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The role of cardiac rehabilitation in patients with atrial fibrillation and heart failure

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Abstract: This review investigates the role and effectiveness of cardiac rehabilitation in individuals diagnosed with atrial fibrillation and heart failure. A comprehensive analysis of existing literature, clinical trials, and observational studies was conducted to assess the outcomes associated with cardiac rehabilitation interventions in this specific patient population. The complex and bidirectional relationship between atrial fibrillation and heart failure underscores the importance of a patient-centered approach that integrates medical, lifestyle, and rehabilitative interventions for optimal care and outcomes. Results suggest improved functional capacity, enhanced quality of life, and potential favorable cardiovascular outcomes. The review brings new insights to the existing literature, emphasizing the importance of personalized cardiac rehabilitation strategies in optimizing the overall well-being of these patients.

Keywords: cardiac rehabilitation; atrial fibrillation; heart failure

1. Introduction

Atrial fibrillation (AF), the most common sustained arrhythmia encountered in clinical practice, is characterized by rapid and irregular electrical activity in the atria, leading to an irregular and often rapid ventricular response. It is estimated that around 2-3% of the general population may have atrial fibrillation, and its prevalence rises with age, affecting a significant percentage of the elderly population [1]. Several risk factors contribute to the development of AF, including age, obesity, hypertension, diabetes, hyperthyroidism, heart failure, coronary artery disease, and certain structural cardiomyopathies [2].

The prevalence of AF among patients with heart failure (HF) is significant (about 10-30%), and the coexistence of these two conditions is well-established in clinical literature [1].

AF and HF involve various common pathophysiological mechanisms [2] that contribute to a complex and often interdependent relationship, frequently creating a vicious cycle where the hemodynamic consequences of each condition exacerbate the other. AF can reduce cardiac output leading to the worsening of heart failure, while heart failure-induced structural changes can promote the initiation and maintenance of this arrhythmia.

Both HF and AF lead to shared consequences, including **impaired cardiac output** (ineffective atrial contractions compromise the atrial contribution to ventricular filling, resulting in reduced cardiac output; in addition, irregular ventricular response in AF may contribute to hemodynamic instability and suboptimal ventricular filling) [3], **tachycardia-induced cardiomyopathy** (persistent tachycardia in AF can induce cardiomyopathy, resulting in impaired ventricular function and structural alterations),

increased oxygen demand (the irregular rhythm of AF elevates myocardial oxygen demand, potentially exacerbating myocardial ischemia), **atrial remodeling** (atrial dilation, fibrotic changes and disruptions in ion channel function create a conducive substrate for the initiation and perpetuation of AF) [3], **neurohormonal activation** (the renin-angiotensin-aldosterone system and sympathetic nervous system influence adverse atrial remodeling), and **fluid retention** (in HF, fluid retention increases atrial stretch particularly in the left atrium which can trigger electrical and structural changes promoting the development of the AF) [1, 3, 4].

When AF and HF come about simultaneously, wide-ranging implications may occur, significantly impacting patients across clinical, psychosocial, and economic dimensions. Recognizing the intricate relationship between these conditions is essential for devising targeted and individualized management strategies to improve outcomes, enhance quality of life, and reduce the associated complications, including thromboembolic events [1, 5].

Cardiac rehabilitation (CR) has emerged as a cornerstone in the management of patients with AF and HF, offering multifaceted benefits across various domains of care. CR interventions encompass tailored exercise training, risk factor modification, psychosocial support, and education, all aimed at improving outcomes and enhancing quality of life. This comprehensive review synthesizes current evidence on the impact of CR on patients with AF and HF.

Methods – search strategy and selection criteria

For our review, we established clear criteria for selecting studies, focusing on randomized controlled trials (RCTs), observational studies, systematic reviews, and meta-analyses that addressed cardiac rehabilitation for patients with both atrial fibrillation and heart failure. We exclusively included English-language articles with full-text availability.

To gather relevant literature, we conducted thorough searches on databases such as PubMed, MEDLINE, EMBASE, and the Cochrane Library. Quality assessment of included studies was paramount. RCTs were evaluated using the Cochrane risk of bias tool, while observational studies underwent assessment with the Newcastle-Ottawa Scale. Systematic reviews and meta-analyses were evaluated using PRISMA guidelines and rigorous methodology.

Two independent reviewers conducted evaluations, resolving discrepancies through discussion or consultation with a third reviewer. This meticulous process ensured the inclusion of high-quality evidence relevant to cardiac rehabilitation interventions for patients with concurrent AF and HF.

Exercise rehabilitation – recommendations

The ESC guidelines managing HF [4] and AF [6] emphasize the importance of exercise rehabilitation as an IA class indication. There is convincing evidence that moderate and regular physical activity improves exercise tolerance and enhances health-related quality of life (QoL) in these patients [1, 2, 7]. Clinical trials and meta-analyses demonstrate a reduction in both all-cause and heart failure-related hospitalizations. Nevertheless, there remains uncertainty regarding the impact of this intervention on mortality or serious adverse events [8, 9, 10].

Moreover, clinical evidence has shown that cardiac rehabilitation and moderate physical activity reduce the duration of arrhythmic episodes in patients diagnosed with paroxysmal and persistent AF [5]. Additionally, several studies, along with the latest ESC Guidelines on Sports Cardiology and Exercise in Patients with Cardiovascular Disease [11], suggest that moderate-intensity endurance training, such as aerobic exercise, may have a favorable impact on reducing AF burden with [12, 13] or without [14] post-catheter ablation, highlighting the significance of the primary and secondary preventive effects of physical activity. It is essential to consider the specifics of each study, including the patient populations, exercise protocols, and follow-up periods.

At the same time, for patients with AF, the 2023 ACC/AHA guidelines suggest, as a class 1 recommendation, performing physical activity that reaches up to 210 minutes/week to improve symptoms, maintain sinus rhythm, increase functional capacity and enhance QoL [15].

High-intensity exercise training can also improve QoL and peak oxygen consumption (VO2) [16, 17]. Still, it is recommended only in supervised rehabilitation programs including patients with stable HF evaluated explicitly by a cardiologist [18].

Clinical evaluation

Before cardiac rehabilitation, patients presenting with AF and HF require a clinical assessment, administration of optimal pharmacotherapy, risk stratification and proper management addressing the underlying etiologies of both conditions [2]. This involves clinical and paraclinical investigations, including electrocardiography (ECG), 24h-ECG recording, echocardiography, and exercise testing.

Cardiopulmonary exercise testing (CPET) is widely regarded as the gold standard evaluating exercise testing [11]. It provides comprehensive information about cardiovascular, respiratory, and metabolic responses during exercise, making it a valuable tool for assessing exercise capacity and identifying physiological limitations [19]. This evaluation method can determine several vital parameters that are essential indicators of a patient's functional capacity. These include **VO2 max** (the maximum amount of oxygen a person can use during intense exercise, reflecting the cardiovascular and respiratory systems' ability to deliver oxygen to the working muscles), **ventilatory threshold** (a point during exercise where ventilation increases disproportionately to oxygen consumption, often associated with the transition from aerobic to anaerobic metabolism), **maximum exercise capacity in metabolic equivalents** (METs - one MET represents the energy expenditure at rest and the MET value is a measure of the intensity of physical activity, also used to include HF into NYHA classes) and **respiratory exchange ratio** (RER - which is the ratio of carbon dioxide produced to oxygen consumed, providing insights into the substrate, carbohydrates or fats, predominantly utilized during exercise) [19].

CPET typically involves a treadmill or a cycle ergometer [7, 20], and it is performed incrementally, gradually increasing exercise intensity while monitoring parameters such as oxygen consumption (VO2), carbon dioxide production (VCO2), heart rate, blood pressure, and respiratory gases [18]. This method provides a dynamic and individualized approach to defining optimal intensity intervals for aerobic exercise. Between the first and the second anaerobic thresholds lies an area of exercise intensity known as the "moderate intensity" zone, which is associated with effective aerobic conditioning, enhancing cardiovascular fitness without excessive reliance on anaerobic metabolism. Consequently, the goal is to prescribe aerobic exercise within this moderate intensity range to optimize cardiovascular adaptations, improve aerobic capacity, and enhance endurance [21, 16].

The information obtained from CPET can also help reveal patterns and abnormalities specific to different pathological conditions or physical deconditioning [19]. For instance, in heart failure, there may be a reduced peak oxygen consumption, while in pulmonary disorders like Chronic Obstructive Pulmonary Disease (COPD), there might be limitations in ventilatory capacity. Hence, it is a valuable tool for clinicians to gain insights into the complex interactions between the cardiovascular, pulmonary, and musculoskeletal systems during exercise, to facilitate the diagnosis and optimal management.

Moreover, CPET typically includes continuous monitoring of heart rate and rhythm to detect specific arrhythmias (ventricular and supraventricular) and conduction disorders [18]. It can also monitor blood pressure (to reveal hypertension, exercise-induced hypotension, or inadequate blood pressure response) and assess heart rate response to exercise, to detect inadequate chronotropic reaction (which may be found in conditions like chronotropic incompetence, autonomic dysfunction, or pharmacological side effects), thus facilitating the identification of suitable interventions or treatments.

Several studies [22, 23] have also investigated ECG alterations during CPET, which can provide indirect indicators of myocardial ischemia, especially during exercise when myocardial oxygen demand increases. These potential ischemic parameters include specific symptoms, abnormal ST-segment changes (depression or elevation), or impaired exercise tolerance (in patients with significant coronary artery disease).

Periodic CPET assessments (3 to 6 months) allow for monitoring progress over time [11]. This objective measurement helps determine the effectiveness of the rehabilitation program and implements adjustments, if necessary, to optimize rehabilitation protocols by identifying the appropriate intensity and progression of exercises.

On the other hand, there are alternative methods to evaluate the patients before including them in rehabilitation programs when CPET assessment is not available, such as the 6-minute walk test (6MWT), a simple and reliable test to estimate exercise intolerance in patients with HF, and "the talk test" which is a practical tool when used in combination with other methods to monitor and prescribe exercise intensity as suggested in a few studies [2], not only in clinical or hospital settings but also widely employed in exercise testing outside hospital environment for those patients who have already underwent medical supervision.

Cardiac rehabilitation in heart failure

a) Exercise capacity and quality of life

Traditionally, it was believed that individuals with HF were vulnerable to exercise, often being advised against engaging in physical activity due to the perception that it could potentially trigger decompensation in an already weakened heart. However, multiple studies have contradicted these concerns by demonstrating that exercise and physical activity are safe for individuals diagnosed with HF and can actually provide significant benefits. Additionally, these studies have highlighted the harmful effects of extended bed rest and immobility among HF patients [24].

Individuals with HF often experience significant decreases in exercise capacity, which can negatively impact their daily activities and overall health-related QoL [9]. Exercise intolerance in individuals with HF is complex, involving a variety of factors encompassing both central and peripheral mechanisms. There is supporting evidence indicating insufficient cardiac output and elevated filling pressures, resulting in an inadequate augmentation of blood flow to active muscles. This shortfall contributes to the early onset of anaerobic metabolism and subsequent muscle fatigue during exercise [24]. Impairments in skeletal muscle function demonstrated through diminished peripheral oxygen extraction and modifications in fiber composition, contractile efficiency, and metabolism, are also influential. Additional factors include endothelial dysfunction, obesity, increased sympathetic activation, vasoconstriction, and elevated levels of inflammatory cytokines [24].

Studies involving patients with HF who underwent exercise training have demonstrated a reversal or a reduction in neurohormonal and inflammatory activation and ventricular remodeling. In addition, exercise training has been associated with improvements in vasomotor and endothelial function, morphological characteristics, skeletal muscle function, and reductions in ventricular filling pressures. These improvements contribute to enhanced exercise performance, and overall QoL for individuals affected by this condition [24].

The HF-ACTION trial [25], the most extensive study on exercise training in patients with HF with reduced ejection fraction, revealed that regular aerobic exercise training was highly well-tolerated, deemed very safe, and resulted in improved QoL. There were also described decreases in both overall mortality or hospitalization rates and cardiovascular mortality or HF hospitalization regardless of age, sex, race, etiology, or severity of HF [24].

Other meta-analyses [26, 27] have continued to affirm the safety and effectiveness of exercise training in HF, showing notable enhancements in QoL for both patients with HF and reduced ejection fraction (HFrEF) and those with heart failure and preserved ejection fraction (HFpEF), along with reductions in hospitalizations related to HF in HFrEF patients [24].

b) Cardiovascular outcomes

CR is generally considered safe and beneficial for patients with HF. However, it is essential for healthcare professionals to carefully assess and tailor exercise programs to individual patients based on their specific conditions and risks. Exercise, an essential component of CR, can initially lead to increased cardiac workload. In some cases, especially if the exercise intensity is not appropriately adjusted or if there are pre-existing severe cardiac issues, there might be a risk of decompensation, including acute pulmonary edema. Furthermore, given the potential arrhythmogenic substrate associated with structural remodeling of the heart, exercise prescription for HF patients is an area of concern that requires careful consideration. Sometimes, continuous electrocardiogram (ECG) monitoring is used during exercise sessions to detect and manage arrhythmias promptly.

CR in these patients may face limitations related to medication management, and HF patients may need careful monitoring during and after exercise sessions. Some studies explored the impact of beta-blocker use on exercise training outcomes and suggested individualized approaches to exercise prescription in patients on beta-blockers [24]. Moreover, examining the effect of ACE inhibitors and, or angiotensin II receptor blockers (ARBs) on post-exercise hypotension, the authors shed light on how these medications may affect blood pressure responses after exercise [28]. Other studies described the relationship between diuretic use, increased serum urea levels, and the effects of exercise training in chronic HF patients. Diuretics, commonly prescribed in this pathology, can influence electrolyte balance, thus emphasizing the importance of individualized approaches for these patients [25].

In summary, CR demonstrates beneficial effects for individuals with HF, and it is included as a class IA indication in HF practice guidelines. Clinicians and healthcare providers must prioritize CR as an integral component of standard care for HF patients.

Cardiac rehabilitation in atrial fibrillation

AF, an easily diagnosed condition with well-defined treatment guidelines, is a prevalent comorbidity among individuals participating in rehabilitation programs. Several controlled trials employ standard laboratory methods and endpoints to assess the efficacy of exercise testing and training in this patient population. In pursuit of this goal, numerous inquiries arise regarding the influence of aerobic and resistance training on patients with AF, including considerations of safety, QoL, clinical outcomes, and central, autonomic, and peripheral adaptations [29].

a) Exercise capacity and quality of life

In general, cardiac rehabilitation, coupled with consistent moderate physical activity, has demonstrated efficacy in decreasing the duration of arrhythmia in individuals with paroxysmal and persistent AF. This highlights its potential as a valuable complement to antiarrhythmic therapies [5]. In cases of permanent AF, it is essential to lower the resting ventricular response rate in patients who find drug treatments insufficient or wish to reduce bradycardia therapies such as digitalis. Reducing the resting ventricular response rate is crucial in enhancing symptoms associated with arrhythmia, physical capacity, distance covered in a 6-minute walk test (6-MWT), and overall QoL [5].

At the same time, when we recommend physical activity to patients with AF, we must ensure that the atrioventricular rhythm is under permanent control, given the fact that a high heart rate can lead to atrial myopathy, and that high-intensity aerobic exercise can promote the occurrence of AF [31].

We would like to highlight that in the latest American Guideline dedicated to AF, it is emphasized that the physical training prescribed for these patients should be aerobic of moderate to vigorous intensity. Regarding the duration of the training, the target should be 210 minutes per week to reduce the frequency and length of the AF episodes, to improve the cardiorespiratory fitness, and to reduce the severity of the symptoms [32].

A particular category of patients is those with AF undergoing ablation procedures. Their inclusion in rehabilitation training programs also resulted in an improvement in their capacity for effort and QoL. Exercise also has favorable effects on comorbidities frequently associated with AF (obesity, hypertension, and diabetes) [33, 34].

b) Cardiovascular outcomes

Buckley et al. [14] highlighted in a review how regular exercise training benefits AF burden and reduces major adverse events, illustrating the presumed role of modifying risk factors, mainly through physiological cardiac remodeling (enlargement in cardiac dimensions, enhanced contractility, and increased blood volume), improvements in atrial health (physiological enlargement of atrial size with a concurrent reduction in fibrosis and inflammation) and also enhancements in vascular health (increased diameter size and improved vascular function).

The latest guidelines from the European Society of Cardiology regarding the diagnosis and management of AF [6] consistently emphasize the significance of CPET and cardiopulmonary fitness. Furthermore, the guidelines advocate for encouraging patients to engage in moderate-intensity exercise and maintain physical activity to prevent the incidence or the recurrence of AF [6].

Nevertheless, based on the results from a review by Nielsen et al. [30], engaging in prolonged, intense physical activity may be linked to AF. Conversely, a sedentary lifestyle may also be connected to an elevated risk of AF. In contrast, an active lifestyle involving high to moderate physical activity appears advantageous and correlated with a reduced risk of AF.

However, attention must also be increased regarding medication prescribed to patients with AF and their participation in exercise training. Attaining sufficient rate control can pose challenges. The apparent choice is beta-blockers, but their use could be limited by potential effects on physical performance. Calcium-channel blockers and digitalis, when used independently, may not be potent enough. Frequently, a combination of carefully titrated medications with negative chronotropic effects is necessary to avoid sinus bradycardia at rest or chronotropic incompetence during exercise [11].

ESC guidelines on sports cardiology and exercise in patients with cardiovascular disease [11] stress that achieving rhythm control is also complicated. Class III antiarrhythmic drugs (sotalol) are often ineffective or relatively contraindicated in younger patients (amiodarone). While class I drugs may help prevent AF recurrences, they should not be used in monotherapy, as this could elevate the risk of developing atrial flutter (AFL). Without proper rate control, AFL might result in 1:1 atrioventricular conduction, leading to high ventricular rates and significant intraventricular slowing, potentially causing hemodynamic compromise.

Finally, the decision to prescribe oral anticoagulants (OAC) is contingent upon the clinical risk profile (estimating CHA2DS2-VASc score). It is recommended to avoid sports involving direct bodily contact or those prone to trauma in patients on OAC.

As a result, enhancements in cardiac rehabilitation align with a comprehensive improvement in patient well-being and serve as essential endpoints in managing individuals diagnosed with AF [5].

Cardiac rehabilitation for both heart failure and atrial fibrillation

a) Exercise capacity and quality of life

There is limited data regarding the effectiveness of comprehensive cardiac rehabilitation in individuals with concurrent pathologies. However, a recent study [1] investigated the influence of cardiac rehabilitation on individuals with both HF and AF in comparison to those with HF but without coexisting AF. The findings revealed a notable enhancement in exercise capacity, QoL, and Hospital Anxiety and Depression Scale (HADS) scores among individuals with HF and concurrent AF following the completion of a comprehensive cardiac rehabilitation program. Notably, there was no significant difference observed between the HF group with coexisting AF and the group without AF.

Another retrospective observational research demonstrates that AF in older patients with HF is linked to diminished peripheral muscle function and functional capacity at the initial assessment. Additionally, a favorable improvement in physical function resulting from exercise-based CR is correlated with a better prognosis, even among individuals with AF [36].

b) Cardiovascular outcomes

The impact of exercise training on cardiovascular outcomes in individuals with HF or AF is supported by evidence. In a population-based cohort study, starting or maintaining regular exercise after the onset of AF was linked to a reduced risk of heart failure and mortality [35].

Considering the heightened impairment in exercise performance observed in patients with both HF and AF (typically manifested by a reduction in peak oxygen uptake-VO2), a recent research article [2] emphasizes that exercise training programs at a moderate intensity hold significant potential for providing substantial benefits for individuals with HF and AF. Particularly, for patients with both HF and AF, the calculation of average heart rate (HR) using telemetry should encompass a more extended period compared to individuals in sinus rhythm.

In the RACE 3 (Rate Control versus Electrical cardioversion for persistent atrial fibrillation) trial, it was demonstrated that in patients with AF and early HF, along with the use of drug treatment (mineralocorticoid receptor antagonists, statins, ACE inhibitors and, or angiotensin receptor blockers), physical rehabilitation programs contribute to the maintenance of sinus rhythm [37].

These results affirm the favorable impact of the rehabilitation program, positioning it as a promising therapeutic intervention for enhancing clinical outcomes in individuals dealing with both HF and AF.

Patient-Centered Focus

In cardiac rehabilitation, prioritizing patient-centered approaches is essential for maximizing treatment effectiveness. By recognizing and accommodating the unique needs and preferences of each individual, healthcare professionals can tailor interventions accordingly. This personalized approach fosters greater patient engagement and adherence to prescribed treatment regimens, establishing a collaborative relationship based on trust and mutual understanding. Furthermore, taking into account individual psychosocial and cultural factors ensures comprehensive care that extends beyond medical management alone. Ultimately, patient-centered care promotes shared decision-making, empowering patients to play an active role in their recovery process and leading to improved satisfaction and health outcomes.

Limitations and future directions

When reviewing literature on cardiac rehabilitation in patients with AF and HF several limitations may arise. Firstly, the heterogeneity of study populations poses challenges in drawing uniform conclusions, given variations in disease severity, comorbidities, and treatment regimens among participants. While there is evidence supporting the benefits of CR in patients with HF, there may be fewer randomized controlled trials (RCTs) specifically focusing on patients with both AF and HF. The lack of high-quality RCTs can limit the strength of evidence available and introduce potential biases in observational studies. Moreover, there may be a lack of consensus on the optimal components and duration of CR programs for patients with AF and HF. Variability in program design and implementation across different healthcare settings can influence outcomes and make it challenging to compare results between studies. Lastly, the possibility of publication bias favoring positive outcomes highlights the need for cautious interpretation of existing evidence.

To overcome these limitations, there is a substantial need for further research efforts. This entails conducting well-designed RCTs with larger sample sizes, extended follow-up durations, and standardized outcome measures. Additionally, comprehensive assessments of patient characteristics and program components are essential. Future research should prioritize refining exercise training methods and evaluating long-term outcomes through rigorous randomized trials.

Conclusions

In conclusion, cardiac rehabilitation presents a valuable opportunity to improve outcomes and enhance quality of life for patients with both AF and HF, despite the complexities posed by these concurrent conditions. While existing literature underscores the efficacy of CR in addressing exercise capacity, symptom management, cardiovascular risk factors, and psychosocial support in AF and HF individually, a nuanced approach is necessary when managing patients with both pathologies. Tailored CR programs that account for the unique challenges, including combined symptom burden, reduced exercise tolerance, and heightened psychosocial distress, are essential for optimizing outcomes in this population. By integrating targeted interventions and closely monitoring patient progress, CR can effectively mitigate the impact of AF and HF, empowering individuals to lead healthier lives and reduce the burden of cardiovascular disease.

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