) at 60%-70% of HRmax between intervals, ending with a 5-minute cooldown period. The frequency of the program was 3 times per week lasting for 12 weeks in total. It was reported a significant reduction in mean time in AF, frequency of symptoms and severity, cardiorespiratory fitness and quality of life in intervention-group. This study demonstrated that the exercise protocol with high intensity is safe as no major adverse events were observed [55].

While this study provides valuable insights into the potential of high intensity exercise for individuals with non-permanent AF, the small sample size and specific inclusion criteria of the study, may restrict the generalization of the results to a broader AF population. Moreover, the duration of 12-weeks was relatively short for this population and long-term effects and sustainability of the observed results remain unclear. Future research with larger sample size and diverse participants, along with prolonged periods of follow-up, would contribute to a more comprehensive understanding of the impact of high intensity exercise on AF population.

In a more recent study by Reed et al. (2022) [57] 86 individuals with persistent and permanent AF participated 2 times per week either to a HIIT program or to a cardiovascular rehabilitation program for a total of 12 weeks. HIIT was performed on an upright cycle ergometer and involved a 23-minute session which consisted of a 2-minute warm-up at 50% of peak power output (PPO) and a 1-minute cool-down at 25% of PPO, 2x8-minute intervals of 30s work periods at 80%-100% of PPO, with 30s AR and 4-minutes of recovery between the blocks. The other group applied for 60 minutes a 10-15minute warm-up of aerobic exercise, 30-minutes of continuous aerobic exercise (walking or jogging, cycling, elliptical, rowing) at moderate to vigorous intensity (67%-95% HRmax) and a 15-minute cool-down of straitening and stretching exercises. It was reported that participants following either HIIT or cardiac rehabilitation program could improve functional capacity, quality of life, physiological parameters such as resting heart rate and time in AF [69].

The study carried out by Reed et al. (2022) [69] provides significant insights into the effects of different exercise programs on individuals with persistent and permanent AF. The inclusion of HIIT and cardiovascular rehabilitation program enables for a comprehensive comparison. The recognition of HIIT as an alternative exercise regimen to continuous training is a noteworthy finding, particularly due to its shorter time, which may improve exercise adherence. On the other hand, the study also highlights the observation of more adverse events in HIIT-group compared

to the other group. This finding raises safety concerns about the application of HIIT in population with persistent and permanent AF. A further assessment of the nature and severity of these adverse events is vital in order to provide an understanding of the risks associated with HIIT in this clinical population.

A case study by Reed et al. (2015) [70], reported that a 74-year-old man with permanent AF who underwent to a 10-week HIIT (23-minute session, 2 x 8-minute interval training blocks of 30s at 80-100% of PPO interspersed with 30s AR, 4 minutes of passive recovery between the blocks) had substantial improvements in physiological parameters such heart rate, blood pressure, aerobic and functional capacity and quality of life [70].

While this case study demonstrated some positive changes in physiological parameters, aerobic and functional capacity and quality of life it is important to acknowledge the limitations of a single case study, as a generalization to a wider AF population may be challenging. In addition, the lack of a control-group complicates the attribution of the observed improvements exclusively to the HIIT intervention. In order to confirm and extend the case study findings, further research with larger sample sizes, inclusion of control-groups and long-term follow-ups is essential.

In the randomized controlled trial (RCT) by Elliot et al. (2023) [71] participated 120 individuals with paroxysmal or persistent AF. 60 participants applied an aerobic exercise program 4x4-minutes at 85%-90% of heart rate reserve (HRR) for 6 months and the rest of them received usual care involving education of physical activity and recommendations for 150 minutes per week of moderate physical activity. At 6 months participants in the exercise-group had a lower AF symptoms severity, increased peak oxygen consumption (VO<sub>2</sub>peak) compared to the control-group. Moreover, after 12 months, 24 out of 60 participants in exercise-group were “AF-free”, while 12 out of 60 participants in the control-group were also free from AF [71].

The RCT’s strength lie in its randomized design and the use of a control-group receiving usual care, contributing to a more robust comparison. Nevertheless, the criteria for defending participants as “AF-free” at 12 months might not reflect the complexity of AF management as the symptom’s severity were assessed via a validated questionnaire.

A case series by Vidal-Almela et al. (2022) [72] stated that 4 men with permanent AF participated in a 3 day per week HIIT program on a cycle ergometer, lasting a total of 10 weeks. Each exercise session involved 16-minutes of HIIT, divided into 2 x 8-minute blocks, interspersed with a 4-minute active or passive recovery period, based on participants’ preference. All participants had a reduction in heart rate following the cool-down, with only one participant showing a reduction in blood pressure. In these series of cases, it is important to note that exercise adherence was not 100% and participants reported symptoms of fatigue, musculoskeletal symptoms and lack of motivation [72].

The inclusion of parameters such as heart rate and blood pressure provide a brief view into the physiological responses

of exercise. However, the small sample size of participants with permanent AF limits the generalizability of the results. Moreover, as mentioned before the lack of control-group makes it difficult to attribute observed effects only to HIIT intervention. On the other hand, the reduction in heart rate is a positive outcome, but the absence of consistent blood pressure reduction among the participants, may raises questions regarding the wider cardiovascular impact. In addition, participation adherence was not 100% and the reported symptoms among participants underscore the potential challenges patients with AF may face during the application of a HIIT program. These symptoms may affect the overall feasibility and sustainability of such interventions in this clinical population.

In another study by Hegbom et al. (2006) [73], 30 participants with chronic AFM were randomized into an exercise-group or to control-group without exercise for 2 months. 15 individuals in the exercise-group applied 3 days per week a session involving a 5-minute warm-up, 3x15-minute aerobic exercise at 70-90% of HRmax on a cycle ergometer, interspersed with strengthening exercises for the core and lower limbs and a 15-minute cool-down with stretches and relaxation. Following a two-month training program for individuals with AF, there were notable improvements in exercise capacity, heart rate variability quality of life and a reduction in resting heart rate [73].

This RCT provided new information about the potential benefits of exercise in individuals with chronic AF, as the exercise protocol involved the combination of aerobic and strengthening exercises. Apart from the small sample size, the short duration of the intervention raises questions regarding the long-term sustainability and lasting effects of the exercise training.

In a study by Terada et al. (2023) [74], 23 individuals with permanent or persistent AF participated twice a week to a supervised HIIT or moderate intensity continuous training (MICE) program lasting for 12 weeks. Each HIIT session lasted 23-minutes and conducted on a cycle ergometer. The session started with a 2-minute warm-up, followed by 2 blocks of 8 intervals of 30s of high intensity at 80-100% PPO, with 30s AR periods. There was a 4-minute AR between the blocks and 1-minute cool-down. On the other hand, MICT session involved a 15-minute warm-up, 30-minutes of continuous aerobic training and 15-minute cool-down. From the results it was observed that a twice weekly HIIT or MICT for 12 weeks did not improved cardiorespiratory fitness. Moreover, only a small percentage of these participants achieved a clinical meaningful increase in cardiorespiratory fitness [74].

This study presents an interesting assessment of the effects of HIIT and MICE on patients with permanent or persistent AF. However, apart from the detailed description of the exercise protocol and the inclusion of both exercise regimes, the findings of this study indicated no significant improvement in cardiorespiratory fitness with the exception of a limited number of participants achieving a clinical meaningful increase. This raise questions about the effectiveness of these exercise interventions in this clinical population.

Another study by Melo et al. (2019) [75], included 37 patients with HF and AF soon after cardiac resynchronization therapy (CRT) implantation. Individuals who were randomized in HIIT-group applied twice a week a 60-min session for 6 months. More specifically, each session began with a 10-min warm-up and concluded with a 5–7-minute cool-down. The main program comprised 4 interval periods at 90-95% of HRmax, interspersed with 3 AR periods at 60-70% of HRmax between interval training periods. The rest of the participants were randomized to a control-group with no exercise intervention. In the post hoc analysis, it was found that HIIT intervention led to improvements in quality of life and VO<sub>2</sub>peak in both groups, with no significant difference between them [75].

It's important to note that participants had undergone CRT and the sample size of participants with AF was limited to 18 across both groups [75]. Moreover, the findings of the study and more specifically the improvement in quality of life and VO<sub>2</sub>peak in both groups demonstrated no significant difference between them, raising questions about the effectiveness of HIIT. In addition, the small sample size of AF participants and the post hoc analysis further complicate the interpretation of the results.

In the study of Skielboe et al. (2017) [56], 76 individuals with paroxysmal or persistent AF were randomized to either low intensity or high intensity exercise-group for 12 weeks. Low intensity was defined as 50% of the maximum perceived exertion (11-13 Borg scale), while high intensity was defined as 80% of the maximum perceived exertion (16-18 Borg scale). Each session involved a 10-minute warm-up at 7-10 Borg, followed by 20-minutes of intervals performed on a cycle ergometer, 20-minutes of various circuit exercises performed on the floor, followed by a 10-minute cool-down. Following the 12-weeks, both exercise-groups had significant improvements in VO<sub>2</sub>peak, with no statistically significant difference between the groups. Moreover, no serious adverse events were observed [56].

The inclusion of both low and high intensity exercise groups, adds a valuable diversity to the assessment of HIIT in AF. The significant improvements observed in VO<sub>2</sub>peak in both groups indicate the potential benefits of exercise training for patients with AF. However, the absence of no significant difference among the groups of low intensity and high intensity raises questions about the necessity of engaging an individual with AF in a high intensity exercise training program as other studies reported adverse events. On the other hand, this study reported no serious adverse events, highlighting the safety of exercising with high intensity.

Moreover, in the study of Kim et al. (2023) [76], participated 74 individuals with AF which were randomized into exercise-group or to a medical-group. Before the main exercise training, participants applied a 10-minute warm-up at 60-70% of HRpeak. The main exercise program performed on a cycle ergometer, consisted of 4-minutes at 85-95% of HRpeak, with 3-minutes of AR at 60-70% of HRpeak between the sessions. A 5-minute cool-down was then conducted at 20-30% of HRpeak. It seems that a 12-month exercise program with high intensity enhances

endothelial function and it is linked to a decrease in circulating pro-inflammatory and thrombogenic factors, leading to lower risk of complications related to blood vessel dysfunction [76]. On the other hand, the duration of the intervention is relatively short in the context of chronic conditions like AF.

## Conclusion

In conclusion, this review sheds light on the potential benefits of HIIT in individuals with AF. While the reviewed limited studies indicate that well-designed HIIT protocols can lead to improvements in various cardiovascular health parameters, including cardiorespiratory fitness, quality of life, physiological parameters and endothelial function, it is vital to interpret their results with caution.

A significant concern highlighted in the literature is the safety of participants with AF. While some studies often emphasize only on the improvement of the primary outcomes, other studies report absence of any adverse events indicating that HIIT can be well-tolerated by this clinical population. Nevertheless, it is important to acknowledge the limitations of these studies because due to the small sample size and non-well design, they may not provide an understanding of the potential risks associated with HIIT in the AF. Another issue was the heterogeneity across the included studies in terms of AF types, participants characteristics and exercise training protocols which introduces variability that complicates the generalization of the results. In addition, the lack of standardized HIIT guidelines in patients with AF further emphasizes the necessity of caution in applying these exercise protocols across various clinical populations.

In order to address these concerns and establish a more robust opinion for HIIT recommendations in AF, future research should assess larger sample size, be well-designed with longer periods of follow-up.

## Ethics approval and Consent to participate

Not applicable.

## Declaration of competing interest

The authors declare that they have no conflict of interest.

## Acknowledgments

None

## References

1. Karamitanha F, Ahmadi F, Fallahabadi H (2023) Difference between various countries in mortality and incidence rate of the atrial fibrillation based on human development index in worldwide: Data from Global Burden of Disease 2010-2019. *Curr Probl Cardiol* 48: 101438.
2. Bhalia S, Pallangyo P, Dalidali A, Salum S, Kawajika R, et al. (2020) Burden and correlates of atrial fibrillation among hypertensive patients attending a tertiary hospital in Tanzania. *BMC Cardiovasc Disord* 20: 235.
3. Jones NR, Taylor CJ, Richard Hobbs FD, Bowman L, Casadei B (2020) Screening for atrial fibrillation: A call for evidence. *Eur Heart J* 41: 1075-1085.



4. Khurshid S, Healey JS, McIntyre WF, Lubitz SA (2020) Population-based screening for atrial fibrillation. *Circ Res* 127: 143-154.
5. Camm AJ, Lip GYH, De Catherina R, Savelieva I, Atar D, et al. (2012) 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: An update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. *Eur Heart J* 33: 2719-2147.
6. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, et al. (2016) 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace* 18: 1609-1678.
7. Schoonderwoerd BA, Smit MD, Pen L, Van Gelder IC (2008) New risk factors for atrial fibrillation: Causes of 'not-so-lone atrial fibrillation'. *EP Europace* 10: 668-673.
8. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, et al. (2021) 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 42: 373-498.
9. Atwood JE, Myers JN, Tang XC, Reda DJ, Singh SN, et al. (2007) Exercise capacity in atrial fibrillation: A substudy of the Sotalol-Amiodarone Atrial Fibrillation Efficacy Trial (SAFE-T). *Am Heart J* 153: 566-572.
10. Brenyo AJ, Aktas MK (2011) Non-pharmacologic management of atrial fibrillation. *Am J Cardiol* 108: 317-325.
11. Brenyo A, Link MS, Barsheshet A, Moss AJ, Zareba W, et al. (2011) Cardiac resynchronization therapy reduces left atrial volume and the risk of atrial tachyarrhythmias in MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy). *J Am Coll Cardiol* 58: 1682-1689.
12. Buckley BJR, Risom SS, Boidin M, Lip GYH, Thijssen DHJ (2022) Atrial fibrillation specific exercise rehabilitation: Are we there yet?. *J Pers Med* 12: 610.
13. Risom SS, Zwisler AD, Johansen JP, Sibiltz KL, Lindschou J, et al. (2017) Exercise-based cardiac rehabilitation for adults with atrial fibrillation. *Cochrane Database Syst Rev* 2: Cd011197.
14. Smart NA, King N, Lamber JD, Pearson MJ, Campbell JL, et al. (2018) Exercise-based cardiac rehabilitation improves exercise capacity and health-related quality of life in people with atrial fibrillation: A systematic review and meta-analysis of randomised and non-randomised trials. *Open Heart* 5: e000880.
15. Zhang Y, Ren P, Tang A, Dong L, Hu X, et al. (2022) Efficacy of exercise rehabilitation in patients with atrial fibrillation after radiofrequency ablation: A meta-analysis of randomized controlled trials. *Evid Based Complement Alternat Med* 2022: 9714252.
16. Borland M, Bergfeldt L, Cider A, Rosenkvist A, Jacobsson M, et al. (2022) Effects of 3 months of detraining following cardiac rehabilitation in patients with atrial fibrillation. *Eur Rev Aging Phys Act* 19: 14.
17. Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, et al. (2023) 2023 ACC/AHA/ACCP/HRS Guideline for the diagnosis and management of atrial fibrillation: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 149: e1-e156.
18. Anderson JL, Heidenreich PA, Barnett PG, Creager MA, Fonarow GC, et al. (2014) ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures: A report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. *J Am Coll Cardiol* 63: 2304-2322.
19. Graham R, Mancher M, Wolman DM, Greenfield S, Stenberg E (2011) Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, in *Clinical Practice Guidelines We Can Trust*. National Academies Press (US).
20. Arnett DK, Goodman RA, Halperin JL, Anderson JL, Parekh AK, et al. (2014) AHA/ACC/HHS strategies to enhance application of clinical practice guidelines in patients with cardiovascular disease and comorbid conditions: From the American Heart Association, American College of Cardiology, and U.S. Department of Health and Human Services. *J Am Coll Cardiol* 64: 1851-1856.
21. Di Benedetto L, Michels G, Luben R, Khaw KT, Pfister R (2018) Individual and combined impact of lifestyle factors on atrial fibrillation in apparently healthy men and women: The EPIC-Norfolk prospective population study. *Eur J Prev Cardiol* 25: 1374-1383.
22. Hannan AL, Hing W, Simas V, Climstein M, Coombers JS, et al. (2018) High-intensity interval training versus moderate-intensity continuous training within cardiac rehabilitation: A systematic review and meta-analysis. *Open Access J Sports Med* 9: 1-17.
23. Jaureguizar KV, Vicente-Campos D, Bautista LR, de la Peña CH, Gomez MJA, et al. (2016) Effect of high-intensity interval versus continuous exercise training on functional capacity and quality of life in patients with coronary artery disease: A randomized clinical trial. *J Cardiopulm Rehabil Prev* 36: 96-105.
24. Du L, Zhang X, Chen K, Ren X, Chen S, et al. (2021) Effect of high-intensity interval training on physical health in coronary artery disease patients: A meta-analysis of randomized controlled trials. *J Cardiovasc Dev Dis* 8: 158.
25. McIntyre WF, Diederichsen SZ, Freedman B, Schnabel RB, Svennberg E, et al. (2022) Screening for atrial fibrillation to prevent stroke: A meta-analysis. *Eur Heart J Open* 2: oead044.
26. Li YG, Lee SR, Choi EK, Lip GY (2018) Stroke prevention in atrial fibrillation: Focus on Asian patients. *Korean Circ J* 48: 665-684.
27. Bizhanov KA, Abzaliyev KB, Baimbetov AK, Sarsenbayeva AB, Lyan E (2023) Atrial fibrillation: Epidemiology, pathophysiology, and clinical complications (literature review). *J Cardiovasc Electrophysiol* 34: 153-165.
28. Cintra FD, Figueiredo MJO (2021) Atrial fibrillation (Part 1): Pathophysiology, risk factors, and therapeutic basis. *Arq Bras Cardiol* 116: 129-139.
29. Schotten U, Verheule S, Kirchhof P, Goette A (2011) Pathophysiological mechanisms of atrial fibrillation: A translational appraisal. *Physiol Rev* 91: 265-325.
30. Kistler PM, Sanders P, Fynn SP, Stevenson IH, Spence SJ, et al. (2004) Electrophysiologic and electroanatomic changes in the human atrium associated with age. *J Am Coll Cardiol* 44: 109-116.
31. Elliott AD, Middeldrop ME, Van Gelder IC, Albeert CM, Sanders P (2023) Epidemiology and modifiable risk factors for atrial fibrillation. *Nat Rev Cardiol* 20: 404-417.
32. Rodriguez CJ, Soliman EZ, Alonso A, Swett K, Okin PM, et al. (2015) Atrial fibrillation incidence and risk factors in relation to race-ethnicity and the population attributable fraction of atrial fibrillation risk factors: The Multi-Ethnic Study of Atherosclerosis. *Ann Epidemiol* 25: 71-76. e1.
33. Ugowe FE, Jackson 2nd LR, Thomas KL (2018) Racial and ethnic differences in the prevalence, management, and outcomes in patients with atrial fibrillation: A systematic review. *Heart Rhythm* 15: 1337-1345.



34. Essien UR, Kornej J, Johnson AE, Schulson LB, Benjamin EJ, et al. (2021) Social determinants of atrial fibrillation. *Nat Rev Cardiol* 18: 763-773.
35. Medi C, Kalman JM, Ling LH, The AW, Lee G, et al. (2011) Atrial electrical and structural changes associated with longstanding hypertension in humans: Implications for the substrate for atrial fibrillation. *J Cardiovasc Electrophysiol* 22: 317-324.
36. Huxley RR, Fillion KB, Konety S, Alonso A (2011) Meta-analysis of cohort and case-control studies of type 2 diabetes mellitus and risk of atrial fibrillation. *Am J Cardiol* 108: 56-62.
37. January CT, Samuel Wann L, Alpert JS, Calkins H, Cigarroa JE, et al. (2014) 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* 130: 2071-2104.
38. Guo Y, Lip GY, Apostolakis S (2012) Inflammation in atrial fibrillation. *J Am Coll Cardiol* 60: 2263-2270.
39. Xu J, Luc JGY, Phan K (2016) Atrial fibrillation: Review of current treatment strategies. *J Thorac Dis* 8: E886-E900.
40. De Ferrari GM, Klersy C, Ferrero P, Fantoni C, Salerno-uriarte D, et al. (2007) Atrial fibrillation in heart failure patients: Prevalence in daily practice and effect on the severity of symptoms. Data from the ALPHA study registry. *Eur J Heart Fail* 9: 502-519.
41. Maisel WH, Stevenson LW (2003) Atrial fibrillation in heart failure: Epidemiology, pathophysiology, and rationale for therapy. *Am J Cardiol* 91: 2d-8d.
42. Anter E, Jessup M, Callans DJ (2009) Atrial fibrillation and heart failure: Treatment considerations for a dual epidemic. *Circulation* 119: 2516-2525.
43. Kotecha D, Piccini JP (2015) Atrial fibrillation in heart failure: What should we do? *Eur Heart J* 36: 3250-3257.
44. Sartipy U, Dahlstrom U, Fu M, Lund LH (2017) Atrial fibrillation in heart failure with preserved, mid-range, and reduced ejection fraction. *JACC Heart Fail* 5: 565-574.
45. Huxley RR, Lopez FL, Folsom AR, Agarwal SK, Loehr LR, et al. (2011) Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: The Atherosclerosis Risk in Communities (ARIC) study. *Circulation* 123: 1501-1508.
46. Garg PK, O'Neal WT, Ogunsua A, Thacker EL, Howard G, et al. (2018) Usefulness of the American Heart Association's life simple 7 to predict the risk of atrial fibrillation (from the REasons for Geographic And Racial Differences in Stroke [REGARDS] Study). *Am J Cardiol* 121: 199-204.
47. Soliman EZ, Rahman AF, Zhang ZM, Rodriguez CJ, Chang TI, et al. (2020) Effect of intensive blood pressure lowering on the risk of atrial fibrillation. *Hypertension* 75: 1491-1496.
48. Elliott AD, Linz D, Mishima R, Kadhim K, Gallagher C, et al. (2020) Association between physical activity and risk of incident arrhythmias in 402 406 individuals: Evidence from the UK Biobank cohort. *Eur Heart J* 41: 1479-1486.
49. Dibben G, Faulkner J, Oldridge N, Rees K, Thompson DR, et al. (2021) Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev* 11: Cd001800.
50. Buckley BJR, Harrison SL, Fazio-Eynullayeva E, Underhill P, Lane DA, et al. (2021) Exercise-based cardiac rehabilitation and all-cause mortality among patients with atrial fibrillation. *J Am Heart Assoc* 10: e020804.
51. Sorace P, Ronai P, Berry R (2019) Atrial fibrillation and exercise: Exercise recommendations 41: 118-123.
52. Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, Minson CT, Nigg CR, et al. (2009) Exercise and physical activity for older adults. 41: 1510-1530.
53. Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, Minson CT, Nigg CR, et al. (2009) American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 41: 1510-1530.
54. Bayles MP (2023) ACSM's exercise testing and prescription. Lippincott Williams & Wilkins.
55. Malmo V, Nes BM, Amundsen BH, Tjonna AE, Stoylen A, et al. (2016) Aerobic interval training reduces the burden of atrial fibrillation in the short term: A randomized trial. *Circulation* 133: 466-473.
56. Skielboe AK, Bandholm TQ, Hakmann S, Mourier M, Kalleose T, et al. (2017) Cardiovascular exercise and burden of arrhythmia in patients with atrial fibrillation: A randomized controlled trial. *PLoS One* 12: e0170060.
57. Osbak PS, Mourier M, Henriksen JH, Kofoed KF, Jensen JB (2012) Effect of physical exercise training on muscle strength and body composition, and their association with functional capacity and quality of life in patients with atrial fibrillation: A randomized controlled trial. *J Rehabil Med* 44: 975-979.
58. Luo N, Merrill P, Parikh KS, Whellan DJ, Pina IL, et al. (2011) Exercise training in patients with chronic heart failure and atrial fibrillation. *J Am Coll Cardiol* 69: 1683-1691.
59. Santema BT, Kloesterman M, Van Gelder IC, Mordi I, Lang CC, et al. (2017) Comparing biomarker profiles of patients with heart failure: Atrial fibrillation vs. sinus rhythm and reduced vs. preserved ejection fraction. *Eur Heart J* 39: 3867-3875.
60. Myrstad M, Malmo V, Ulmoen SR, Tveit A, Loennechen JP (2019) Exercise in individuals with atrial fibrillation. *Clin Res Cardiol* 108: 347-354.
61. Su L, Fu J, Sun S, Zhai G, Cheng W, et al. (2019) Effects of HIIT and MICT on cardiovascular risk factors in adults with overweight and/or obesity: A meta-analysis. *PLoS One* 14: e0210644.
62. Yu H, Zhao X, Wu X, Yang J, Wang J, et al. (2023) High-intensity interval training versus moderate-intensity continuous training on patient quality of life in cardiovascular disease: A systematic review and meta-analysis. *Scientific Reports* 13: 13915.
63. Yue T, Wang Y, Liu H, Kong Z, Qi F (2022) Effects of high-intensity interval vs. moderate-intensity continuous training on cardiac rehabilitation in patients with cardiovascular disease: A systematic review and meta-analysis. *Front Cardiovasc Med* 9: 845225.
64. Kato M, Ogano M, Mori Y, Kochi K, Morimoto D, et al. (2019) Exercise-based cardiac rehabilitation for patients with catheter ablation for persistent atrial fibrillation: A randomized controlled clinical trial. *Eur J Prev Cardiol* 26: 1931-1940.
65. Chen YW, Apostolakis S, Lip GY (2014) Exercise-induced changes in inflammatory processes: Implications for thrombogenesis in cardiovascular disease. *Ann Med* 46: 439-455.
66. Green DJ, Hopman MTE, Padilla J, Laughlin MH, Thijssen DHJ (2017) Vascular Adaptation to Exercise in Humans: Role of hemodynamic stimuli. *Physiol Rev* 97: 495-528.
67. Wisløff U, Støylen A, Loennechen JP, Bruvold M, Rognum Ø, et al. (2007) Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: A randomized study. *Circulation* 115: 3086-3094.

68. Hollekim-Strand SM, Bjørgaas MR, Albrektsen G, Tjønnha AE, Wisløff U, et al. (2014) High-intensity interval exercise effectively improves cardiac function in patients with type 2 diabetes mellitus and diastolic dysfunction: A randomized controlled trial. *J Am Coll Cardiol* 64: 1758-1760.
69. Reed JL, Terada T, Vidal-Almela S, Tulloch HE, Mistura M, et al. (2022) Effect of high-intensity interval training in patients with atrial fibrillation: A randomized clinical trial. *JAMA Netw Open* 5: e2239380-e2239380.
70. Reed JL, Nery PB, Birnie DH, Tulloch HE, Pipe AL, et al. (2015) High-intensity interval training improves cardiovascular health, exercise capacity, and quality of life in permanent atrial fibrillation: A case study. *Appl Physiol Nutr Metab* 40: 1321-1323.
71. Elliott AD, Verdicchio CV, Mahajan R, Middeldorp ME, Gallagher C, et al. (2023) An exercise and physical activity program in patients with atrial fibrillation: The ACTIVE-AF randomized controlled trial. *JACC Clin Electrophysiol* 9: 455-465.
72. Vidal-Almela S, Terada T, Cole CA, O'Neil CD, Comeau K, et al. (2022) A case series of acute responses to high-intensity interval training in four males with permanent atrial fibrillation. *Eur Heart J Case Rep* 6: ytac320.
73. Hegbom F, Sire S, Heldal M, Orning OM, Stavem K, et al. (2006) Short-term exercise training in patients with chronic atrial fibrillation: Effects on exercise capacity, AV conduction, and quality of life. *J Cardiopulm Rehabil* 26: 24-29.
74. Terada T, Almela SV, Way KL, Lurette D (2023) The effects of high-intensity interval training and moderate-to-vigorous intensity on cardiorespiratory fitness in patients with permanent or persistent atrial fibrillation. *Eur J Prev Cardiol* 30.
75. Melo X, Abreu A, Santos V, Cunha P, Oliveira M, et al. (2019) A post hoc analysis on rhythm and high intensity interval training in cardiac resynchronization therapy. *Scand Cardiovasc J* 53: 197-205.
76. Kim S, Lee S, Han D, Jeong I, Lee HH, et al. (2023) One-year aerobic interval training improves endothelial dysfunction in patients with atrial fibrillation: A randomized trial. *Intern Med* 62: 2465-2474.