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Effects of High-Intensity Interval Training vs. Moderate-Intensity Continuous Training on Quality of Life and Mental Health in Post-Myocardial Infarction Patients: A Randomized Controlled Trial

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Keywords
Anxiety · Cardiovascular disease · Depression · Health-related quality of life · High-intensity interval training · Randomized controlled trial

Abstract

Introduction: This study aimed to investigate the effects of two exercise-based programs over a short-term 6-week period, compared to a control group (no exercise program), on the quality of life (QoL) and mental health of patients with myocardial infarction (MI). ***Methods:*** In this randomized controlled trial, 72 patients with MI were individually randomized (1:1:1) into three groups: HIIT, MICT, and control. Both training programs consisted of 6 weeks of supervised treadmill exercise, three sessions per week. MICT was performed at ≈70–75% of peak heart rate (HR), while HIIT was performed at ≈85–95% of HRpeak. The control group followed standard medical recommendations. Outcome measures included assessments of QoL (SF-36) and anxiety and depression (HADS). ***Results:*** In the exercise groups, 6 out of the 8 SF-36 dimensions showed a significant improvement after 6 weeks. The HIIT group exhibited noteworthy enhancements in physical functioning (p = 0.022) and general health dimensions (p = 0.015) compared to the MICT group. Baseline anxiety and depression scores, albeit modestly elevated, substantially decreased following the 6-week exercise interventions in both exercise groups, exhibiting statistical significance compared to the control group (p < 0.001). No significant differences were found between the HIIT and MICT in terms of mental health. ***Conclusion:*** Both exercise programs were equally effective in improving QoL and mental health in MI patients. However, the HIIT group showed greater improvements in physical functioning and general health dimensions than the MICT group. Our findings emphasize that abstaining from exercise-based post-MI programs correlates with lower QoL, and higher anxiety and depression scores. This

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underscores the significance of implementing exercise-based rehabilitation strategies to optimize the recovery and well-being of patients with MI.

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Efeitos do treino intervalado de alta intensidade vs. treino contínuo de intensidade moderada na qualidade de vida e na saúde mental de doentes pós-enfarte do miocárdio: um ensaio controlado aleatório

Palavras Chave
Ansiedade · Depressão · Doença cardiovascular · Ensaio clínico randomizado · Qualidade de vida relacionada à saúde · Treino intervalado de alta intensidade

Resumo

Introdução: Este estudo teve como objetivo investigar os efeitos de dois programas baseados em exercício durante seis semanas em comparação com um grupo de controlo (que não realizou nenhum programa de exercício), na qualidade de vida (QV) e na saúde mental de pacientes que sofreram um enfarte agudo do miocárdio (EAM). ***Métodos:*** Neste ensaio clínico randomizado, 72 pacientes após EAM foram aleatoriamente distribuídos (1:1:1) em três grupos: treino intervalado de alta intensidade (HIIT), treino contínuo de intensidade moderada (MICT) e controlo. Ambos os programas de treino consistiram em seis semanas de exercício supervisionado na passadeira, três sessões por semana. O MICT foi realizado a uma intensidade de ≈ 70–75% da frequência cardíaca máxima (FCmáx), enquanto o HIIT foi realizado a ≈85–95% da FCmáx. O grupo controlo seguiu apenas as recomendações médicas habituais. Foi avaliado a QV (questionário SF-36), a ansiedade e a depressão (questionário HADS) antes e após as intervenções. ***Resultados:*** Nos grupos de exercício, seis das oito dimensões do questionário SF-36 mostraram melhorias significativas após as seis semanas. O grupo HIIT exibiu melhorias notáveis nas dimensões funcionamento físico (p = 0,022) e saúde geral (p = 0,015) em comparação com o grupo MICT. Os níveis iniciais de ansiedade e depressão, embora moderadamente elevados, diminuíram substancialmente após as intervenções em ambos os grupos de exercício, exibindo valores estatisticamente significativos em comparação ao grupo controlo (p < 0,001). Não foram encontradas diferenças significativas entre os grupos HIIT e MICT na saúde mental. ***Conclusão:*** Ambos os programas de exercício foram igualmente eficazes na melhoria da QV e da saúde mental em pacientes após EAM. No entanto, o grupo HIIT mostrou melhorias maiores nas dimensões da funcionalidade física e da saúde geral em comparação ao grupo MICT. Os nossos resultados enfatizam que a não participação num programa de exercício pós-EAM está correlacionado com uma menor QV e níveis mais elevados de ansiedade e depressão. Isso sublinha a importância de implementar estratégias de reabilitação baseadas em exercício para otimizar a recuperação e o bem-estar dos pacientes com EAM.

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Introduction

Diseases of the circulatory system are the leading cause of death globally. In 2021, myocardial infarction (MI), strokes, and other circulatory diseases caused more than one in four deaths worldwide [1, 2]. In Portugal, despite a 6.2% decrease in 2021 compared to the previous year, diseases of the circulatory system remained the leading cause of death, closely matching the burden of cancer [3]. The chronic nature of MI negatively impacts patients' quality of life (QoL), with growing recognition of the association between anxiety and depressive symptoms' and higher morbidity and mortality rates [4]. Comparative research by Unsar et al. [5] has demonstrated that individuals with MI experience lower QoL across multiple domains, including mobility, hearing, breathing, elimination, usual activities, mental function, discomfort, symptoms, vitality, sexual activity, and overall score when compared to those without the disease, underscoring the imperative for medical and lifestyle interventions aimed at enhancing QoL, preserving physical and psychosocial independence, and reducing long-term healthcare and social care utilization [5]. Physical exercise is therefore essential to maximize physical, psychological, and social well-being by promoting the development of motor learning skills and cognitive function, which influence QoL [6, 7].

Cardiac rehabilitation (CR) aims to ensure the best possible social, psychological, and physical conditions for patients with cardiac disease. CR is crucial for providing cardiac patients with a strong foundation to lead a healthy lifestyle, improve exercise capacity, and enhance QoL [8–11]. It is also linked to various positive outcomes, including reductions in waist circumference [12], body mass index (BMI) [12, 13], blood glucose and triglyceride

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levels, [14, 15]' and anxiety and depression [16]. A Cochrane review published in 2016 revealed that exercise-based CR in post-MI patients enhanced QoL, decreased the risk of cardiovascular mortality, and resulted in short-term reductions in hospital admissions when compared to a no-exercise control group [17]. Programs of 6–12 weeks' duration resulted in the largest improvements [18]. The American College of Sports Medicine (ACSM) guidelines state that only moderate-to high-intensity continuous training or intermittent training at least three times a week can effectively improve cardiorespiratory fitness, while training <2 times a week will not yield significant improvements in healthy adults [19].

Some studies have found that moderate-intensity continuous training (MICT) can reduce cardiovascular risk and mortality [20]. MICT has traditionally been a foundation of aerobic-based exercise prescription at the intensity of 50–75% heart rate (HR) [21], resulting in short- and long-term clinical benefits in cardiovascular, lung, and skeletal muscle functions, endurance, QoL, inflammation, anxiety and depressive symptoms, stress, and cognitive functions for CAD patients [18, 20, 22, 23]. Despite these undeniable benefits of participation in CR, adherence rates remain low [24]. Patients report several barriers to participating in traditional CR including low motivation, poor self-efficacy, and time constraints [25]. However, high-intensity interval training (HIIT) has recently emerged as an alternative or adjunct strategy to MICT. HIIT involves repeated bouts of relatively higher-intensity exercise (85–100%) interspersed with periods of lower-intensity recovery [24].

A case report examined the physiological parameters of post-MI patients compared to healthy participants who belonged to CR programs of HIIT and MICT and concluded that MICT is more demanding for post-MI patients, which may explain the lower adherence to this exercise training [26]. With traditional CR programs having low attendance rates (mean: 66 ± 18%, range: 37–85% session attendance) [27], there is a need to examine the feasibility of other innovative exercise programs within CR settings. Stavrinou et al. [28] reported that HIIT twice weekly increased VO_2peak by 10.8%, while training three times a week increased VO_2peak by 13.6%. Advantageous HIIT requires less time and yields similar or even greater improvements in VO_2peak [18, 22], body composition [23, 29], HR response to exercise [30], and myocardial function [26] compared to MICT. However, there is a notable gap in the scientific literature regarding the comparative effects of HIIT versus MICT on QoL and mental health of patients with MI. Thus, the primary objective of this study was to investigate the impact of two community-based exercise programs employing HIIT and MICT protocols on QoL and mental health (anxiety and depression) in patients with MI, with a comparative analysis against a control group receiving no exercise program.

Methods

This study was a single-blinded randomized controlled trial (RCT) that follows the CONSORT guidelines for RCTs (http://www.consort-statement.org).

Participants

Seventy-two patients with MI were recruited from among those entering the cardiology unit at the Hospital of Evora (Portugal) between March 2018 and November 2021. The sample size was calculated using G*Power software to ensure adequate statistical power and precision. We selected an effect size (ES) of 0.3, based on previous literature and pilot data [31] to estimate the magnitude of the differences between the two exercise regimens (HIIT and MICT) and the control group. With a predefined sample power of 0.6 and an error probability of 0.05, corresponding to a 95% confidence level, we aimed to achieve a balance between the risk of type I and type II errors [31]. This calculation yielded a minimum sample size of 66 participants (22 per group) necessary to detect significant changes in our outcomes of interest (QoL, anxiety, and depression). Additionally, we anticipated potential dropout rates and accordingly increased the sample size to ensure the robustness and reliability of our findings. The inclusion criteria were age 18–80 years, left ventricular ejection fraction ≥50%, and New York Heart Association (NYHA) functional class I or II. Patients were excluded from the study if they met the following criteria: severe exercise intolerance, uncontrolled arrhythmia, uncontrolled angina pectoris, severe kidney or lung disease, musculoskeletal or neuromuscular conditions preventing exercise testing or training, and signs or symptoms of ischemia.

The patients underwent a clinical evaluation performed by a cardiologist. A supervised graded exercise test to assess volitional fatigue, risks, or symptoms of ischemia was performed on a treadmill using the Bruce protocol [32, 33] before the 6-week intervention period. The test was performed under non-fasting conditions with medication. Electrocardiography was performed continuously, and blood pressure was measured using an arm cuff every 3 min. As a high proportion of patients with MI are prescribed β-blocker therapy, this relative method of exercise intensity takes into the likely to have a

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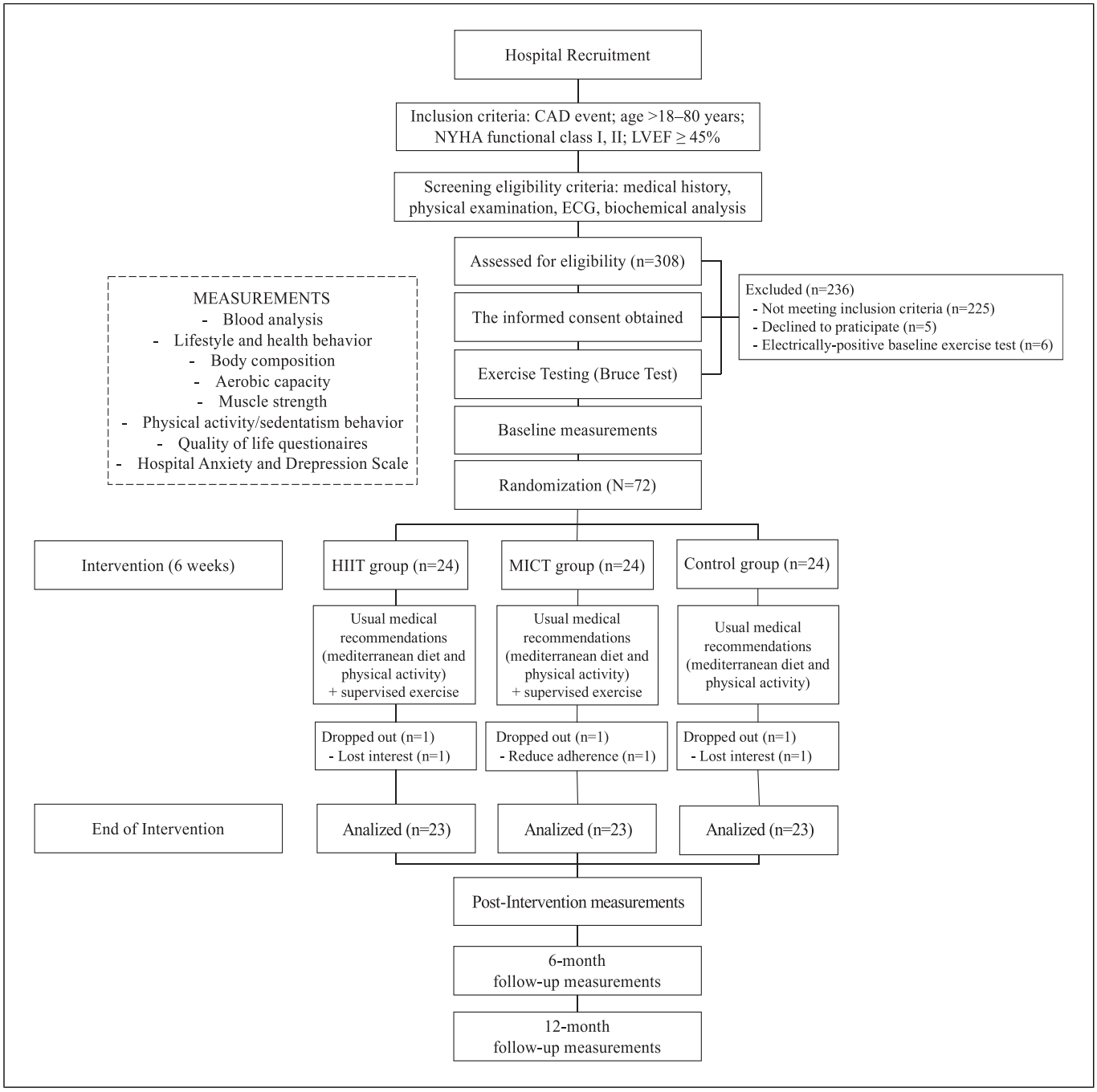

Fig. 1. Diagram of the study.

lower HR peak achieved by these patients during the exercise test. At the end of the test, the cardiologist validated the participation of each patient in the program.

The recruitment ended when a previously calculated sample size was obtained. All the patients had a medical history and provided written informed consent.

Randomization and Masking

After the baseline assessment and before the start of the exercise programs, the 72 patients were randomly assigned in a 1:1:1 allocation ratio to one of three groups: HIIT, MICT (traditional), or control (usual medical recommendations) (Fig. 1). To ensure allocation

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concealment, patients in each group were seen at a specific prescheduled time, and appointments for each group did not coincide with those for any patients in the other groups. The three groups were similar in terms of age, extent of coronary artery disease, coronary risk factors, type of coronary event, and left ventricular ejection fraction.

Outcome Measures and Assessments

Risk Factor Screening

At the second visit, the patient's blood pressure, height, weight, and waist circumference were recorded by a physiologist at the University of Evora's laboratory. Patients were asked to take any medications that they were taking during the assessments. Initially, each patient completed a standardized questionnaire that included demographic data, medical history, medication use, family history of CVD, and smoking status. Body mass index was calculated using the standard formula: *weight (kg)/height (m)* [2], and waist circumference was manually measured according to standard procedures outlined in the ACSM guidelines [32]. VO_2peak was calculated from the equation for men: $VO_2\text{max} = 14.8 - (1.379 \times T) + (0.451 \times T^2) - (0.012 \times T^3)$ [34], and for women: $VO_2\text{max} = (4.38 \times T) - 3.9$ [35], where "T" is the total test time, expressed in minutes and fractions of a minute, as determined during the supervised graded exercise using the Bruce protocol [33].

Quality of Life, Anxiety, and Depression

After risk factor screening, the patients completed the patient-reported QoL questionnaire and the Hospital Anxiety and Depression Scale (HADS), validated for use in Portuguese patients [36, 37]. The QoL questionnaire consisted of the SF-36 (Quality Metric, Lincoln, RI, USA), which includes eight domains: physical functioning, role-physical, role-emotional, social functioning, mental health, vitality, bodily pain, and general health [36]. For all reported QoL instruments, higher scores correspond to better QoL as perceived by the patient. The HADS has been widely used to screen anxiety and depression among cardiac patients in hospitals [37]. The HADS questionnaire has two subscales: anxiety and depression, each consisting of items rated on a four-point Likert scale. The total HADS score ranged from 0 to 42, with 0–14 considered low, 15to 28 considered moderate, and 29 to 42 considered high. For each subscale (anxiety and depression subscales), the scores ranged from 0 to 21, where 0–7 was considered low, 8–14 was moderate, and 15–21 was considered high [37]. The questionnaires were administered at the beginning and completion of 18 sessions of community-based exercise programs.

Exercise Training Protocols

After hospital discharge, educational interventions, dietary advice, and psychological support were provided to all patients. The exercise program consisted of 6 weeks of supervised treadmill exercise, with three sessions per week (Fig. 2). To ensure that training exercise intensity was reflective of medication effects, all patients were instructed to take their usual medications during the exercise program. If the medication was changed, the cardiologist informed the team about the change. A cardiologist validated the participation of each patient. Patients performed each exercise session in a group, with a maximum of 3 patients per session. If a session was missed, it was made up of that week or the following week so that patients could complete the total number of sessions planned at the baseline.

Each training session was initiated with a 5–10-min warm-up at 50–60% HRpeak and ended with 5 min of cool-down at 40% HRpeak. The HIIT group performed 4 × 4-min high-intensity intervals at 85%–95% HRpeak, followed by a 1-min recovery interval at 40% HRpeak [38], as predicted by a supervised graded exercise test on a treadmill using the Bruce protocol [32, 33]. During the exercise, the patients were motivated to gradually increase their exercise intensity toward 6–9 (hard to very hard) on a 0- to 10-Borg scale [39]. The MICT protocol (usual care) consisted of a continuous bout of moderate-intensity exercise to elicit 70–75% HRpeak, rating of perceived exertion 3–5 (fairly light to somewhat hard) [39], for 27.5 min to equate the energy expenditure with the HIIT protocol (Fig. 3).

A physiologist supervised the training sessions. Minute-to-minute HRs were recorded with polar HR monitoring (Polar Electro Oy, Kempele, Finland) during exercise, and blood pressure was measured at the beginning and end of each session. As training intensity increased, the patient's HR, rate of perceived exertion (Borg scale) [39], and cardiac symptoms were also considered. Buchheit et al. [40] and Levinger et al. [41] demonstrated that the Borg Scale (RPE) shows a strong correlation with HR, ventilation, and VO_2 in individuals with and without CAD, and the correlation is not impacted by β-blocker medication, a commonly used HR-modulating medication in patients with MI. The control group did not receive any follow-up on exercise beyond general advice regarding the importance of exercise and diet.

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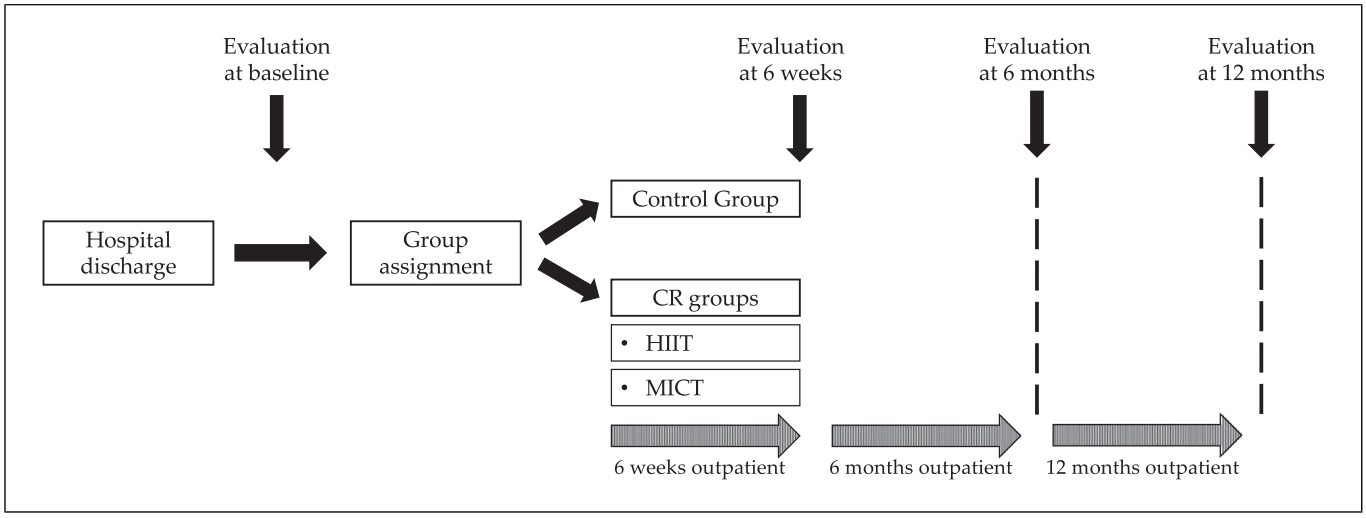

Fig. 2. Study design and time frame.

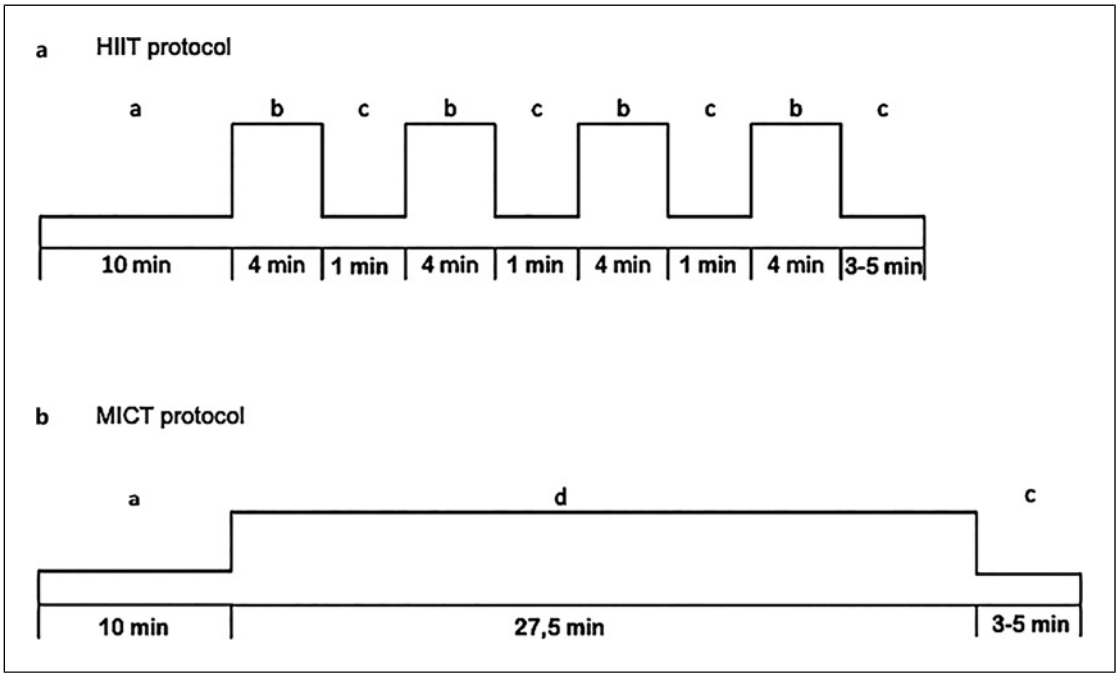

Fig. 3. Summary of the exercise training protocol. **a** HIIT protocol. **b** MICT protocol.

Ethical Considerations

All studies were conducted in accordance with the Declaration of Helsinki and were registered with ClinicalTrials.gov (NCT03538119). Ethical approval was obtained from the University of Evora Ethics Committee (Reference No. 17039). All the patients provided written informed consent before participating in the study.

Statistical Analysis

The assumptions of normality and homogeneity were tested using the Kolmogorov-Smirnov and Levene tests, respectively. As most of the sample variables did not follow a normal distribution, nonparametric statistical analyses were conducted. Between-group comparisons were performed using the Kruskal-Wallis test, and

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within-group comparisons were performed using the Friedman test, followed by post hoc pairwise comparisons. Means and standard deviations were calculated for all variables. The delta value (Δ: *momentx* – *momentx*-1) and the corresponding proportional change delta value (Δ%: [(*momentx* – *momentx*-1)/*momentx*-1] × 100) were computed for all variables: post-intervention vs. baseline. The ES was calculated using Cohen's method because the data were not normally distributed [42]. The ESs were classified based on Cohen's thresholds (small: 0.10; medium: 0.30; and large: 0.50) [43, 44]. Analyses were performed using the SPSS software package (version 24.0 for Windows, IMB Statistics). A p value ≤0.05 was considered statistically significant. A code was assigned to each patient to preserve anonymity.

Results

The demographic and clinical characteristics are summarized in Table 1. Comorbidities and medications also did not differ significantly between the groups ($p >$ 0.05). Two people had already been diagnosed with depression, and two others had been diagnosed with anxiety disorders prior to this study.

In the exercise groups, 6 of the 8 SF-36 dimensions improved significantly after 6 weeks of the community-based exercise program compared to the control group. These dimensions encompassed physical functioning, role-physical, role-emotional, mental health, vitality, and general health (Table 2). In contrast to the control group, HIIT and MICT participants reported superior QoL outcomes at all assessment time points except for the baseline measurement. Furthermore, within the community-based exercise programs, participants engaged in the HIIT regimen exhibited statistically significant temporal enhancements in physical functioning ($p = 0.022$) and general health ($p = 0.015$) when juxtaposed with their counterparts in the MICT group (Table 2). The ES calculated for changes from baseline to the 6-week mark revealed that in the HIIT group, ES values were categorized as small for bodily pain ($d = 0.2$), medium for social functioning ($d = 0.4$), and large for physical functioning ($d = 2.9$), role-physical ($d = 2.7$), role-emotional ($d = 1.6$), mental health ($d = 2.3$), vitality ($d = 1.9$), and general health scores ($d = 1.7$). In contrast, within the MICT group, the ES was identified as small for bodily pain ($d = 0.1$), medium for social functioning ($d = 0.3$), and large for physical functioning ($d = 2.5$), role-physical ($d = 1.7$), role-emotional ($d = 1.3$), mental health ($d = 1.8$), vitality ($d = 1.3$), and general health scores ($d = 1.0$).

Anxiety scores were modestly elevated at baseline (mean HIIT = 6.5 ± 4.8, mean MICT = 6.7 ± 4.4, and mean control = 6.5 ± 4.6 points), demonstrating a subsequent decline following participation in the 6-week community-based exercise program within the exercise groups (mean HIIT = 5.2 ± 4.6, mean MICT = 5.5 ± 4.4 points). However, no significant differences were observed between the exercise groups in the post-MI patients. Correspondingly, mirroring the trends observed for depression scores, a large subset of patients exhibited clinically elevated levels of depression at baseline (mean HIIT = 3.5 ± 3.4, mean MICT = 3.6 ± 3.4, and mean control = 3.6 ± 3.6), as illustrated in Table 3. The frequency of clinically elevated depression scores dropped following the completion of the 6-week community-based exercise program within the exercise groups (mean HIIT = 3.0 ± 3.3 and mean MICT = 3.2 ± 3.3). In contrast, although not significant, the control group experienced an increase in depression scores (mean control = 3.7 ± 3.6 points). The HIIT and MICT groups showed a significant difference of 1.04 and 0.48 points in anxiety scores, and 0.70 and 0.54 points in depression scores compared to the control group ($p < 0.001$). The ES computed for the interval spanning from baseline to 6-week mark unveiled a medium ES in depression scores ($d = 0.4$) and a large ES in anxiety scores ($d = 1.0$) within the HIIT group. Similarly, the MICT group exhibited medium ES for depression scores ($d = 0.4$) and large ES for anxiety scores ($d = 0.9$) during this time frame.

Concerning blood biomarkers (Table 4), there were no differences across groups at baseline. However, significant within-group changes were observed from baseline to post-intervention in both exercise protocols. The HIIT group showed significant results compared to the MICT group in HbA1c (Δ% HIIT: 10.4%, $p < 0.001$ vs. Δ% MICT: 32.3%, $p < 0.001$) and TSH (Δ% HIIT: 16.5%, $p = 0.007$ vs. Δ% MICT: 3.1%, $p = 0.201$). After the 6-week intervention, the control group showed worse results, except for cholesterol variables, specifically HDL-C (Δ% control: 15.9%, $p =$ 0.002). However, it continues to be considered dyslipidemia as defined by the American College of Cardiology, whereas the exercise-based groups showed improvements in lipid profile levels from baseline to post-intervention, approaching normal values. Similar improvements were observed in blood sugar and thyroid variables in the exercise-based groups, but not in the control group.

The respective ESs from baseline to post-intervention in the HIIT group were small for FBG ($d = 0.47$) and endocrine variables: T4 ($d = 0.44$), T3 ($d = 0.47$), and TSH ($d = 0.41$); medium in HbA1c ($d = 0.65$) and hsCRP ($d =$ 0.80); and large for the cholesterol variables: TC

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Table 1. Patient characteristics at baseline

	HIIT (n = 23)	MICT (n = 23)	Control (n = 23)
Demographics			
Age, years, mean±SD	55±9	55±10	57±11
>70 years, *n* (%)	2 (8.7)	3 (13.0)	4 (17.4)
Gender (male/female)	20/3	20/4	20/3
Retired, *n* (%)	2 (8.7)	7 (30.4)	7 (30.4)
Anterior MI, *n* (%)	3 (13.0)	4 (17.4)	2 (8.7)
VO_2peak, mL/kg/min, mean±SD	24.7±9.0	23.4±6.3	23.5±11.0
Risk factors or comorbidities			
Diabetes mellitus, *n* (%)	10 (43.5)	9 (39.1)	10 (43.5)
Hypertension, *n* (%)	13 (56.5)	13 (56.5)	14 (60.9)
Dyslipidemia, *n* (%)	14 (60.9)	15 (65.2)	15 (65.2)
BMI, kg/m^2, mean±SD	28.2±4.5	29.4±3.9	29.4±4.3
Waist circumference, cm, mean±SD	98.4±14.5	101.1±10.3	101.1±10.8
Active smoker, *n* (%)	6 (26.1)	4 (17.4)	4 (17.4)
Nonsmoker, but has been, *n* (%)	9 (39.1)	13 (56.5)	12 (52.2)
Family history of CVD, *n* (%)	14 (60.9)	16 (69.6)	16 (69.6)
Sedentarism, *n* (%)	13 (56.5)	19 (82.6)	19 (82.6)
Sleep <5 h, *n* (%)	6 (26.1)	9 (39.1)	11 (47.8)
Current medication			
ACE inhibitor, *n* (%)	21 (91.3)	23 (100)	22 (95.7)
Antidepressants, *n* (%)	3 (13.0)	2 (8.7)	4 (17.4)
ARBs, *n* (%)	16 (69.6)	7 (73.9)	11 (47.8)
Antiplatelet, *n* (%)	22 (95.7)	22 (95.7)	23 (100)
CCBs, *n* (%)	2 (8.7)	5 (21.7)	5 (21.7)
β-Blockers, *n* (%)	21 (91.3)	22 (95.7)	22 (95.7)
Diuretics, *n* (%)	2 (8.7)	4 (17.4)	6 (26.1)
Insulin, *n* (%)	5 (21.7)	5 (21.7)	11 (47.8)
Statin, *n* (%)	22 (95.7)	22 (95.7)	23 (100)

ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor blockers; BMI, body mass index; CCBs, calcium channel blockers; CVD, cardiovascular disease; HIIT, high-intensity interval training; MI, myocardial infarction; MICT, moderate-intensity continuous training; VO_2peak, maximal oxygen consumed. Data are reported as mean ± standard deviation or number and percent population (%).

(d = 1.35), HDL-C (d = 1.17), LDL-C (d = 1.33), and TG (d = 1.12). In the MICT group, the respective ESs were small for HbA1c (d = 0.37), FBG (d = 0.27), T3 (d = 0.33), and TSH (d = 0.24); medium for TC (d = 0.68), LDL-C (d = 0.66), and TG (d = 0.60); and large for hsCRP (d = 0.81) and HDL-C (d = 1.05).

Adherence

Only 1 patient from each group discontinued the intervention, resulting in 96% adherence to both the HIIT and MICT protocols. There were no reports of adverse events in either protocol (HIIT and MICT) during and after the exercise interventions.

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Table 2. Changes in scores of individual SF-36 dimensions both before and after 6 weeks of community-based exercise programs (HIIT vs. MICT) compared to the control group

Variables		Baseline	Post-intervention	*p* value	Cohen's d (95% CI)
Physical functioning	HIIT	65.0±2.6	75.3±4.2	<0.001[a,c]	2.938 (1.918; 3.958)
	MICT	64.0±2.6	71.5±3.4	<0.001[b]	2.513 (1.671; 3.356)
	Control	63.6±0.6	64.1±0.7	0.491	0.172 (0.181; 0.525)
Role-physical	HIIT	62.7±0.7	72.7±4.1	<0.001[a]	2.669 (1.760; 3.579)
	MICT	62.4±0.9	69.7±0.9	<0.001[b]	1.681 (1.118; 2.245)
	Control	61.5±3.5	61.8±0.9	0.827	0.066 (−0.199; 0.330)
Role-emotional	HIIT	69.3±4.8	76.3±0.8	<0.001[a]	1.624 (1.071; 2.177)
	MICT	68.1±1.1	74.1±0.9	<0.001[b]	1.254 (0.825; 1.683)
	Control	67.3±4.5	67.6±6.3	1,000	0.048 (−0.233; 0.328)
Social functioning	HIIT	73.8±4.6	80.0±3.0	<0.001	1.587 (1.024; 2.151)
	MICT	74.0±4.4	78.3±3.1	<0.001	1.153 (0.741; 1.565)
	Control	75.3±4.7	75.0±0.9	0.808	−0.086 (−0.290; 0.118)
Mental health	HIIT	71.0±3.8	78.7±3.1	<0.001[a]	2.308 (1.548; 3.067)
	MICT	69.8±4.3	76.6±3.3	<0.001[b]	1.755 (1.160; 2.350)
	Control	70.3±4.6	69.5±4.6	0.074	−0.171 (−0.399; 0.058)
Vitality	HIIT	59.8±5.6	69.3±4.6	<0.001[a]	1.851 (1.228; 2.473)
	MICT	61.4±5.2	67.7±4.2	<0.001[b]	1.334 (0.886; 1.782)
	Control	59.9±4.9	60.3±6.3	0.670	0.069 (−0.208; 0.346)
Bodily pain	HIIT	58.1±6.9	65.7±6.5	<0.001	1.138 (0.741; 1.535)
	MICT	61.7±1.3	66.6±5.3	<0.001	0.849 (0.544; 1.153)
	Control	60.7±7.1	63.1±7.6	0.007	0.330 (0.129; 0.530)
General health	HIIT	57.8±2.9	81.2±14.4	<0.001[a,c]	1.698 (1.030; 2.365)
	MICT	56.7±13.0	71.0±14.7	<0.001[b]	1.028 (0.510; 1.545)
	Control	55.1±13.4	58.4±18.6	0.827	0.207 (−0.318; 0.731)

Control, control group (n = 23); HIIT, high-interval intensity training (n = 23); MICT, moderate-intensity continuous training (n = 23). Values are reported as mean ± standard deviation; 95% CI, 95% confidence interval. [a]Significant differences between HIIT and control, $p < 0.05$. [b]Significant differences between MICT and control, $p < 0.05$. [c]Significant differences between HIIT and MICT, $p < 0.05$.

Table 3. Changes in the scores of individual HADS dimensions before and after 6 weeks of community-based exercise programs (HIIT vs. MICT) compared to the control group

Variables		Baseline	Post-intervention	*p* value	Cohen's d (95% CI)
Anxiety	HIIT	6.54±4.76	5.16±4.59	<0.001[a]	1.006 (0.611; 1.402)
	MICT	6.70±4.35	5.52±4.44	<0.001[b]	0.908 (0.682; 1.336)
	Control	6.49±4.59	6.20±4.70	0.491	0.108 (−0.166; 0.382)
Depression	HIIT	3.48±3.35	3.00±3.33	<0.001	0.429 (0.278; 0.687)
	MICT	3.60±3.42	3.16±3.25	<0.001	0.401 (0.205; 0.618)
	Control	3.56±3.61	3.70±3.56	0.827	0.066 (−0.199; 0.270)

Control, control group (n = 23); HIIT, high-interval intensity training (n = 23); MICT, moderate-intensity continuous training (n = 23). Values are reported as mean ± standard deviation; 95% CI, 95% confidence interval. [a]Significant differences between HIIT and control, $p < 0.05$. [b]Significant differences between MICT and control, $p < 0.05$. [c]Significant differences between HIIT and MICT, $p < 0.05$.

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Table 4. Changes in individual blood biomarker levels before and after 6 weeks of community-based exercise programs (HIIT vs. MICT) compared to the control group

Variables		Baseline	Post-intervention	*p* value	Cohen's d (95% CI)
Total cholesterol, mmol/L	HIIT	175±35.2	151±21.8	<0.001[a]	−1.351 (−1.198; −0.714)
	MICT	173±38.5	150±30.4	<0.001	−0.677 (−1.023; −0.331)
	Control	171±32.8	168±38.8	0.835	−0.062 (−0.436; 0.312)
HDL-C, mmol/L	HIIT	43±6.7	54±12.3	<0.001[a]	1.170 (0.640; 1.701)
	MICT	43±9.0	52±9.4	<0.001[b]	1.053 (0.598; 1.508)
	Control	40±9.1	47±12.0	0.002	0.588 (0.234; 0.942)
LDL-C, mmol/L	HIIT	117±38.0	85±32.8	<0.001[a]	−1.330 (−1.857; −0.804)
	MICT	120±45.1	92±39.4	<0.001[b]	−0.659 (−0.950; 0.367)
	Control	117±50.4	119±51.4	0.144	0.039 (−0.227; 0.304)
Triglycerides, mmol/L	HIIT	200±60.6	137±51.2	<0.001[a]	−1.119 (−1.544; −0.693)
	MICT	187±91.7	138±72.1	<0.001[b]	−0.598 (−0.856; -0.341)
	Control	188±78.0	187±62.7	1.00	0.036 (−0.207; 0.135)
HbA1c, %	HIIT	6.1±1.3	5.4±0.8	<0.001[a,c]	−0.645 (−0.992; −0.298)
	MICT	5.8±0.6	5.4±0.4	<0.001	−0.370 (−0.506; −0.233)
	Control	6.2±0.9	6.2±1.0	0.670	0.008 (−0.227; 0.227)
FBG, mg/dL	HIIT	118±28.3	106±22.5	0.002[a]	−0.466 (−0.776; −0.155)
	MICT	114±20.2	109±16.2	0.007[b]	−0.271 (−0.537; −0.004)
	Control	122±25.0	122±29.4	0.532	0.003 (−0.245; 0.251)
hsCRP, mg/L	HIIT	1.5±1.7	0.4±0.7	<0.001[a]	−0.796 (−1.312; −0.280)
	MICT	1.1±1.1	0.4±0.5	<0.001[b]	−0.805 (−1.280; −0.329)
	Control	1.3±0.8	1.1±1.0	0.532	0.004 (−0.604; −0.004)
TSH, mU/L	HIIT	1.6±0.7	1.3±0.9	0.007[a,c]	−0.407 (−0.830; 0.016)
	MICT	1.9±0.8	1.7±0.7	0.201	−0.242 (−0.543; 0.058)
	Control	1.8±1.4	2.4±2.2	0.007	0.089 (−0.109; 0.760)
T4, ng/dL	HIIT	0.9±0.2	1.0±0.1	0.006	0.439 (0.086; 0.793)
	MICT	0.9±0.1	1.0±0.1	0.007	0.089 (0.300; 1.138)
	Control	1.0±0.4	1.1±0.4	0.022	0.188 (0.035; 0.341)
T3, ng/dL	HIIT	3.7±0.7	3.4±0.5	0.002[a]	−0.465 (−0.844; −0.085)
	MICT	3.7±0.5	3.5±0.5	0.002[b]	−0.327 (−0.561; −0.094)
	Control	4.4±2.6	5.3±3.9	0.144	0.260 (−0.156; 0.675)

Control, control group ($n = 23$); FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; HbA1c (%), hemoglobin A1C; HIIT, high-interval intensity training ($n = 23$); hsCRP, high-sensitive C-reactive protein; LDL-C, low-density lipoprotein cholesterol; MICT, moderate-intensity continuous training; SBP, systolic blood pressure; TSH, thyrotropin; T3, tri-iodothyronine; T4, thyroxine. Values are reported as mean ± standard deviation or number and percent population (%). [a]Significant differences between HIIT and control, $p < 0.05$. [b]Significant differences between MICT and control, $p < 0.05$. [c]Significant differences between HIIT and MICT, $p < 0.05$.

Discussion

The positive impact of exercise on post-MI mortality has been recognized since the 1950s [45]. However, its potential to improve QoL and mental health has only been acknowledged more recently [46, 47]. Although CR programs have demonstrated improvements in QoL, anxiety, and depression in post-MI patients, most studies to date are limited by cross-sectional designs and fail to compare the effects of different types of exercise programs before and after participation in a community-based CR program [48]. Notably, only one RCT has compared HIIT and MICT in terms of QoL in post-MI patients, and that was a home-based intervention [49]. As such, new research is needed to better assess the efficacy of HIIT compared to the traditionally recommended, MICT. An in-depth investigation into the impact of exercise intensity in CR programs is necessary, as there is still no ideal intensity dose for this population. To our knowledge, this study is the first RCT in Portugal

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comparing the effects of HIIT and MICT during a 6-week community exercise program on QoL, anxiety, and depression, with a control group that followed only standard medical recommendations, shedding light on the potential benefits of these exercise modalities that used validated questionnaires. Our comparative analysis demonstrated significant improvements in 6 out of 8 domains of QoL, and a reduction in anxiety, and depression symptoms, and clinical values of biochemical analyses in both the HIIT and MICT groups after completing a community-CR programs, compared to the control group. These findings highlight the benefit of exercise training, even when the program duration is relatively short, involving only a few weeks or sessions. This supports the established role of exercise as a well-founded intervention for patients with MI, as it has been shown to improve physical, clinical, and psychological outcomes.

When analyzing QoL separately in physical and psychological domains, we found that both HIIT and MICT led to significantly greater improvements in the physical QoL domain, including "physical functioning," "role-physical," "vitality," and "general health" components, compared to the control group. Interestingly, the type of intensity program had a significant impact on "physical functioning" and "general health," with HIIT showing significantly greater improvements compared to MICT in these components of the SF-36. These findings align with the existing literature [50–54]. A recent systematic review and meta-analysis [52] concluded that the physical component summary was significantly higher in the HIIT group compared to the MICT group (SMD = 0.23, 95% CI 0.05–0.41, Z = 2.45, $p = 0.014$) in patients with CAD. Ulbrich et al. [53] studied 22 chronic heart failure patients (mean age 53.8 ± 8 years) who were randomized to MICT ($n = 10$) and HIIT ($n = 12$) and observed significant improvements in all domains from baseline in both groups ($p < 0.05$), with between-group differences for functional capacity (SF-36). A systematic review with meta-analysis by Griffiths et al. [54] analyzed 21 studies with 24 ESs, 14 of which compared HIIT with physical QoL, and 17 compared HIIT with general QoL. The included studies covered a wide variety of populations, including patients with heart failure with reduced ejection fraction, and individuals after CR, among others. They found a statistically significant improvement in both physical (SMD = 0.405, 95% CI: 0.110–0.700, $p = 0.007$) and general health (SMD = 0.554, 95% CI 0.210–0.898, $p = 0.002$) following an HIIT program. Hence, the authors [54] concluded that practicing HIIT leads to statistically significant improvements in both physical and overall QoL in clinical populations, with a small to moderate ES. In conjunction with the results of the present study, the findings indicate that the magnitude of improvement in QoL is greater with increasing exercise intensity. These QoL improvements may also be explained by a growing body of evidence, suggesting that exercise involving HIIT induces greater benefits and is more effective in improving body composition and cardiorespiratory fitness compared to MICT [18, 23]. This, in turn, leads to improvements in the physical components of QoL, as a result, as we observed.

Regarding psychological QoL dimensions, the exercise groups had statistical significance after the 6-week assessment period in "role-emotional" and "mental health" components compared to the control group. Similar to the current analysis, a recent systematic review and meta-analysis [53] reported an improvement in mental (SMD = 0.473, 95% CI: 0.043–0.902, $p = 0.031$) following a program of HIIT. These results support those from Martland et al. [55], who reported significant improvements in mental well-being with suggestions for improvements in psychological distress with an HIIT intervention. This work concluded that these improvements had a small-to-medium ES. In our study, there were no significant differences between the exercise groups in the dimensions of psychological QoL, meaning that HIIT appears to be an effective strategy for achieving improvements in psychological well-being as does the MICT intervention. Additionally, it has also been observed that group interventions favor the development of bonds among individuals through the exchange of experiences and feelings during these activities, improving the individual's well-being and mental health [55].

Quality of Life

Both HIIT and MICT interventions appear effective in improving physical dimensions of QoL, but HIIT seems to be a particularly efficient strategy for enhancing well-being, especially in physical aspects of QoL, offering a more time-efficient exercise option. On the other hand, these physical and psychological domains of QoL were not improved by patients in the control group. These results coincide with those of previous studies with a significant impact of CVD significantly impacting an individual's QoL by increasing functional dependence [56], reaffirming that exercise-based CR post-MI induces positive effects in QoL [57–59]. Lovlien et al. [60] demonstrate that even low-intensity exercise-based CR can notably enhance health-related QoL in acute MI patients. Most previous systematic reviews have deemed QoL data for exercise-based CR to be insufficient or

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unsuitable for meta-analysis because of the significant heterogeneity [17, 61–63]. In 2015, a systematic review of RCTs revealed QoL improvements in 14 out of 20 studies for MI patients undergoing exercise-based CR compared to usual care [17]. A 2018 meta-analysis (41 RCTs, N = 11,747), spanning studies from 1975 to 2017, indicated a modest positive effect of exercise-based CR on QoL. However, it favored "psychosocial management" as more effective overall [64]. Subsequently, a 2019 systematic review of 14 RCTs, encompassing 1,739 individuals with post-acute coronary syndrome, reported clinically significant positive effects on SF-36 domains at 6 months (role-physical and general health) and one domain at 12 months (physical function) [61]. Comparatively, a study found that the QoL improvement from 11 weeks of low-intensity MICT paralleled that of HIIT during the early stages of acute MI [65]. An RCT involving MI patients concluded that both aerobic interval training and usual care rehabilitation improved QoL and reduced resting HR [64]. Lastly, in a cohort study, 37 MI patients (mean age, 66 years) who underwent a 5-week CR program showed improvements in QoL [66]. However, in our study, no significant differences were observed between the exercise groups in 6 of 8 QoL dimensions. Thus, studies in post-MI patients with gradual but intensive increases in physical fitness during CR have shown that physical, psychological, and social recovery becomes increasingly obvious and statistically significant [67–70].

Mental Health

Regarding mental health, we found high levels of anxiety and depression at the beginning of our study, which is alarming given that anxiety and depressive symptoms have been associated with a higher risk of subsequent cardiac events [71]. Akhtar et al. [72] showed that up to 50% of patients with MI suffer from symptoms of anxiety and/or depression 1 week after MI. Additionally, in a prospective study of 288 MI patients, 37.2% had depressive symptoms, 41.0% had anxious symptoms, and 51% experienced both [73]. Thus, it appears that psychological distress, including anxiety and depression, is common among MI patients, and reducing these symptoms is crucial for improving overall recovery and long-term outcomes.

After 6 weeks, the HIIT and MICT groups demonstrated significant improvements in symptoms of anxiety and depression compared to the control group. It has been established that an exercise-based CR program contributes to decreased levels of anxiety and depression [74]. The control group had worse mental health scores after 6 weeks, emphasizing the potential harm of not following a CR program post-MI. Additionally, Bakker et al. [75] observed that anxiety correlated with greater self-reported sedentary behavior in patients with CVD, suggesting the need for further investigation into the interaction between depression, anxiety, and sedentary behavior in cardiovascular diseases. Also, a 2019 meta-analysis highlighted the effectiveness of exercise in reducing anxiety and depression after MI. [63]. These findings further support the positive impact of exercise on mental well-being post-MI.

In the HIIT group, anxiety and depression on the HADS scale decreased by 1.4 and 0.5 points, respectively ($p < 0.001$), while in the MICT group, anxiety decreased by 1.2 points and depression decreased by 0.4 points ($p < 0.001$). HIIT may be superior to MICT in reducing depression and anxiety levels [76, 77]. However, no significant differences were observed in our study among exercise groups in post-MI patients. The same was verified in the study of Yu et al., [53] where the difference in mental health levels between the HIIT and MICT groups was not statistically significant (SMD = 0.07, 95% CI – 0.05–0.20, Z = 1.13, $p = 0.259$). Notably, Nytrøen et al. [77] observed the effectiveness of HIIT in reducing anxiety and depression following MI [63]. Compared to the control group, the HIIT and MICT groups had a significant difference of 1.04 and 0.48 points in anxiety scores and 0.70 and 0.54 points in depression scores. The ES from baseline to the 6-week mark revealed medium ES for depression scores ($d = 0.4$) and large ES for anxiety scores ($d = 1.0$) in the HIIT group. Similarly, the MICT group exhibited medium ES in depression scores ($d = 0.4$) and large ES for anxiety scores ($d = 0.9$) during this time frame. Consistent with our results, several meta-analyses and systematic reviews have reported that structured exercise-based CR programs are associated with small-to-moderate reductions in depressive symptoms [78–80].

In summary, these findings underscore the significant role of exercise-based programs in enhancing QoL, and anxiety and depression levels among CR patients. Notwithstanding, failing to carry out exercise programs post-MI may exacerbate well-being and mental health, reinforcing the importance of these interventions in the care of post-MI patients.

Study's Strengths

Regarding patient adherence, it is notable that only 1 patient in each group discontinued the intervention, resulting in a remarkable adherence rate of 96% for both the HIIT and MICT protocols. The strengths of our study lie in its randomized design, the use of objective outcome

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measures, and blinded assessors. Furthermore, individualized training intervention that maintains consistent relative intensity following the HIIT principle adds value. Importantly, our study's positive efficacy findings are encouraging, particularly given the significant improvements achieved within a relatively short 6-week duration, involving 3 sessions per week, totaling 18 sessions per patient. We believe that this type of intervention could be included in routine CR to significantly improve psychological outcomes in patients with MI and offer added value over standard CR.

Study Limitations

This study has several limitations. First, only 13–17% of the patients in this study were women. The lower proportion of women referred to and attending CR is a problem, which is not specific to this setting. Second, there was no psychotherapy, psychological counseling, stress management, or consultation with a psychiatrist. We aimed to understand the role that exercise programs could play in these variables, as these patients would not have had access to any CR programs without this study. We believe that, with the addition of clear, patient-oriented psychological recommendations, there could have been a more significant improvement in more dimensions of QoL and mental health. Additionally, when considering the results of this study, the possible confounding effects of concomitant medications must be considered, although no changes were observed during the study period. Furthermore, the control group did not provide activity diaries, making it impossible to assess physical activity levels during the 6-week intervention period, which could have influenced the observed effects. Exercise interventions, particularly those that include group activities and social engagement, have been shown to help alleviate mental health issues and foster a sense of community and support among the participants.

Conclusions

Our RCT revealed substantial improvements across multiple dimensions of QoL, highlighting notable gains in physical functioning, role-physical, role-emotional, mental health, vitality, and general health within both the HIIT and MICT groups. The HIIT group had a more effective impact on physical functioning and general health across all QoL dimensions than the MICT group. Furthermore, both exercise groups showed significant reductions in anxiety and depression levels, underscoring the beneficial impact of structured exercise-based CR on psychosocial well-being, and reinforcing the importance of these interventions in the care of post-MI patients. In contrast, individuals who did not participate in the CR program post-MI did not show similar improvements in these variables. Thus, our study emphasizes the crucial role of CR exercise programs in promoting QoL and mental health during recovery from MI.

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Statement of Ethics

This study protocol was reviewed and approved by the University of Evora's research ethics system (Ethical Approval No. 17039). All work was conducted following the Declaration of Helsinki and registered at (NCT03538119). The informed consent was obtained from all individual participants included in the study and was approved by the University of Evora's research ethics system (Ethical Approval No. 17039).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conceptualization, resources, and supervision: C.G., J.B., J.P., and A.R.; methodology and validation: C.G. and J.P.; formal analysis, data curation, writing – review and editing, project administration, and funding acquisition: C.G., J.B., and A.R.; investigation and writing – original draft preparation: C.G.; and visualization: C.G., J.B., A.A., and A.R. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author C.G. upon reasonable request.

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