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SYSTEMATIC REVIEW

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Effect of Exercise Training with Consideration of Potential Moderating Variables in Patients with Atrial Fibrillation: A Systematic Review and Meta-Analysis

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Abstract

Background Exercise-based cardiac rehabilitation (CR) shows promise as an adjunctive treatment for patients with atrial fibrillation (AF). Previous evidence has highlighted its beneficial impact in this population. However, studies exhibit significant heterogeneity and often fail to differentiate between AF types. Furthermore, the specific influence of training variables such as exercise modality or intensity on the exercise-induced effects remains unclear. Therefore, the aim of our review was to assess the effect of exercise training (i.e., aerobic, resistance, and combined exercise), on exercise capacity, quality of life (QoL), resting heart rate (HR), AF burden, and symptoms in AF.

Methods Electronic searches were conducted in PubMed, Embase, and Web of Science up to May 2025. Standardised mean difference (SMD) or mean difference (MD) were estimated in controlled and multi-intervention studies. Effect size indices were pooled using a random-effects model when at least three studies reported a specific outcome. Additionally, subgroup analyses were carried out based on AF type.

Results Most of the studies used moderate intensity exercise (MIE). Across included studies, peak oxygen uptake (VO_2 peak) ($n = 5$, $N = 1{,}519$), 6-min walk test (6MWT) ($n = 5$, $N = 1{,}344$), QoL ($n = 9$, $N = 1{,}596$), resting HR ($n = 6$, $N = 490$), AF burden ($n = 5$, $N = 412$), and AF symptoms ($n = 4$, $N = 428$) were reported. The results showed that aerobic exercise improves VO_2 peak to a greater extent than usual care, regardless of AF type ($MD_+ = 4.24$ [95%CI = 0.87; 7.45] ml/kg/min). Compared to usual care, aerobic exercise only diminished resting HR in non-permanent AF ($MD_+ = -12.79$ [95%CI = −15.90: −9.67] bpm). No differences were found for improving QoL and 6MWT ($p > .050$). The effect of exercise on AF burden and symptoms has been poorly studied. No pooled analyses were performed by including multi-intervention studies. The findings showed no influence of the aerobic intensity or modality.

Conclusion Aerobic exercise improves VO_2 peak in patients with permanent and non-permanent AF. MIE reduces resting HR in patients with permanent AF, while no differences were found in non-permanent AF. In contrast, the limited and heterogeneous RCT evidence available is insufficient to demonstrate superior improvements in the

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6MWT or QoL compared to usual care. Further research is needed to determine the impact of CR on AF burden and symptoms, and to elucidate how exercise modality and intensity influence outcomes.

Key Points

1. Aerobic exercise significantly improves VO_2 peak in patients with permanent and non-permanent AF.
2. MIE reduces resting HR in patients with permanent AF, while CR does not demonstrate superior improvements in the 6MWT or QoL compared to usual care.
3. Further research is necessary to elucidate how exercise modality and intensity influence outcomes and to determine the impact of cardiac rehabilitation on AF burden and symptoms.

Keywords Cardiac rehabilitation, Exercise capacity, Quality of life, AF symptoms, AF burden, Meta-analysis

Background

Atrial fibrillation (AF) stands as the most prevalent cardiac arrhythmia, affecting 1–2% [1, 2] of the population. Its prevalence is expected to increase exponentially in upcoming years due to population aging, improved detection methods, and the growing burden of comorbidities [3, 4]. AF can be classified into various types based on presentation and duration, including first diagnosed AF, paroxysmal (terminates spontaneously or with intervention within seven days of onset), persistent (sustained beyond seven days or termination by cardioversion), and permanent (accepted by the patient and physician with no attempts to restore sinus rhythm) [5]. The global impact of AF on both patients and physicians is substantial, with increased risk of stroke, heart failure (HF), dementia, and overall mortality [5]. Additionally, individuals with AF suffer from impaired functional capacity and quality of life (QoL) [6, 7]. This condition also entails a great economic burden for healthcare systems, with the estimated yearly AF medical cost in the US ranging from 6 to 26 billion dollars [8].

In recent years, there has been a growing interest in the role of exercise as an adjunctive therapy in the management of chronic diseases, including AF [9]. Multicomponent cardiac rehabilitation (CR) programmes include exercise training, health-education, management of cardiovascular risk factors, and psychological support [10]. To design an exercise-based CR programme tailored for patients with AF, careful consideration of multiple variables is essential, such as exercise modality, duration, and intensity. Concerning exercise modality, the three most commonly employed are aerobic exercise, resistance exercise, or combined aerobic and resistance exercise (henceforth referred to as combined exercise). In turn, aerobic exercise, can be categorised based on intensity: low-intensity exercise (LIE), moderate-intensity exercise (MIE), and high-intensity interval exercise (HIIE). Various methods exist to assess aerobic exercise intensity, including objective measures like blood lactate, the percentage of peak oxygen uptake (VO_2 peak), peak heart rate (HR peak), and workload from incremental testing, as well as subjective ratings such as the Borg scale [11, 12].

HIIE is characterised by alternating short bursts of high-intensity exercise (e.g., >85% VO_2 peak or above the second lactate threshold) with low intensity or passive recovery (e.g., below the first lactate threshold) [13]. On the contrary, LIE and MIE, which can be performed continuously or intermittently, are characterised by long-duration exercise bouts performed at low (e.g., below the first lactate threshold) or moderate (e.g., between the first and second lactate thresholds) intensity, respectively [14].

On the other hand, one-repetition maximum (1RM) serves as the gold standard for prescribing resistance exercise intensity in healthy individuals. However, within exercise-based CR, limitations arise in estimating 1RM due to the requirement for sophisticated equipment and patient capacity. In this context, the RPE emerges as a viable alternative, demonstrating a direct correlation with 1RM [15, 16]. Evidence also highlights the impact of exercise volume (number of repetitions per sets and repetitions per exercise), intervention duration and exercise frequency (exercise sessions per week) on the exercise-induced effects with cardiovascular disease [17].

The latest 2024 ESC guidelines for the management of AF now include a class I indication for: "A tailored exercise programme in individuals with paroxysmal or persistent AF to improve cardiorespiratory fitness and reduce AF recurrence" [18]. This recommendation stems from accumulating evidence, as previous systematic reviews and meta-analyses in patients with AF have consistently demonstrated the positive impact of exercise-based CR on VO_2 peak, the distance covered in the six-minute walk test (6MWT), and resting HR, contributing to enhance patient QoL [19–23]. However, no previous systematic reviews or meta-analyses have addressed the effect of CR on AF symptoms or AF burden. Additionally, the results of previous systematic reviews are controversial displaying considerable heterogeneity which could be due to potential moderator variables, such as the components of CR programme (i.e., multicomponent CR or exercise-based CR), patient characteristics (e.g., AF type), and exercise-related variables (e.g., aerobic exercise method).

For instance, Zhang et al. [24] conducted a meta-analysis to determine the efficacy of exercise-based CR in patients with non-permanent AF after radiofrequency ablation. The results of the included studies on 6MWT, VO_2 peak, resting HR, and left ventricular ejection fraction (LVEF) exhibited high heterogeneity. These discrepancies could be attributed to the inclusion of a wide array of interventions such as yoga, electrical stimulation, or inspiratory muscle exercise, which prevented the authors from evaluating the isolated impact of exercise-based CR. Similarly, Shi et al. [22] selected studies which recruited patients with AF irrespective of the type and also included other interventions in their meta-analyses (i.e., Qigong and yoga). Consequently, their findings regarding QoL were also controversial, lacking assessment of the potential impact of the type of AF on the exercise-induced effect. Furthermore, new research has emerged since the publication of previous reviews, warranting an update on the subject [25, 26].

Hence, the aim of the current systematic review was to assess the effect of exercise training (i.e., aerobic exercise, resistance exercise, and combined exercise), either as a standalone intervention (i.e., exercise-based CR) or combined with other therapies (i.e., multicomponent CR), on exercise capacity (i.e., VO_2 peak and 6MWT), QoL, resting HR, AF burden, and AF symptoms in patients with AF.

Methods

This systematic review with meta-analysis was performed following the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) [27]. The protocol of this review was prospectively published in the PROSPERO database (CRD42023446915).

Data Search and Sources

Systematic searches were conducted in PubMed, Embase, and Web of Science (i.e., Core Collection [Science Citation Index Expanded and Conference Proceeding Citation Index]) from inception to May 2025. A search strategy based on free-text terms related to participants (e.g., "atrial fibrillation"), intervention (e.g., "exercise"), and outcomes (e.g., "walking capacity") was developed. The selected free-text terms were combined using Boolean operators (i.e., AND, OR) and searched in the title, abstract, and keywords fields (when available) across the databases (see Electronic Supplementary Material [ESM]). Conference proceedings were also searched on the Web of Science Core Collection. On the other hand, backward citation searches (i.e., checking reference lists) of systematic reviews identified through database searches and forward citation searches of included studies were also conducted [28]. Finally, corresponding authors of included studies were contacted in an attempt to identify ongoing or unpublished studies that fulfilled the inclusion criteria.

Study Selection

Eligibility criteria were established according to the PICOS (participants, interventions, comparisons, outcomes, and study design) guideline as follows: (a) participants: male and female adult (aged ≥ 18 years) patients with AF (i.e., paroxysmal, persistent, and/or permanent), irrespective of LVEF. Studies that included patients with AF treated with thoracoscopic ablation or undergoing left atrial appendage closure were excluded; (b) interventions: inpatient or outpatient exercise training programmes lasting at least two weeks, regardless of the setting (i.e., supervised or unsupervised exercise programmes), and based mainly on aerobic exercise (i.e., LIE, MIE, or HIIE), resistance exercise, or combined exercise, either alone or in addition to psychosocial and/or educational interventions. In order to be included in the review, exercise variables (e.g., intensity and volume) according to the exercise modality (i.e., aerobic exercise, resistance exercise, or combined exercise), must have been reported in the manuscript. Studies involving yoga, traditional Chinese medicine or respiratory exercises were excluded because they include relaxation or meditation techniques, which could confound our analysis; (c) comparisons: usual care interventions and/or non-exercise groups (henceforth control group [CG]). The different dosages of exercise regimens (e.g., modality and intensity) were also allowed as comparators; (d) primary outcomes: (i) exercise capacity measured by VO_2 peak, (ii) walking capacity measured by the 6MWT, and (iii) QoL measured by questionnaire; and secondary outcomes: (i) resting HR, (ii) AF burden, and (iii) AF symptoms; and (e) study design: randomised and non-randomised studies. Finally, studies written in English or Spanish were included. The original publication was included in the review when more than one publication of the same study was retrieved.

Two review authors (N.S. and C.B.) independently assessed all identified studies and consulted a third author (A.M) to resolve disagreements.

Data Extraction and Coding Study Characteristics

Two authors (N.S. and J.M.S.) extracted information from the selected studies using an approved data extraction sheet and a third review author (L.F.) was consulted in case of disagreement.

The information extracted from the studies was classified as follows: (a) study characteristics (publication year, country, journal, and study design [i.e., randomised or non-randomised]); (b) patient characteristics (sample size, sex [i.e., males, females, or mixed sample], men percentage, age, LVEF, type or class of AF [i.e., paroxysmal, persistent, and/or permanent], type of intervention (e.g., rate or rhythm control [i.e., catheter ablation or antiarrhythmic drugs], and medical treatment); (c) intervention characteristics (CR programme [exercise-based CR or multicomponent CR], setting [i.e., supervised, unsupervised, or mixed], exercise modality [i.e., aerobic exercise, resistance exercise, or combined exercise], aerobic exercise method (if applicable) [i.e., LIE, MIE, or HIIE], intervention length [weeks], sessions a week, and intervention description [e.g., session length, intensity, training mode, and number of sets]); (d) CG details (instructions given to patients and activity monitoring); and (e) statistical information (e.g., mean and standard deviation [SD]) of the selected primary and secondary outcomes. Regarding the classification of LVEF, we considered reduced LVEF (< 40%), mildly-reduced LVEF (41–49%), and preserved LVEF (> 50%), according to the 2021 European Society of Cardiology Guidelines for the management of HF [29]. Concerning aerobic exercise intensity, this was categorised as follows: LIE (RPE ≤ 12), MIE (RPE 13–16), and HIIE (RPE: ≥ 17). When alternative variables were used to prescribe the aerobic exercise intensity, equivalences were employed [12]. Furthermore, we deemed resistance exercise as an exercise modality only when the studies explicitly reported the exercise variables used (e.g., intensity and volume) and when these variables adhered to the definition of resistance exercise.

Dealing with Missing Data

Corresponding authors were contacted to seek clarification and obtain additional data in cases where the information provided in the manuscript was unclear or missing. If no response was received, the respective study was excluded from the current systematic review.

Methodological Quality Assessment

The methodological quality of the selected studies was assessed using the Tool for the assEssment of Study qualiTy and reporting in EXercise (TESTEX) scale [30]. The TESTEX scale comprises 12 items, each scored as "yes" (1 point) or "no" (0 points), depending on whether the criterion is satisfied or not. The maximum possible score is 15. The criteria used to carry out methodological quality assessment can be found in Table S1 (see ESM). Based on the overall scores obtained, methodological quality was judged as excellent [12–15], good [9–11], fair [6–8], or poor (< 6). Two review authors (C.B. and J.M.S.) independently assessed the methodological quality of the selected studies, with involvement from a third author (L.F.) in cases of disagreement.

Computation of Effect Size and Statistical Analyses

The mean difference (MD) with its 95% confidence interval (CI) was used as the effect size (ES) index. The MD was calculated by subtracting the mean change in the comparison group (i.e., CG or intervention group [IG] performing other exercise regimen) from the mean change in the IG and was then corrected by a factor for small samples [31]. Additionally, for outcomes measured using different units, the standardised mean difference (SMD) along with its 95% CI served as the ES index. The SMD was computed as the MD divided by the pooled standard deviation at pre-intervention. The magnitude of SMD was classified as trivial (< 0.20), small (0.20–0.49), medium (0.50–0.79), or large (≥ 0.80) [32]. When MD and/or SMD were not applicable (non-continuous variables), the original finding reported in the manuscript was used instead. We used the terms 'MD_+' and 'SMD_+' to refer to the MD and SMD calculated from the pooled analysis, representing the overall ES across all included studies. In studies conducting more than two measurements (e.g., follow-up), ES indices were calculated using the initial two measurements (i.e., pre- and post-interventions). Moreover, within multi-intervention studies, the groups performing higher intensity exercises (e.g., HIIE vs MIE) or combined exercise (e.g., combined exercise vs aerobic exercise) were identified as the IG when determining ES indices. A positive ES denotes an increase in favour of the IG for exercise capacity, QoL, and muscle strength, while a negative ES denotes a decrease in favour of the IG for resting HR, AF burden, and AF symptoms. A random-effects model was used to conduct pooled analyses, in which the weighting factor is the inverse variance, defined as the sum of the within-study and the between-study variance [33]. Subgroup analyses were performed based on AF type (i.e., paroxysmal/persistent vs. permanent) to determine the influence of this variable on the exercise-induced effect. If subgroup analyses did not reach statistical significance ($p > .050$), the results were reported without considering the type of AF. Regarding heterogeneity, the chi-square test was used to identify statistical heterogeneity and the I^2 index was used to quantify the percentage of variation across studies due to heterogeneity. I^2 values of 25%, 50%, and 75% were interpreted as low, moderate, and high heterogeneity, respectively [34]. On the other hand, robust variance estimation (RVE) was employed to carry out meta-analysis where multiple dimensions of an endpoint were obtained from the same patients to avoid statistical dependence [35]. RVE was not used when the degree of freedom was <4 to avoid type 1 error [36]. Pooled analyses were conducted separately in controlled studies and multi-intervention studies. Meta-analysis was conducted only if three or more studies, or analysis units, were included for the specific endpoint. In cases where there were fewer than three studies or analysis units, the results were discussed qualitatively instead. All analyses were performed using STATA software (version 16.0; Stata Corp LLC, College Station, TX, USA).

Deviations from Registered Protocol

Deviations from the intended protocol were: (i) RVE was used to pool those outcomes where several measurements were obtained from the same participants; and (ii) sensitivity and publication bias analyses were not conducted due to the low number of pooled studies.

Results

Study Selection

Figure 1 shows the flow chart diagram of the study selection process. A total of 5,177 references were retrieved

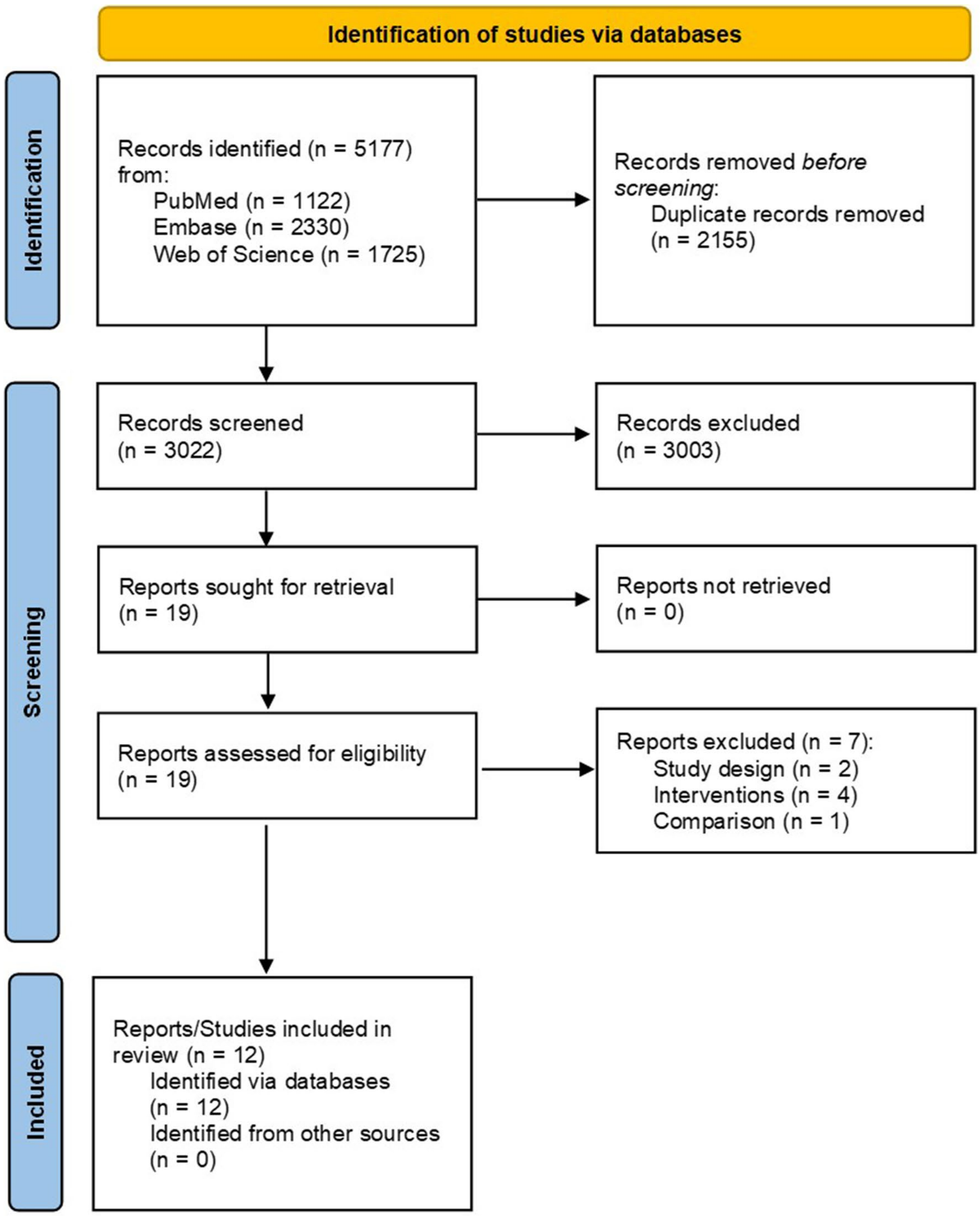

Fig. 1 PRISMA study identification and selection flow chart

from the electronic database searches. We removed 2,155 duplicates and 3,022 references were forwarded to the first stage of the study selection process. After reviewing titles and abstracts, 3,003 studies were excluded and 19 were included for full-text analysis and checked against inclusion criteria (second stage). Twelve studies met the inclusion criteria [25, 26, 37–46] and seven were excluded from qualitative synthesis for the following reasons: (a) study design ($n = 2$; crossover design [47] and retrospective study [48]); (b) interventions ($n = 4$; no exercise prescription and exercise recommendations instead [49–52]); and (c) comparison ($n = 1$; tele-monitored exercise programme [53]). Efforts were made to identify unpublished studies; however, no additional studies were identified from other sources, and all included studies had been published in peer-reviewed journals.

Study Characteristics

Study and patient characteristics can be found in Table 1. The studies included were from 8 countries and were published from 2006 to 2023. All 12 (100%) selected studies were randomised. The 12 studies enrolled 831 patients, 522 in the IG and 309 in the CG. The mean ± SD age of the IG was 64.2 ± 6.3 years and the mean ± SD age of the CG was 62.4 ± 4.1 years. Eleven (91.7%) studies recruited both male and female patients [26, 37–46] and one study (8.3%) recruited exclusively male patients [25]. Regarding the type of AF of the patients recruited, six (50.0%) studies included both paroxysmal and persistent AF [37, 38, 40, 41, 44, 46], four (33.3%) studies exclusively included patients with permanent AF [25, 42, 43, 45], one (8.3%) included patients with persistent AF [39], and one (8.3%) recruited both persistent and permanent AF [26]. Two (16.7%) studies included patients with AF who had undergone catheter ablation [39, 44]. Eleven (91.7%) studies recruited patients with preserved LVEF (≥ 50%) [26, 37–46] and one (8.3%) focused on patients with reduced LVEF [25].

A summary of the intervention characteristics and reported outcomes of the included studies can be found in Tables S2 (controlled studies) and S3 (multi-intervention studies) (see ESM). In relation to the type of comparison, nine (75.0%) studies compared, at least, one IG with a non-IG (i.e., controlled studies) [25, 37–44] (Table S2), and three (25.0%) conducted a comparison with another IG in a multi-intervention study [26, 45, 46] (Table S3). Four (33.3%) studies conducted a multicomponent CR programme [37, 38, 42, 44]. Seven (58.3%) studies carried out a supervised centre-based exercise programme [25, 26, 38, 40, 42, 43, 46], four (33.3%) combined centre and home-based exercise sessions [37, 39, 41, 44], and one (8,4%) did not report this information. Lastly, Borland et al. [45] was a multi-intervention study that compared a home-based intervention with a mixed (supervised and home-based) programme. Of the nine controlled studies, eight (88.9%) performed aerobic exercise and one (11.1%) combined exercise. Regarding the aerobic exercise method, six (66.7%) studies implemented MIE [25, 37–39, 43, 44], two (22.2%) utilised HIIE [40, 41], and one (11.1%) incorporated LIE [42]. Among the multi-intervention studies, one (33.3%) compared HIIE with MIE [26], one (33.3%) compared the progression of MIE to HIIE with LIE [46], and one (33.3%) compared combined exercise (i.e., resistance exercise and MIE) with MIE [45]. In regards to the aerobic intensity prescription, out of all the included studies, six (50.0%) used the Borg 6–20 RPE scale [38, 43–46], four (33.3%) HR percentages [37, 40–42], one (8.3%) peak power output percentages, and one (8.3%) did not specifically disclose this information [39]. Among the two studies that also performed resistance exercise, one (50%) used 1RM percentages [39] and one (50.0%) used the Borg 6–20 RPE scale [45]. The mean ± SD duration of the interventions was 14.7 ± 5.7 weeks and patients conducted a mean total of 32.0 ± 18.4 sessions. Nine (75.0%) studies trained during 12 weeks [25, 26, 38, 41–46] and three (25.0%) during 24 weeks [37, 39, 40]. The frequency of the training sessions varied from two days a week in four studies [26, 38, 42, 46], three days a week in six studies [25, 39–41, 43, 44], and more than three days a week in two studies [37, 45].

Concerning the outcomes measured, six (50.0%) studies measured VO_2 peak [25, 38, 40, 41, 44, 46], five (45.4%) distance covered in the 6MWT [26, 38, 39, 43, 44], ten (83.3%) QoL [25, 26, 37–44], six (54.5%) resting HR [25, 26, 39, 41, 43, 45], four (36.4%) AF-related symptoms [26, 37, 41, 44], and five (45.4%) AF burden [26, 37, 39, 41, 46]. We were able to conduct meta-analysis of four variables: VO_2 peak, 6MWT, quality of life, and resting HR. Briefly, out of the nine studies that reported QoL, eight (66.7%) used the Short-Form 36 (SF-36) questionnaire [26, 37, 40, 41, 43–45], three (25.0%) employed the Minnesota Living with Heart Failure Questionnaire (MLHFQ) [25, 40, 43], and one (9.1%) applied four different questionnaires (i.e., Quality of life in patients with Atrial Fibrillation [AF-QoL], Atrial Fibrillation Effect on Quality of life [EFEQT], the Patient Health Questionnaire [PHQ], and the EuroQol 5D questionnaire [EQ-5D]) [38]. Among the five studies that measured the burden of AF, three (27.3%) assessed the percentage of time that patients spent in AF with a 24–48 h Holter-ECG [26, 37] or an implantable loop recorder [41]. The remaining two studies reported the number of patients with a recurrence of AF [39] or the ratio of ECGs with AF to the total ECGs [46]. Bittman et al. [37] also analysed the percentage of AF beats on a 48-hour Holter monitor and a doctor-reported burden of AF scale. Among the four studies that assessed the severity of AF symptoms, two used the Toronto AF symptom severity scale (AFSS) [26, 37], one the Canadian

Table 1 Study and patient characteristics

Study	Group	Study characteristics	Patient characteristics			
		Country; study design; journal	AF type (%); Catheter ablation (%)	LVEF	Final sample size; men percentage; age	Pharmacological treatment (n; %)
Controlled studies						
Alves et al. [25], 2022	IG (AE; MIE)	Brazil; Randomised study; Heart rhythm	Permanent (100)	≤ 40%	13; 100%; 58.0 ± 3.0 y	Amiodarone (1; 8) BB (13; 100) Digoxin (8; 62)
	CG				13; 100%; 58.0 ± 2.0 y	Amiodarone (1;8) BB (13; 100) Digoxin (11; 85)
Bittman et al. [37], 2022	IG (AE; MIE)	Canada; Randomised study; CJC Open	Paroxysmal (85) Persistent (15)	≥ 50%	34; 68%; 63.7 ± 8.6 y	Amiodarone (5; 15) Other AAD (14; 41) CV (13; 38) Ablation (5; 15) BB (22; 65)
	CG		Paroxysmal (92) Persistent (8)		38; 55%; 61.0 ± 9.7 y	Amiodarone (2; 5) Other AAD (10; 26) CV (8; 21) Ablation (5; 13) BB (16; 42)
Joensen et al. [38], 2019	IG (AE; MIE)	Denmark; Randomised study; J Rehabil Med	Paroxysmal (57) Persistent (43)	≥ 50%	28; 61%; 62.2 ± 10.0 y	Amiodarone (3; 11) Flecainide (3; 11) BB (18; 64)
	CG		Paroxysmal (38) Persistent (62)		24; 71%; 60.2 ± 8.9 y	Amiodarone (2; 8) Flecainide (4; 17) BB (16; 67)
Kato et al. [39], 2019	IG (CE; MIE)	Japan; Randomised study; Eur J Prev Cardiol	Persistent (100) Catheter ablation (100)	≥ 50%	28; 71%; 67.0 ± 10.0 y	Amiodarone (1; 4) BB (9; 32) Digoxin (0%) CCB (5; 18%) Second ablation (2; 7)
	CG				31; 90%; 65.0 ± 8.0 y	Amiodarone (1; 3) BB (8; 26) Digoxin (1; 3) CCB (8; 26) Second ablation (4; 13)

Table 1 (continued)

Study	Group	Study characteristics	Patient characteristics			
		Country; study design; journal	AF type (%); Catheter ablation (%)	LVEF	Final sample size; men percentage; age	Pharmacological treatment (n; %)
Kim et al. [40], 2023	IG (AE; HIIE) 1 year (a)	Korea; Randomised study; Intern Med	Paroxysmal (67) Persistent (33)	≥ 50%	21; 77%; 65.3 ± 4.0 y	
	IG (AE; HIIE) 6 months (b)		Paroxysmal (43) Persistent (57)		23; 73%; 64.0 ± 6.3 y	Amiodarone (10; 11) Sotalol (4; 3.6) BB (54; 49) Digoxin (1; 0.9) CCB (24; 21.8)
	CG		Paroxysmal (52) Persistent (48)		30; 61%; 62.4 ± 5.4 y	
Malmo et al. [41], 2016	IG (AE; HIIE)	Norway; Randomised study; Circulation	Paroxysmal (58) Persistent (42)	≥ 50%	26; 77%; 56.0 ± 8.0 y	AAD (16; 62) Amiodarone (7; 27) Flecainide (7;2 7) Sotalol (2; 8) BB (8; 31) Digoxin (1; 4) CCB (4; 15)
	CG		Paroxysmal (56) Persistent (44)		25; 88%; 62.0 ± 9.0 y	AAD (15; 60) Amiodarone (2; 8) Flecainide (9; 36) Sotalol (4; 16) BB (7; 28) Digoxin (0) CCB (5; 20)
Nourmohammadi et al. [42], 2019	IG (AE; LIE)	Iran; Randomised study; ARYA Atheroscler	Permanent (100)	≥ 50%	25; 40%; 52.7 ± 7.4 y	Amiodarone (2; 8) Flecainide (1; 4) Sotalol (0; 0) BB (9; 36) Digoxin (5; 20) CCB (7; 28)
	CG				25; 52%; 59.9 ± 7.5 y	Amiodarone (3; 12) Flecainide (0; 0) Sotalol (0; 0) BB (6; 24) Digoxin (7; 28) CCB (3; 12)

Table 1 (continued)

Study	Group	Study characteristics	Patient characteristics			
		Country; study design; journal	AF type (%); Catheter ablation (%)	LVEF	Final sample size; men percentage; age	Pharmacological treatment (n; %)
Osbak et al. [43], 2011	IG (AE; MIE)	Denmark; Randomised study; Am Heart J	Permanent (100)	≥ 50%	24; 75%; 69.5 ± 7.3 y	BB (0.67 ± 0.48) # Digoxin (0.38 ± 0.50) #
	CG				23; 74%; 70.9 ± 8.3 y	BB (0.57 ± 0.51) # Digoxin (0.39 ± 0.50) #
Risom et al. [44], 2016	IG (AE; MIE)	Denmark; Randomised study; Am Heart J	Paroxysmal (72) Persistent (28) Catheter ablation (100)	≥ 50%	95; 70%; 60.0 ± 9.0 y	Amiodarone (20; 19) CV (49;47) Ablation (41;39) BB (55;52) Digoxin (11; 10) CCB (22; 21)
	CG		Paroxysmal (72) Persistent (28) Catheter ablation (100)		100; 73%; 59.0 ± 12.3 y	Amiodarone (12; 11) CV (54;51) Ablation (5; 13) BB (56; 53) Digoxin (7; 7) CCB (28; 27)
Multi-intervention studies						
Borland et al. [45], 2020	IG (CE; MIE)	Sweden; Randomised study; Transl Sports Med	Permanent (100)	≥ 50%	40; 74%; 74.0 ± 4.0 y	Heart rate regulators (37; 80)
	IG (AE; MIE)				47; 68%; 74.0 ± 6.0 y	Heart rate regulators (42; 84)
Reed et al. [26], 2022	IG (AE; HIIE)	Canada; Randomised study; JAMA Netw Open	Permanent (61) Persistent (39)	≥ 50%	32; 67%; 68.0 ± 8.0 y	AAD (1; 2) BB (29; 67) Digoxin (7; 16) CCB (15; 35)
	IG (AE; MIE)		Permanent (61) Persistent (39)		39; 65%; 71.0 ± 7.0 y	AAD (4; 9) BB (26; 61) Digoxin (5; 12) CCB (9; 21)

Table 1 (continued)

Study	Group	Study characteristics	Patient characteristics			
		Country; study design; journal	AF type (%); Catheter ablation (%)	LVEF	Final sample size; men percentage; age	Pharmacological treatment (n; %)
Skielboe et al. [46], 2017	IG (AE; MIE)	Denmark; Randomised study; PloS One	Paroxysmal (43) Persistent (57)	≥ 50%	37; 59%; 61.4 ± 3.0 y	AAD Ic (11; 30) BB (23; 62) Digoxin (4; 11) CCB (11; 30)
	IG (AE; LIE)		Paroxysmal (55) Persistent (45)		33; 58%; 63.8 ± 3.3 y	AAD Ic (5; 15) BB (22; 67) Digoxin (2; 6) CCB (8; 24)

AAD, antiarrhythmic drugs; AAD Ic: antiarrhythmic drugs class Ic; AE, aerobic exercise; AF, atrial fibrillation; BB, Beta-blockers; CCB, calcium channel blockers; CG, control group; CE, combined exercise; CV, cardioversion; HIIE; high-intensity interval exercise; IG, intervention group; LIE, low-intensity exercise; LVEF, left ventricular ejection fraction; MIE, moderate-intensity exercise

\# Values are reported as mean ± standard deviation.

Cardiovascular Society Severity of AF scale (CCS-SAF) [37], one the EHRA symptoms score [46], and another the AF Symptoms and Severity Checklist [41].

Methodological Quality Assessment

The results of the methodological quality assessment can be found in Table 2. Additionally, the statements supporting the judgement of each item are reported in Table S4 (see ESM). In summary, the mean ± SD score was 9.3 ± 2.2 (range 6–13). Reviewers judged four (33.3%) studies to have fair quality [25, 38, 40, 42], six (50.0%) to have good quality [26, 37–39, 41, 43, 44], and two (16.7%) to have excellent quality [45, 46]. The noteworthy results showed that only four (33.3%) studies conducted intention-to-treat analyses [26, 44–46]. Out of the eight controlled studies, only one (8.3%) monitored physical activity in those patients allocated to the CG [37]. Finally, none of the included studies conducted mid-intervention assessments to adjust exercise intensity throughout the intervention period.

Outcomes

Peak Oxygen Uptake (VO_2 peak)

Six studies used VO_2 peak as an endpoint, of which five were controlled studies [25, 38, 40, 41, 44] and one a multi-intervention study [46]. Therefore, pooled analyses were conducted for controlled studies (Supplementary Fig. 1). There was no statistically significant difference in the VO_2 peak improvement between patients with permanent AF and non-permanent AF ($p = .830$). Therefore, the results are reported regardless of AF type. Compared to usual care, there was a statistically significant improvement ($p < .001$) in VO_2 peak of 4.24 ml/kg/min (95% CI = 0.87; 7.45). In the multi-intervention study, the results showed no differences between MIE and LIE for enhancing VO_2 peak in patients with non-permanent AF (MD = −0.74 [95% CI = −4.65; 3.17] ml/kg/min; Table S3).

Six-minute Walk Test (6MWT)

Five studies measured the distance covered in the 6MWT, of which four were controlled studies [38, 39, 43, 44] and one was a multi-intervention study [26]. Therefore, pooled analyses were conducted for controlled studies (Supplementary Fig. 2). Subgroup analysis did not reach statistical significance ($p = .082$) and the results were reported regardless of AF type. No differences were found between the IG and the CG for enhancing the distance covered in the 6MWT (MD_+ = 22.63 [95% CI = −17.16; 62.43] m). The heterogeneity test reached statistical significance with high inconsistency ($p = .007$; $I^2 = 80\%$). In the multi-intervention study, the results showed no differences between HIIE and MIE for enhancing the distance covered in the 6MWT in patients

Table 2 Methodological quality assessment of included studies judged using TESTEX scale

Study	Study quality					Study reporting								
	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Overall	Judgement
Alves et al. [25]	1	1	0	1	0	0	0	1	1	0	0	1	6	Fair
Bittman et al. [37]	1	1	0	1	1	2	0	1	1	1	0	1	10	Good
Joensen et al. [38]	1	0	0	1	1	2	0	1	1	0	0	1	8	Fair
Kato et al. [39]	1	0	0	1	1	3	0	1	1	0	0	1	9	Good
Kim et al. [40]	1	1	0	1	1	0	0	1	1	0	0	1	7	Fair
Malmo et al. [41]	1	0	0	1	1	3	0	1	1	0	0	1	9	Good
Nourmohammadi et al. [42]	1	1	0	1	0	0	0	1	1	0	0	1	6	Fair
Osbak et al. [43]	1	1	1	1	1	2	0	1	1	0	0	1	10	Good
Risom et al. [44]	1	1	1	1	0	2	2	1	1	0	0	1	11	Good
Borland et al. [45]	1	1	1	1	1	3	2	1	1	NA	0	1	13	Excellent
Reed et al. [26]	1	1	1	1	1	0	2	1	1	NA	0	1	10	Good
Skielboe et al. [46]	1	1	1	1	1	2	2	1	1	NA	0	1	12	Excellent

Item 1, eligibility criteria specified; Item 2, randomisation specified; Item 3, allocation concealment; Item 4, group similar at baseline; Item 5, blinding of assessor; Item 6, outcome measures assessed in 85% of patients; Item 7, intention-to-treat analysis; Item 8, between-group statistical comparisons reported; Item 9, point measures and measures of variability for all reported outcome measures; Item 10, activity monitoring in control groups; Item 11, relative exercise intensity remained constant; Item 12, exercise volume and energy expenditure; NA, non-applicable item due to study design

with persistent or permanent AF (MD = 8.03 [95% CI = − 36.78; 52.84] m; Table S3).

Quality of Life (QoL)

Ten studies assessed QoL, eight were controlled studies [25, 37, 38, 41–44] and two were multi-intervention studies [26, 45]. Subgroup analyses based on AF type using RVE were not performed due to the low number of included studies. Meta-analysed data from the controlled studies revealed no statistically significant differences between both groups for improving QoL (8 studies; SMD_+ = 1.11 [95% CI = − 0.02; 2.25]; $p = .053$). In relation to the multi-intervention studies, Borland et al. [45] found in patients with permanent AF that those in the combined exercise group had greater improvements in the "Role physical" domain of the SF-36 questionnaire compared to the aerobic exercise group (SMD = 0.36 [95% CI = 0.03; 0.69]), while no differences were found between the two groups in the remaining dimensions (see Table S2). In patients with permanent or persistent AF, Reed et al. [26] reported a greater enhancement of the "Mental health" domain of the SF-36 questionnaire in the HIIE group compared to the MIE group (SMD = 0.34 [CI = 0.01; 0.67]), and no differences were found in the other dimensions (see Table S3).

Resting Heart Rate (resting HR)

Six studies evaluated the patients' resting HR, four were controlled studies [25, 39, 41, 43] and two were multi-intervention studies [26, 45]. Pooled analyses were conducted for controlled studies (Supplementary Fig. 3). Subgroup analyses based on AF type reached statistical significance ($p < .001$). The CR-induced effect on resting HR was greater in those studies which recruited patients with permanent AF (2 studies; MD_+ = − 12.79 [95% CI = − 15.90: − 9.67] bpm) compared to non-permanent AF (2 studies; MD_+ = − 2.36 [95% CI = − 5.47; 0.75] bpm). The results of the included studies did not show inconsistency both in patients with permanent AF ($p = .645$; $I^2 = 0\%$) and non-permanent AF ($p = .763$; $I^2 = 0\%$). Regarding the multi-intervention studies, Reed et al. [26] found no significant differences between HIIE and MIE for reducing resting HR in patients with persistent or permanent AF (MD = 0.69 [95% CI = − 6.33; 4.94] bpm) (Table S2). Similarly, Borland et al. [45] reported no differences between aerobic exercise and combined exercise for reducing resting HR in patients with permanent AF (MD = 1.98 [95% CI = − 2.22; 6.18] bpm) (Table S3).

Atrial Fibrillation Burden (AF Burden)

Five studies measured the burden of AF, three were controlled [37, 39, 41] and two were multi-intervention [26, 46]. Nonetheless, we were not able to calculate ES in two of the included studies due to the nature of the variables

[39, 46], and meta-analyses were not conducted. Malmo et al. [41] found no differences between the IG and the CG in diminishing AF burden (MD = −7.38 [95% CI = −15.10; 0.33] %). On the contrary, Bittman et al. [37] found an increase of AF burden in the IG compared to the CG (MD = 9.10 [95% CI = 1.81; 16.39] %) (Table S2). In multi-intervention studies, Reed et al. [26] found an increase in AF burden in the HIIE group compared to the MIE group (MD = 6.24 [95% CI = 1.34; 11.15] %). In contrast, Skielboe et al. [46] in the intention to treat analysis and after controlling for confounders, reported no differences between the HIIE group and the LIE group in AF burden (incidence rate ratio = 0.74 [95% CI = 0.29; 1,91], $p = .538$). Similarly, no differences were found between the two groups in AF recurrence ($p = .465$). Lastly, Kato et al. [39] was the only study included in our review that evaluated the effect of CR on AF recurrence in patients with persistent AF after catheter ablation. They found a non-significant change in the relative risk of AF recurrence (RR = 0.83 [95% CI = 0.33; 2.10]), after six months of MIE (Table S3).

Atrial Fibrillation Symptoms (AF Symptoms)

Four studies assessed AF symptoms, of which three were controlled studies and one was a multi-intervention study. Bittman et al. [37] found a statistically significant reduction of AF symptoms in favour of the IG compared to the CG (SMD = −0.47 [95% CI = −0.84; −0.10]) when the CCS-SAF questionnaire was used. Malmo et al. [41] also found a significant reduction in the frequency and severity of AF symptoms in favour of the IG (SMD = −0.48 [CI = −0.92; −0.05], and (SMD = −0.68 [95% CI = −1.13; −0.23], respectively). On the contrary, Bittman et al. [37] and Risom et al. [44] reported no differences between the two groups in AF symptoms when the AFSS questionnaire and EHRA were used, respectively (Table S2). However, Bittman et al. [37] reported a statistically significant reduction of global well-being in the IG compared to the CG (SMD = −0.76 [95% CI = −1.14; −0.38]). In the multi-intervention study, Reed et al. [26], found an increase in the duration of AF symptoms in the HIIE compared to the MIE group (SMD = 0.46 [95% CI = 0.12; 0.79]) (Table S3).

Discussion

The current systematic review was conducted to determine the most common exercise characteristics used in CR programmes and investigate the effect of exercise-based and multicomponent CR programmes in patients with AF while considering the influence of possible moderating variables such as AF type and exercise characteristics (e.g., modality and intensity). Most of the studies performed aerobic exercise as the training modality and used MIE as the aerobic exercise method, while the effect of combined exercise has been poorly investigated. In addition, none of the included studies performed resistance exercise. The results showed that aerobic exercise, performed alone or combined with other interventions (i.e., multicomponent programmes), is suitable for improving VO_2 peak in patients with permanent and non-permanent AF. Interestingly, we also found that MIE reduces resting HR in patients with permanent AF, while no differences were found, regardless of the aerobic exercise intensity (i.e., MIE and HIIE), in patients with non-permanent AF. By contrast, it appears that CR programmes do not increase the distance covered in the 6MWT or the QoL to a greater extent than usual care in patients with AF. Our findings also elucidated that very few studies have investigated the effect of CR programmes on AF burden and symptoms, and their results are controversial. In addition, only one study investigated the influence of exercise modality and two the influence of aerobic exercise intensity. The results showed no influence of these variables on the exercise-induced effect in patients with AF.

The finding that aerobic exercise increases VO_2 peak in patients with AF is consistent with previous reviews and meta-analyses [21–23, 54]. Additionally, the improvement of 4.24 ml/kg/min, exceeds the clinically meaningful change for patients with cardiovascular disease (1 ml/kg/min or 10%) [55]. This is particularly relevant considering that patients with AF experience reduced physical capacity compared to the general population and undergo a more rapid physical decline with age [56]. For every 1 ml/min/kg increase in VO_2 there is a relative risk reduction of 9% in all-cause mortality (hazard ratio 0.91; [95% CI, 0.87–0.95]) [57]. The results of our meta-analysis would imply a mortality risk reduction of 38.16% in patients with AF. Regarding the mechanisms of VO_2 peak increase, there is evidence showing that aerobic exercise ameliorates both central (e.g., cardiac function) and peripheral (e.g., endothelial function) impairments which, in turn, improves VO_2 peak.

Contrary to the improved VO_2 peak, we observed no exercise-induced effect on the 6MWT, which is unexpected given previous systematic reviews and meta-analyses [21–23, 54]. Smart et al. [23] found a significant improvement in 6MWT of 46.93 m in the exercise versus control group (95% CI 26.44 to 67.42; $p < .001$, $I^2 = 66\%$), exceeding the minimal clinically important difference of 41.8 m for patients with AF [58]. These differences could be attributed to the fact that Smart et al. [23] included a broader range of physical activities such as yoga, Pilates, Tai Chi, hydrotherapy, functional electrical stimulation, and inspiratory muscle training. Additionally, the most recent Cochrane review provided evidence indicating that exercise-based CR increased the 6MWT, albeit with high heterogeneity [59]. The significant heterogeneity observed among the studies included in our review may account for the absence of improvement in 6MWT. Nonetheless, VO_2 peak remains the standard method for measuring functional capacity [60].

Our meta-analysis revealed a reduction in resting HR, which was statistically significant only in patients with permanent AF, where it could hold a greater significance given that rate control is the primary strategy for this subgroup. Therefore, CR could serve as an effective tool for rate control in patients with AF, reducing the dependency on medical treatment [5, 61]. Such a decrease in resting HR could also translate into enhanced QoL and reduced mortality [62]. Past studies have demonstrated a J-shaped relationship between HR and mortality in AF patients, with elevated HR correlating with increased mortality rates [63]. These results are in line with previous reviews [21, 23, 64]. Ortega-Moral et al. [21] also found a significant reduction in resting HR exclusively in permanent AF. However, the magnitude of the effect found in our study (reduction of 12 beats per minute) is higher than previous evidence. The meta-analysis of Smart et al. [23] found a reduction in resting HR of 4.61 beats per minute (95% CI −7.42 to −1.80; $p = .001$). The mechanisms contributing to improved ventricular rate control through exercise are likely associated with increased cardiac parasympathetic activity [65, 66]. Most patients have relatively high sympathetic tone, increasing atrial susceptibility to AF. Regular physical exercise on a non-elite level reverses the autonomic balance towards a stronger parasympathetic tone, improving rhythm regulation and reducing AF burden.

The majority of studies included in our review did not find a significant reduction in AF burden in the exercise group [39, 41, 46]. This contrasts with previous research [59]. A recent study found that a 1-hour reduction in daily physical activity over the past week increased the likelihood of AF the next day by 24%, indicating an acute protective effect of regular activity [67]. Reducing AF burden could impact patients' symptoms, but also, reduce the risk of stroke, HF and mortality [68]. A possible explanation for these conflicting findings may be the lack of consensus on the definition and measurement of AF burden. AF burden is variably defined as the duration of the longest episode, number of episodes or AF beats, or the percentage of time in AF during a monitoring period, and is assessed using ECGs, Holter monitors, or continuous loop recorders [68]. Longer monitoring systems increase the likelihood of AF detection. Out of the three controlled studies that measured AF burden in our review, only one used an implantable loop recorder [41], while the others utilised Holter monitoring [37, 39]. Exercise training did reduce AF burden in the study that used continuous ambulatory monitoring [41], consistent with previous evidence [20]. Notably, one study even reported an increase in AF burden with exercise compared to the non-exercise group, as assessed by Holter monitoring and AFSS score [37]. Despite this, the same study observed a reduction in AF burden according to the physician-reported CCS-SAF score. Despite these results, we found no substantial evidence supporting the concern that exercise might increase AF burden, based on the increased incidence of AF among elite athletes [69].

Only one study included in our review evaluated the effects of exercise after catheter ablation and it showed no statistically significant differences in AF recurrence between the CR and usual care group (RR 0.83; 95% CI, 0.33 to 2.10) [39]. These results contrast with recent clinical trials suggesting that physical activity could improve ablation success, which has recurrence rates of 20–30%. The ARREST-AF trial demonstrated that exercise, accompanied by weight loss and risk factor management before catheter ablation, improved long-term maintenance of sinus rhythm over a 3- to 4-year period in patients with AF [70]. In addition, the LEGACY trial showed that long-term sustained weight loss, combining exercise and a nutritional program, also favoured maintenance of sinus rhythm [71].

Unlike previous literature, we found no significant improvement of QoL following exercise [21–23, 54, 59, 64], despite the well-documented burden of AF on morbidity. Individuals with AF experience lower QoL than healthy counterparts and, in some cases, even lower than those recovering from myocardial infarction. However, the effect approached significance ($p = .53$), warranting further investigation in a larger cohort. This result may be partly explained by the use of different QoL questionnaires across studies. The optimal tool for assessing QoL in AF remains uncertain. The use of generic QoL questionnaires like the SF-36 has drawn criticism because they lack the sensitivity needed to capture AF-specific symptoms and the unique barriers faced by these individuals [72].

In recent years, there has been a growing interest in the advantages of HIIE compared to MIE in AF, owing to its promising outcomes in other cardiovascular conditions [73, 74]. However, we encountered a scarcity of studies assessing the impact of exercise intensity in AF patients, leading to inconclusive findings. Both studies included in our review found no differences in functional capacity, resting HR or QoL between HIIE and MIE [26, 46]. Favouring HIIE, Reed et al. [64] reported a significant improvement in QoL, specifically in the "mental health" subscale of the SF-36, in the HIIE group, consistent with prior evidence. Martland et al. [19], in their meta-review, observed similar trends, with 25% of patients with cardiometabolic disorders experiencing enhancements in QoL following HIIE compared to controls. Nonetheless, Reed et al. [26] also observed a significant increase in AF burden and symptoms in the HIIE group. Concerns about the potential of HIIE to increase AF risk have persisted over the years and are rooted in research demonstrating elevated AF rates among athletes [69]. However, this result was not supported by Skielboe et al. [46], who reported no significant differences in AF burden between the HIIE and LIE group. It is worth noting that their HIIE protocol deviates from standard definitions, as the intervention began with MIE and only progressed to HIIE towards the end of the programme. Additionally, the authors faced challenges controlling the exercise amount and intensity in the LIE group, possibly resulting in smaller differences between the two aerobic protocols. In fact, both groups achieved the same physiological effect from the intervention (VO_2 peak). In summary, current evidence does not favour HIIE over MIE, as both similarly improve functional capacity and resting HR. However, HIIE may be more time-efficient—an advantage given that lack of time is a common barrier to exercise adherence.

Only two studies performed combined exercise programmes [39, 45], of which one study investigated the influence of exercise modality on outcomes [45]. Borland et al. [45] compared CE with aerobic MIE training in 80 patients with permanent AF. They found no differences in QoL between the two exercise modalities, except for a significant improvement in the "role physical" subscale of the SF-36 questionnaire in the CE group. This contrasts with Shi et al. [22], who demonstrated that aerobic exercise significantly improved QoL compared to CE. Contrary to Borland et al. [45], Shi et al. [22] included yoga and Qigong as part of the aerobic exercise interventions, which incorporate meditation, consciousness and breathing exercises as part of the practice. These components alone have been shown to enhance QoL, potentially accounting for the differences observed [75]. Although Borland et al. [45] found no differences in QoL between CE and aerobic exercise, they did observe greater muscle strength and improvement in exercise capacity measured with the maximum workload achieved in a cycloergometer in the CE compared to MIE (18% vs. -3% W; $p < .0001$). This suggests that CE may be a valuable adjunct for AF patients, as gains in muscle strength and power support physical independence and improve QoL [76].

Finally, our findings align with the most recent 2023 ACC guidelines for the management of AF, which recommend moderate-to-vigorous aerobic exercise training to a target of 210 min per week to reduce AF symptoms and burden, increase maintenance of sinus rhythm, functional capacity, and QoL [61]. However, only one study in our review met this 210-minute-per-week target (Borland et al. [45]), indicating that even shorter weekly exercise durations may still offer benefits.

Strengths and Limitations

To the best of our knowledge, this is the first systematic review and meta-analysis that addresses the effect of exercise on AF burden and symptoms. Additionally, the effect of exercise has been studied considering the influence of training variables, such as the aerobic exercise method or exercise modality. In this regard, studies were carefully classified based on the exercise intervention characteristics, regardless of the definition given by the authors in the study. Furthermore, studies conducting other type of physical therapies (e.g., yoga and inspiratory muscle training) were excluded to diminish intervention heterogeneity. Finally, we have also taken into account the influence of the type of AF on the exercise-induced effect, which had not been addressed previously. On the other hand, some limitations need to be highlighted. Firstly, the number of studies included was low, which prevented us from conducting meta-analysis of variables such as AF burden and symptoms. Secondly, the results of subgroup analyses should be interpreted with caution due to the low number of included studies. Thirdly, there is inconsistency in the definition of training programmes across the studies included in our review; for instance, some studies describe their interventions as HIIE but do not conform to the standard HIIE protocols. Finally, the influence of other potential moderator variables was not tested.

Conclusion

In conclusion, aerobic exercise, either alone or in combination with other interventions, improves VO_2 peak in patients with both permanent and non-permanent AF and reduces resting HR in permanent AF. No effect was found on QoL, or the distance covered in 6MWT, possibly attributable to the scarcity of exercise-based randomised controlled trials in this population and the variability in QoL reporting. The number of studies investigating the effect of CR programmes on AF burden and symptoms was insufficient to draw any conclusions. It is imperative to development guidelines specifying the frequency, duration, intensity and mode of exercise training programs for the management of patients with AF. To achieve this, further research is needed regarding the impact of training variables on the exercise-induced effect through rigorous RCTs in this population. This understanding could help tailor CR programmes to meet the specific needs of patients with AF, maximizing the potential benefits of these interventions.

Abbreviations

AAD	Antiarrhythmic drug
AAD Ic	Antiarrhythmic drug class Ic
AE	Aerobic exercise
AF	Atrial fibrillation
AF-QoL	Atrial fibrillation quality of life
AFSS	Atrial Fibrillation Symptom Severity Scale

BB	Beta-blockers
CCB	Calcium channel blockers
CCS-SAF	Canadian Cardiovascular Society Severity of Atrial Fibrillation Scale
CD	Cool down
CE	Combined exercise
CG	Control group
CI	Confidence interval
CR	Cardiac rehabilitation
CV	Cardioversion
d/w	Days per week
ECG	Electrocardiogram
EHRA	European Heart Rhythm Association score
EQVAS	Visual analogue scale assessing self-estimated health status
ES	Effect size
HF	Heart failure
HIIE	High-intensity interval exercise
HR	Heart rate
IG	Intervention group
LIE	low-intensity exercise
LVEF	Left ventricular ejection fraction
MCS	Mental component score
MD	Mean difference
MIE	Moderate-intensity exercise
MLHF	Minnesota Living with Heart Failure
NA	Non-applicable
PCS	Physical component score
PHQ	Patient health questionnaire
PPO	Peak power output
QoL	Quality of life
RE	Resistance exercise
RM	One repetition maximum
RPE	Rate perceived exertion
RVE	Robust Variance Estimation
SF-36	36-item Short Form Survey Instrument
SMD	Standardised mean difference
VO2 peak	Peak oxygen uptake
WU	Warm-up
6MWT	6-minute walk test

Supplementary Information

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Supplementary Material 1

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Author Contributions
L.F., V.C, and A.M., designed the systematic review, established the electronic search equation, and performed the searches. N.S., C.B., and A.M. performed the study selection, N.S., J.M.S., and L.F. carried out the data extraction, and C.B., J.M.S, and L.F. performed the risk of bias assessment. J.M.S, A.C., and L.F. carried pooled analyses, and C.B., N.S., and V.C. wrote the first draft of the manuscript. J.M.S., A.M., and A.C. critically revised the content of the manuscript and wrote the final version of the manuscript, which was finally approved by all authors. All authors have read and agreed to the published version of the manuscript.

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Data Availability
The dataset generated from the current study is available from the corresponding author on reasonable request.

Declarations

Ethics Approval and Consent to Participate
Not applicable.

Consent for Publication
Not applicable.

Competing Interests
Agustín Manresa-Rocamora, Laura Fuertes-Kenneally, Noemí Sempere-Ruiz, Carles Blasco-Peris, Alicia Ibáñez-Criado, Vicente Climent-Paya, and José Manuel Sarabia declare no conflicts of interest.

Supplementary Information
This article includes supplementary materials with additional data on the pooled analysis of VO_2 peak (Supplementary Fig. 1), the 6MWT (Supplementary Fig. 2), and resting HR (Supplementary Fig. 3). It also contains a methodological quality assessment (Tables S1 and S4) and a summary of the intervention characteristics and reported outcomes of the included studies (Table S2 and S3).

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