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ORIGINAL ARTICLE

HRV-guided training vs traditional HIIT training in cardiac rehabilitation: a randomized controlled trial

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Abstract High-intensity interval training is the gold standard for cardiac rehabilitation although current revascularization therapy focuses on the recovery of autonomic nervous system balance through heart rate variability (HRV). The main objective was to analyze the effect of HRV-guided training versus high-intensity interval training on cardiorespiratory fitness, heart rate variability, quality of life, and training volume at high intensity, as well as exercise adherence, safety, and feasibility in ischemic patients. This is an 8-week cluster randomized controlled trial with an HRV-based training group (HRV-G) and a traditional HIIT group (HIIT-G). Maximal oxygen consumption, heart rate, and blood pressure were measured during the Bruce protocol treadmill test. HRV was measured with the HRV4Training application, and quality of life with the MacNew QLMI. The repeated measures ANCOVA was used with the age and the baseline scores as covariables. Forty-six patients (mean age 55 ± 11.03 years) were randomized and assigned either to HRV-G (n = 23) or HIIT-G (n = 23). Both groups improved maximal oxygen consumption and METS ($P > .05$). However, the resting systolic blood pressure was lower in HRV-G (4.3 ± 1.2 mmHg, $P = .05$). In HRV-G, the resting diastolic, maximal diastolic, and systolic blood pressure decreased (5.4 ± 5.96 mmHg, $P = .007$; 11.4 ± 12.46 mmHg, $P = .005$; and

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Key points
What is known about the topic?
- HIIT-guided training is safe and feasible in cardiac rehabilitation but standardized training programs provoke varying physiological responses among patients.
- HRV is a powerful health and mortality predictor post myocardial infarction as it is an indicator of the interaction between the autonomous nervous system and the cardiovascular system. It could be used as a tool for training individualization.
What does the study add?
- Both HRV-guided training and HIIT traditional training improved cardiorespiratory fitness (VO_2max and METS) in cardiomyopathy patients, although HRV-guided training showed a more beneficial effect on blood pressure and heart rate parameters.
- The age was an interfering factor for HRV domains.
- Both training programs are safe and feasible for cardiac rehabilitation.
- Lower volumes of high-intensity training present a better cardioprotective effect than a standardized HIIT training program.

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5 ± 5.98 mmHg, $P = .013$, respectively) whereas the recovery heart rate increased significantly (−21.5 ± 23.16 beats/min, $P = .003$). The LnrMSSDcv ([$LnrMSSD_{SD}/LnrMSSD_{MEAN}$] × 100) was lower in HRV-G (1.23 ± 0.91 mmHg, $P = .03$) while the training volume at high intensity was higher in HIIT-G (31.4 ± 29.2 min, $P = .024$). HRV-guided training presents a better cardioprotective effect than HIIT-G at a lower high-intensity training volume.

Keywords Heart rate variability · High-intensity interval training · Cardiac rehabilitation · Autonomous nervous system · VO_2max · LnrMSSD

Introduction

Ischemic heart disease (IHD) is the leading cause of death and one of the main causes of disability [1], resulting in increased health system costs. Ischemic cardiopathology has been associated either with atherosclerosis and the factors involved in the atherosclerotic process or with the left ventricular dysfunction [2]. According to Shaffer, McCraty, and Zerr [3], this left ventricular failure depends on the integration between efferent heart regulation by the cardiovascular center and afferent signals sent to the brain from the heart's intrinsic nervous system, which contribute to beat-to-beat changes. Consequently, heart function depends on the balance between sympathetic and parasympathetic outflow. This highlights the relevance of autonomic nervous system (ANS) function in regulating the heart as an additional factor that increases the risk of relapse or death in IHD.

In this regard, heart rate variability (HRV) is being used as a measure of neurocardiac function that reflects the heart-brain interactions and the ANS dynamics [3]. HRV is defined as the fluctuation in the interval between consecutive heartbeats and the fluctuation between consecutive instantaneous heart rates [4]. According to Rodas, Pedret-Carballido, Ramos, and Capdevila [4], HRV is inversely correlated with the heart rate and therefore, with the sympathetic branch of the ANS, in such a way that the higher the heart rate and the sympathetic nervous activation, the lower the HRV. This is a key aspect in cardiac rehabilitation since cardiovascular diseases increase sympathetic system predominance, which is reflected in a high resting heart rate and low HRV [5], thus manifesting worse cardiovascular system adaptation and a negative state of health. For all these factors, HRV should be considered as an essential outcome to control in cardiac rehabilitation programs together with the heart rate, maximal oxygen consumption (VO_2max), and blood pressure.

National and international heart societies have developed general cardiac rehabilitation guidelines [6] for the treatment of IHD based on a multidisciplinary program including physical exercise, psychological and nutritional control, risk factors revision, and educational trends implemented together with pharmacological treatment. However, the response to certain pharmacological therapies do not give the expected results [7], and the cardiac rehabilitation programs are not followed as they should be [8] owing to limited political or economic support, and a lack of knowledge or interest by healthcare professionals or patients. Nevertheless, exercise programs have developed over recent years that show the greater effectiveness of high-intensity interval training (HIIT) over moderate-intensity continuous training in improving the maximal oxygen consumption (VO_2max), left ventricular ejection fraction, end-diastolic volume, quality of life, blood parameters, and functionality in patients with IHD [9, 10]. HIIT-based training is thus the recommended exercise program nowadays for cardiac rehabilitation. Regardless of this, there is still insufficient evidence from high-quality, large-sample, multicenter RCTs to reach any consistent conclusion [10–12] because of the wide range of HIIT-training methodologies used. Moreover, although HIIT is a promising tool for improving the HRV in healthy individuals and patients with metabolic syndrome [13], there is still little evidence with regard to cardiomyopathy [14, 15], due to it has been included in the research for a few years now.

HRV analysis has also been established as a useful method for assessing the heart's ability to adapt to both endogenous and exogenous loads [16], hence it can be used for assessment of individual responses to training loads. This is particularly useful when considering that an individual's cardiovascular system can be affected by IHD to varying degrees [2]. Therefore, the exercise dose given to each patient should be closely controlled and individualized, avoiding overstimulation of the cardiovascular system during training while increasing safety and efficiency. Nonetheless, serious adverse events still occur in cardiac rehabilitation [17] perhaps because such training is often carried out in groups, and it is recognized that group training using the same standardized training program can result in a wide range of reactions in terms of performance and physiological adaptations [18]. Consequently, HRV has recently been used as a biomarker of the autonomic nervous system to help design an individualized day-to-day training session that optimizes the physiological response to workloads. This has been the case in several studies carried out with elite or amateur athletes [19] and with cancer survivors [20]. However, there is scant evidence that HRV-guided training results in better cardiac rehabilitation outcomes than other pre-determined exercise [21, 22].

HRV can be influenced by several factors such as circadian rhythms, core body temperature, metabolism, hormones, intrinsic rhythms generated by the heart, the body position, or mental and physical stress [3, 23] which create a dynamic physiological control system that is never static. Therefore, researchers should be aware of methodological issues related to HRV measurements so that the studies could be compared around the world. Even so, HRV measurements have become more accessible nowadays owing to the progress in technology and computer science. Electrocardiography and photoplethysmography can be used to detect the interbeat interval, and short recording periods (e.g., 60 s) can be employed with the same reliability as longer ones. This is the case with validated heart rate monitors, such as Polar i10, or low-cost smartphone applications, such as HRV4Training. Considering all the above, the main objective of this study was to analyze changes in VO_2max in cardiac rehabilitation patients following an HRV-guided training program versus a HIIT training program. The secondary objectives were (i) to assess changes in other cardiovascular parameters, heart rate variability, quality of life, the training volume at high intensity, exercise adherence, safety, and feasibility after each exercise program, and (ii) to determine the relationship between the variables measured. The hypotheses were that both groups would have improved VO_2max, blood pressure, heart rate parameters, HRV, and quality of life, but that the HRV-guided training would be safer and more feasible because program individualization would result in less high-intensity training volume.

Materials and methods

Trial design

This study consisted of an 8-week cluster-randomized controlled trial in which the patients who enrolled in a cardiac rehabilitation program were assigned to an HRV-based training group (HRV-G) or a traditional high-intensity training group (HIIT-G). The trial protocol was approved by the University of Almería's Bioethics Committee (UALBIO2019/026) and was prospectively registered with ClinicalTrials.gov: NCT04150952. The protocol was also published prior to the study [19]. The study was conducted according to the World Medical Association Declaration of Helsinki and reported following the Consolidated Standards of Reporting Trials (CONSORT) guidelines [24].

Participants

The sample comprised patients affected by ischemic cardiopathology and treated at University Hospital Torrecárdenas in Almería, Spain. Details relating to the eligibility criteria, recorded patient information, and the consent form are available elsewhere [19].

Interventions

The 8-week interventions were divided into two phases: the familiarization period (the first 2 weeks) and the training period (the subsequent 6 weeks), in which the HIIT-G followed a predefined, high-intensity short training program, while the HRV-G trained according to their individual and daily HRV scores. The schema suggested by Kiviniemi et al. [25] was followed and Fig. 1 shows the HRV fluctuations during the training period in the HRV-G. For both training groups, high intensity was considered >85% of the peak heart rate. The groups trained 3 days/week for 1 h/day (24 training sessions). The total training period went from October 2021 to July 2022. All the intervention details can be found in the Carrasco-Poyatos et al. [19] trial protocol.

Outcomes

The study's primary outcome was the VO_2max. The secondary outcomes were: (i) the resting, maximal

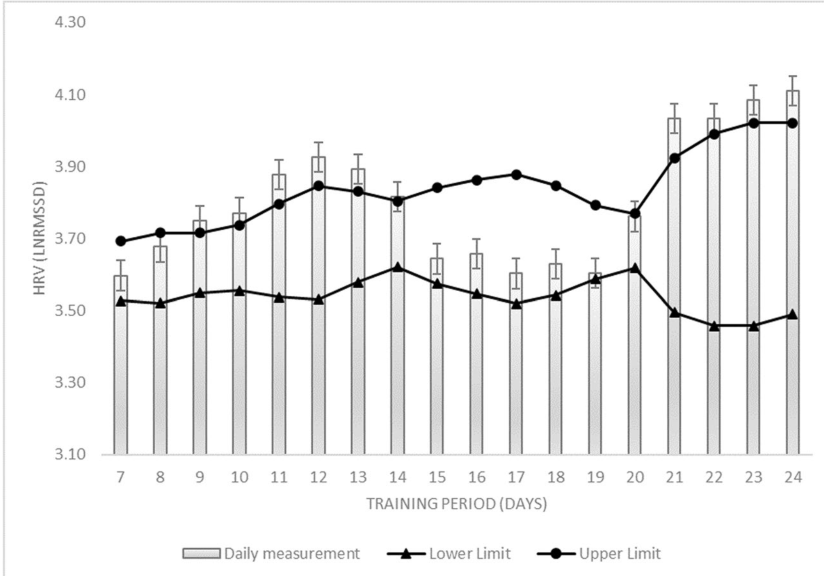

Fig. 1 HRV fluctuations during TR period in HRV-G

and recovery blood pressure and heart rate, and metabolic equivalents (METS); (ii) heart rate variability; (iii) quality of life; (iv) training volume at high intensity; and (v) exercise adherence, safety, and feasibility. The outcomes were recorded during the first and the last intervention weeks of the program, except for exercise adherence, feasibility, and safety, which were recorded daily.

As recommended for heart disease patients [21, 26], the Bruce protocol treadmill test was used to assess the VO_2max, heart rate, and blood pressure. The VO_2max was calculated using the formula described by McConnell and Clark [$VO_2max = 2.282(time) + 8.545$] [27]. In this way, METS were calculated using the equivalence of 1 MET = 3.5 ml/kg/min. Electrocardiograms were taken at rest, during the test, and 2 min after the test to record the resting, maximal, and recovery heart rate. Systolic and diastolic blood pressure was also measured at the same time. It was considered a good test if the peak heart rate was ≥85% of that predicted and the rate of perceived exertion (RPE) ≥ 18 [28].

Heart rate variability was recorded prior and after the training program following the procedure used in other sport contexts [29]. The HRV4Training smartphone application, validated by Plews et al. [30], was used for the purpose. The measure was 60 s long and was taken in a seated position just before starting the first and the last training session of the program. The temporal-domain variables recorded were the standard deviation of al R-R intervals (SDNN), the root mean square of successive differences (rMSSD), and the percentage of successive normal sinus RR intervals >50 ms (pNN50), while the frequency-domain ones were low frequencies (LF) and high frequencies (HF) because of their relationship to parasympathetic activation [31]. To assume a normal distribution, the Napierian logarithm of the variable rMSSD (LnrMSSD) was calculated together with its coefficient of variation ($LnrMSSD_{CV} = [LnrMSSD_{SD} / LnrMSSD_{MEAN}] \times 100$), as this appears to be more sensitive to training changes [32]. For the frequency-domain variables, the LF/HF quotient was also calculated to determine the sympathetic-parasympathetic balance [33]. A pre-session LnrMSSD of the familiarization period was used to obtain the individual normality range for the exercise prescribed in the HRV-G, following the Plews, Laursen, Kilding, and Buchheit procedure [34].

Quality of life was measured with the validated Spanish version of the MacNew QLMI [35] which comprises the physical, emotional, and social dimensions. The high-intensity training volume was determined by the minutes that the training heart rate was 85–100% of the peak heart rate. Adherence was determined by the number of sessions attended. Safety was measured as the number of adverse events, recorded as low, moderate, or severe [36], together with their relationship to the exercise program. Feasibility was recorded as the attendance to the session periodization according to the heart rate reached and the RPE score. These variables were recorded by the multidisciplinary group (a physician, a physiotherapist, a nurse, and a physical-exercise graduate) during each exercise session.

Sample size and power

Assuming a standard deviation of 6.6 ml/kg/min for the VO_2max [37] and an estimated error (d) of 2.7, a total of twenty-three subjects would be a valid sample size for each arm, providing a 95% confidence interval (CI) ($n = CI^2 \times d^2/SD^2$). Thus, the final sample sizes for the HRV-G (n = 22) and HIIT-G (n = 19) provide a power of 90% and 85%, respectively, if between and within a variance of 1. The calculations to establish the sample size were performed using RStudio 3.15.0 software. The significance level was set at $P \leq 0.05$.

Randomization and blinding

Participants were randomly allocated to each group using a block randomization method, which was implemented through a central telephone registration system. The treatment was randomly assigned to the groups via a coin toss. The block size was determined according to the statistical power provided. Both the participants and the research staff were blinded. Only the multidisciplinary group knew about the interventions so that they could adapt, where appropriate, the training sessions or respond to an adverse event. An excel sheet was used to implement the patients' randomization process as well as to record the data. This process was carried out by the principal researcher.

Statistical methods

Prior to data analysis, the Kolmogorov-Smirnov test was used to determine the normal distribution of the variables. Levene's test was also performed to determine the homogeneity of variance. An unpaired two-tailed t-test was employed to compare groups at baseline for the continuous variables, while the Fisher exact test was utilized for categorical data. Differences between groups were found in age, so the repeated measures ANCOVA was used with the age and the baseline scores as covariables. Treatment effects are presented as adjusted and unadjusted between group differences. The standardized mean differences (Cohen's effect size) were calculated together with the 95% confidence intervals to determine the treatment magnitude. An effect size value of 0.20 indicates a small effect, 0.50 a moderate effect, and 0.8 a large effect [38]. A bivariate Pearson and Spearman correlation was utilized to assess the relationships between the variables. The correlation thresholds were 0.1, small; 0.3, moderate; 0.5, large; 0.7, very large; and 0.9, nearly perfect [38]. Statistical analyses were performed using SPSS Statistics version 25 (IBM). The level of significance was set at $P \leq 0.05$ and all P values were 2-tailed.

Results

Eighty-five patients were screened from April to September 2021, of which 46 were randomized and allocated to HRV-G (n = 23) or HIIT-G (n = 23). The total training period was from October 2021 to July 2022, which was undertaken in a phased manner every 8 weeks. At the end of the intervention, 22 and 19 cases, respectively, were included in the statistical analysis. The participant flow is detailed in Fig. 2. The baseline demographic and clinical characteristics of each group are shown in Table 1. Both groups were similar in all aspects measured except for the age, with HRV-G being statistically older than HIIT-G ($X \pm SD_{Dif} = \pm 7.4$ years, $t = 2.25$ [.75, 14.1], $P = .03$). Therefore, age was used as a covariable.

The results for the main objective indicate a large effect in the VO_2max and METS increment after both training interventions (HRV-G = −6.96 ± 8.35 ml/kg/min; HIIT-G = −4.57 ± 6.53 ml/kg/min) although there were no intra- or inter-group differences when adjusting for age.

With respect to the secondary objectives, in the inter-group analysis, HRV-G presented lower resting systolic blood pressure than HIIT-G ($X \pm SD_{HRV\text{-}G} = 115.4 \pm 5.96$ mmHg, $X \pm SD_{HIIT\text{-}G} = 119.7 \pm 7.16$ mmHg, $F = 4.024$, $P = .05$, $d = .096$). Moreover, the resting diastolic blood pressure and the maximal

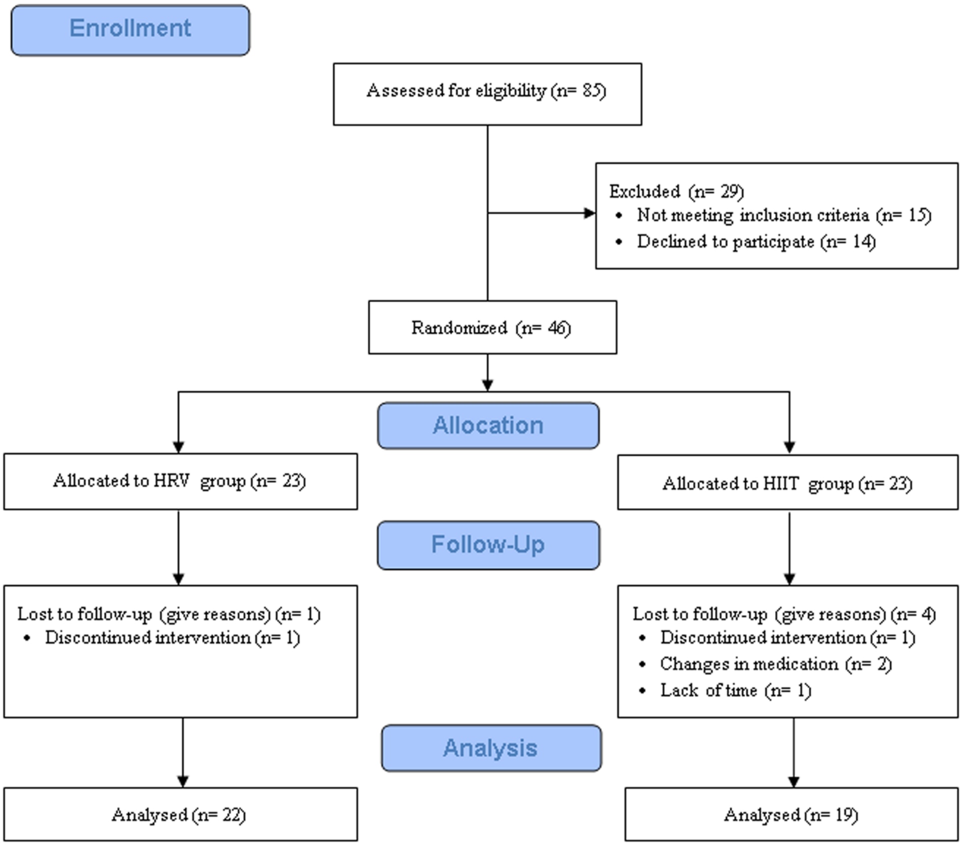

Fig. 2 Participant flow diagram

diastolic and systolic blood pressure decreased by 5.4 ± 5.96 mmHg, 11.4 ± 12.46 mmHg, and 5 ± 5–98 mmHg, respectively, in the HRV group. The recovery heart rate was higher in both exercise groups, but was only statistically significant in HRV-G (−21.5 ± 23.16 beats/min) (Table 2).

There were also statistical differences in the LnrMSSDcv between groups, which was lower in the HRV-G than in the HIIT-G ($X \pm SD_{\text{HRV-G}} = 13.17 \pm 5.35$ mmHg, $X \pm SD_{\text{HIIT-G}} = 14.4 \pm 4.44$ mmHg, $F = 5.075$, $P = .03$, $d = .118$) but the baseline scores and the age were conditioning this result statistically ($F = 7.12$, $P = .011$, $d = .283$). However, the LnrMSSDcv increased in both groups in the intra-group analysis (Table 2), and this change was also significantly affected by the covariates ($F = 6.357$, $P = .016$, $d = .143$). There were no significant inter-group differences in the quality of life.

Furthermore, the HRV-G group accomplished 159.3 ± 53.82 out of 432.7 ± 156.18 min at an intensity >85% heart rate peak (HRPeak), meaning 36.81% of the total training time. In contrast, the HIIT-G group trained at high intensity for 190.7 ± 24.64 out of 417 ± 69.76 min, meaning 45.73% of the total training time. These results were statistically different, favoring HIIT-G ($X \pm SD_{\text{Dif}} = 31.4 \pm 29.2$ min; $P = .024$; $d = 42.89$ [−58.63, −4.29]) (Fig. 3).

Regarding adherence and feasibility, 69.1% ($n = 15$) of the HRV-G and 68.3% ($n = 13$) of the HIITG attended > 80% of the sessions. The remaining percentage attended > 70% of the sessions. Only one participant in HRV-G withdrew from the training session. During the intervention, there were 12 adverse events (Table 3) — ten of these occurred in the HRV-G (7 of low level and 3 of moderate level) and two in the HIIT-G (1 of low level and 1 of moderate level). None of them required hospitalization. Taking into account the age, there were no significant differences between

Table 1 Baseline demographic and clinical characteristics for each group

Variables	HRV-G (*n* = 22)	HIIT-G (*n* = 19)	*P* value
Age (years)	58.4 ± 9.95	51 ± 11.13	**.03**
Sex			
Male	22 (100)	16 (84.2)	.053
Female	0 (0)	3 (15.8)	.053
Height (m)	1.7 ± .06	1.7 ± .06	.723
Weight (kg)	81.2 ± 10.6	86.4 ± 14.8	.198
BMI (kg/m^2)	27.3 ± 3.32	28.6 ± 3.9	.234
Resting blood pressure			
Systolic (mmHg)	120.9 ± 9.59	122.1 ± 7.69	.665
Diastolic (mmHg)	66.8 ± 5.68	63.7 ± 7.69	.069
Resting heart rate (beats/min)	72.7 ± 14.32	71.8 ± 14.51	.813
Resting heart rate variability			
SDNN (ms)	84.2 ± 61.01	68.8 ± 61.61	.428
LnrMSSD (ms)	1.9 ± .29	1.8 ± .28	.443
LnrMSSDcv (ms)	11.74 ± 3.1	13.31 ± 5.35	.248
pNN50 (ms)	49.4 ± 23.41	44.4 ± 19.52	.463
LF (Hz)	.09 ± .07	.06 ± .07	.27
HF (Hz)	.15 ± .17	.07 ± .04	.062
LF/HF (Hz)	.79 ± .51	.78 ± .45	.925
Diagnosis			
ST-EMI	6 (27.3)	6 (31.6)	.197
NST-EMI	4 (18.2)	3 (15.8)	.248
Angina	12 (54.5)	10 (52.6)	.099
Time since event	33.3 ± 5.2	34.2 ± 4.9	.824
Comorbidities			
Hypertension	9 (40.9)	10 (52.6)	.689
Family history	10 (45.4)	9 (47.4)	.721
Diabetes	2 (9.1)	1 (5.3)	.18
Current smoking	1 (4.5)	0 (0)	.987
Mental health	1 (4.5)	0 (0)	.785
Fibromyalgia	0 (0)	1 (5.2)	.856
Lupus	0 (0)	1 (5.2)	.963
Medications			
Beta-blocker	12 (54.5)	10 (52.6)	.112
Anti-hypertensive	10 (45.4)	9 (47.4)	.258
Antiplatelet	18 (81.2)	18 (94.7)	.812
Statin	19 (86.4)	18 (94.7)	.698
Anti-anginal	7 (31.8)	7 (36.8)	.897
Diuretic	5 (22.7)	6 (31.6)	.657

Data for continuous variables is presented as mean ± SD, and for categorical variables as mean (%). SDNN (ms), LnrMSSD (ms), and pNN(50) are the temporal parameters used for HRV measurement. LF (Hz), HF (Hz), and LF/HF(Hz) are the frequency parameters used for HRV measurement. *ST-EMI*, ST elevation myocardial infarction; *NST-EMI*, non-ST elevation myocardial infraction

groups ($X \pm SD$ = .34 ± .46 numbers, F = 2.257, P = .141, d = .056).

With respect to the relationship between variables, the maximal oxygen uptake and the METS were statistically correlated with the McNew Physical Score (r = .329, r^2 = .068, P = 0.036). Conversely, the LnrMSSD_{CV} was inversely correlated with the McNew total score (r = −.328, r^2 = .018, P = 0.036).

Table 2 Intra-group changes after the interventions

Variables	*n*	Pre-training		Post-training		Unadjusted intra-group effects				Adjusted intra-group effects		
						P	95% CI for mean difference		Cohen's *d*	Time*Group		
		Mean	SD	Mean	SD		Lower	Upper		*F*	*P*	ES η^2
Cardiopulmonary												
Resting systolic blood pressure (mmHg)												
HRV-G	22	120.9	9.59	115.4	5.96	**.038**	.34	10.57	11.54	.449	.507	.012
HIIT-G	19	122.1	7.69	119.7	7.16	.12	−.67	5.41	6.32			
Resting diastolic blood pressure (mmHg)												
HRV-G	22	66.8	5.68	61.3	3.51	**.0003**	2.81	8.1	5.96	8.185	**.007**	.177
HIIT-G	19	63.7	7.69	64.2	5.07	.667	−3.05	2	5.24			
Resting heart rate (beats/min)												
HRV-G	22	72.7	14.32	67.4	11.03	.089	−.9	11.81	14.33	1.655	.206	.042
HIIT-G	19	71.8	14.51	71.9	14.39	.951	−3.63	3.42	7.32			
Maximal systolic blood pressure (mmHg)												
HRV-G	22	154.1	13.3	142.7	10.77	**.0003**	5.84	16.89	12.45	9.025	**.005**	.192
HIIT-G	19	141.3	12.45	144.7	13.48	.325	−10.52	3.67	14.72			
Maximal diastolic blood pressure (mmHg)												
HRV-G	22	75.9	5.1	70.9	2.94	**.001**	2.35	7.65	5.98	6.767	**.013**	.151
HIIT-G	19	73.9	7.92	74.7	6.97	.563	−3.6	2.02	5.84			
Maximal heart rate (beats/min)												
HRV-G	22	133.2	14.22	130.9	8.8	.412	−.344	8.01	13	.609	.44	.016
HIIT-G	19	138	12.37	140.8	13.71	.232	−7.38	1.91	9.64			
Maximal oxygen uptake (ml/kg/min)												
HRV-G	22	29.7	6.6	36.6	8.76	**.001**	−10.66	−3.25	8.35	.782	.382	.02
HIIT-G	19	33.6	9.01	38.2	7.47	**.007**	−7.71	−1.42	6.53			
METS												
HRV-G	22	8.5	1.89	10.5	2.5	**.001**	−3.05	−.93	2.39	.784	.382	.02
HIIT-G	19	9.59	2.58	10.9	2.14	**.007**	−2.21	−.41	1.87			
Recovery systolic blood pressure (mmHg)												
HRV-G	22	147.3	18.1	142.3	12.32	.178	−2.46	12.46	16.83	.282	.598	.007
HIIT-G	19	146.8	14.93	144.2	13.46	.399	−3.76	9.03	13.27			
Recovery diastolic blood pressure (mmHg)												
HRV-G	22	73.2	6.46	70.4	3.75	.083	−.39	5.84	7.02	.004	.948	.000
HIIT-G	19	74.5	7.97	73.2	7.49	.399	−1.88	4.51	6.63			
Recovery heart rate (beats/min)												
HRV-G	22	100.3	19.45	121.8	13.18	**.0003**	−31.82	−11.27	23.16	9.822	**.003**	.205
HIIT-G	19	111.5	22.1	119.2	21.35	.068	−15.98	.62	17.22			
Heart rate variability												
SDNN (ms)												
HRV-G	22	84.17	61.01	81.85	78.58	.873	−27.63	32.27	67.55	.155	.696	.001
HIIT-G	19	68.8	61.61	76.63	62.76	.726	−54.04	38.38	95.87			
LnrMSSD (ms)												
HRV-G	22	1.91	.3	1.86	.32	.443	−.08	.19	.31	.035	.873	.005
HIIT-G	19	1.84	.3	1.86	.31	.893	−0.25	.22	.48			

Table 2 (continued)

Variables	n	Pre-training		Post-training		Unadjusted intra-group effects				Adjusted intra-group effects		
						P	95% CI for mean difference		Cohen's d	Time*Group		
		Mean	SD	Mean	SD		Lower	Upper		F	P	ES η^2
$LnrMSSD_{CV}$ (ms)												
HRV-G	22	11.74	3.1	13.17	2.71	.09	−3.1	.24	3.78	6.36	**.016**	.032
HIIT-G	19	13.31	5.3	14.4	4.44	.329	−3.35	1.18	4.7			
pNN50 (ms)												
HRV-G	22	49.42	23.41	43.95	24.95	.363	−6.77	17.72	27.61	.226	.337	.006
HIIT-G	19	44.39	19.52	44.78	24.13	.948	−12.87	12.08	25.89			
LF (Hz)												
HRV-G	22	.09	.07	.06	.05	.091	−0.005	.065	.08	1.393	.245	.094
HIIT-G	19	.06	.07	.09	.09	.412	−0.08	.04	.12			
HF (Hz)												
HRV-G	22	.15	.17	.08	.53	.075	−0.008	.15	.18	.0002	.989	.107
HIIT-G	19	.07	.04	.12	.11	.17	−0.11	.02	.13			
LF/HF (Hz)												
HRV-G	22	.79	.51	.78	.5	.935	−0.32	.34	.74	.248	.123	.009
HIIT-G	19	.78	.45	.84	.5	.71	−0.39	.27	.68			
Quality of life												
McNew global score												
HRV-G	22	4.8	1.34	5.3	1.18	.067	−1.13	.13	1.43	1.883	.178	.047
HIIT-G	19	5.7	.75	5.8	.8	.446	−0.49	.36	.88			
McNew emotional score												
HRV-G	22	4.5	1.08	5	1.07	.082	−1.06	.07	1.27	.177	.677	.005
HIIT-G	19	5.3	.83	5.5	.74	.103	−0.64	.06	.73			
McNew physical score												
HRV-G	22	4.8	1.46	5.3	1.27	.191	−1.15	.23	1.56	2.85	.1	.07
HIIT-G	19	5.9	.84	5.77	1.2	.636	−0.48	.66	1.18			
McNew social score												
HRV-G	22	5.1	1.61	5.7	1.3	.14	−1.23	.16	1.56	4.456	.125	.061
HIIT-G	19	6	.76	6	1.06	.453	−0.58	.59	1.22			

HRV-G, HRV-guided training group; *HIIT-G*, HIIT-based training group; *SDNN*, the standard deviation of al R-R intervals; *LnrMSSD*, the logarithm in a base 10 of the root mean square of successive differences; $LnrMSSD_{cv}$ = ([$LnrMSSD_{SD}$ / $LnrMSSD_{MEAN}$] × 100; *pNN50*, the percentage of successive normal sinus RR intervals > 50 ms; *LF*, low frequencies; *HF*, high frequencies; *LF/HF*, low frequencies/high frequencies. ANCOVA for repeated measures with covariates in the adjusted model: age and baseline scores

Discussion

The study results show that both the HRV and HIIT interventions generated a non-significant tendency to improve the cardiorespiratory fitness (VO_2max and METS) of the cardiac rehabilitation patients, conditioned by age. However, the resting diastolic blood pressure and the maximal diastolic and systolic blood pressure were only reduced in the HRV-G, while the heart rate recovery statistically increased. In this regard, the $LnrMSSD_{CV}$ was lower in the HRV-G than in the HIIT-G, but age had a statistical influence on this inter-group difference. On the other hand, the interventions were not statistically different regarding quality of life, adherence, safety, and feasibility, but there were statistical correlations between the

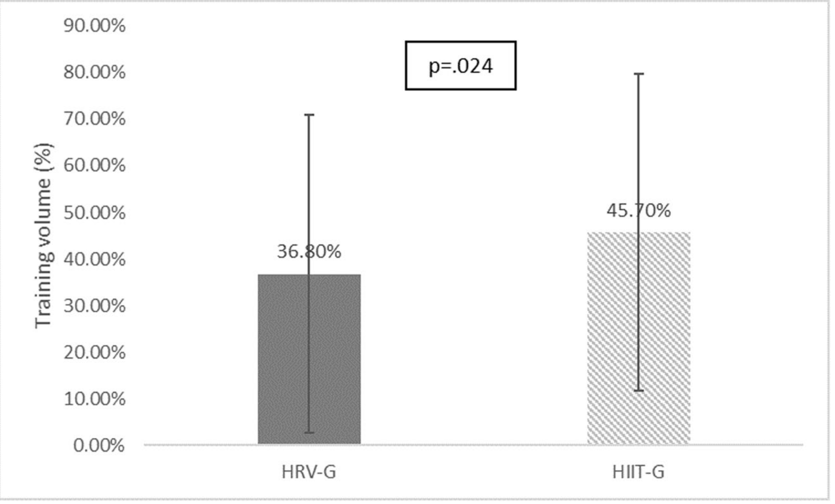

Fig. 3 Training volume at high intensity

Table 3 Adverse events

Event	Group	Type	Severity	Related to exercise	Remained in the study	Reason for the event
Familiarization period (weeks 1 and 2)						
#1	HRV-G	Dizziness	Moderate	No	Yes	Cardiovascular disease
#2	HIIT-G	Dizziness	Moderate	No	No	Cardiovascular disease
Training period (weeks 3–8)						
#3	HRV-G	Dizziness and fatigue	Low	Yes	Yes	Cardiovascular disease
#4	HRV-G	Dizziness	Low	Yes	Yes	Cardiovascular disease
#5	HRV-G	Fatigue and high heart rate	Low	No	Yes	Cardiovascular disease
#6	HRV-G	Fatigue	Low	No	Yes	Low physical condition
#6	HRV-G	Muscle overload	Low	No	Yes	Low physical condition
#7	HRV-G	Chest pain	Moderate	No	Yes	Cardiovascular disease
#8	HRV-G	Psychological	Moderate	No	Yes	Fear
#9	HRV-G	Muscle overload	Low	No	Yes	Low physical condition
#10	HRV-G	Dizziness	Low	No	Yes	Fatigue
#11	HIIT-G	Dizziness	Moderate	Yes	Yes	Cardiovascular disease
#12	HIIT-G	Chest pain	Low	No	Yes	Anxiety

McNew QLMI, the VO_2max, the METS, and the $LnrMSSD_{CV}$.

The VO_2max and METs increased significantly with large effect sizes in both exercise groups; however, these increases were not significant when age was used as a covariable. Moreover, the exercise groups were not statistically different regarding these cardiorespiratory variables. Our results are in line with those obtained by Manresa-Rocamora et al. [22] after implementing a similar 6-week training protocol (HRV-guided vs predefined HIIT training), or Beherens et al. [21] in terms of improved VO_2max resulting from 4 weeks of HRV-guided training. It appears that the duration of the interventions (4, 6, or 8 weeks) is not such a determinant when HRV-guided training is employed, since in both the short-term intervention and in the longer ones, the VO_2max can be significantly improved in ischemic patients. Nevertheless, the training intensity does appear to be a differentiating factor.

Our results agree with the meta-analysis of Ballesta-García et al. [9] and Li et al. [10] that it is the intensity of the parameter that produces greater cardiovascular system adaptations, such as the increase in the cross-sectional area of the muscle, adaptations in the energy reserves, or the increased synchronization of the motor units. Moreover, an increment in the 2 METS following cardiac rehabilitation is associated with lower rates of cardiovascular events, cardiovascular hospitalizations, and unplanned coronary angiographies [39]. However, considering the age of the participants, the results are weak. Aging is associated with a progressive impairment of cardiovascular functioning [40], which pre-determine the type, intensity, and duration of the interventions.

In this regard, and in accordance with Manresa-Rocamora et al. [22], our HRV-guided training group spent significantly less time training at high intensity (−31.4 ± 29.2 min) while obtaining the same results as the HIIT predefined training group. Therefore, confirming that suggested by McGregor et al. [11], high-intensity training is recommended to improve VO_2max and METS in cardiac rehabilitation although, if the HIIT-training dose is given when the patient is ready (ascertained by the basal HRV scores), the same results are obtained with lower HIIT training volumes, making HRV-guided training the optimal option for this purpose. Nonetheless, in future studies, the effect of age should be taken into account among this population.

Regarding the other cardiovascular variables, following the interventions, a positive effect of the HRV-guided training was observed in the resting and maximal blood pressure, while the heart rate recovery increased statistically. Even so, no significant changes in these variables were obtained in HIIT-G. Focusing on blood pressure, similar results were reported by Taylor et al. [41] after a moderate-intensity predefined cardiac rehabilitation program, while no significant changes were shown in other studies [12, 15]; indeed, it is a missing parameter in other trials on this population [24, 42]. A reduced resting heart rate and blood pressure is linked to increased vagal activity [4] and an improved chronotropic response to an exercise stimulus, which in turn is associated with a decreased risk for cardiovascular disease and mortality [4]. Consequently, we recommend the HRV-guided intervention for cardiac rehabilitation.

These results appear to be controversial when we allude to the increased heart rate at recovery found in both exercise groups. Nevertheless, our results are in line with those obtained in the above-mentioned study [24], and with Villalebeitia-Jaureguizar et al. [36] after an 8-week HIIT vs moderate predefined training, both of which were with coronary artery disease patients. According to Pecanha et al. [43], it is accepted that heart rate recovery is predominantly promoted by vagal reactivation immediately after exercise (i.e., 0–2 min), whereas an interaction between vagal reactivation and sympathetic withdrawal is behind the heart rate recovery behavior from the second to the fifth minute of recovery. As has been pointed out, autonomic function is altered after suffering cardiovascular disease [7, 43], with sympathetic activity becoming predominant; this might explain the heart rate recovery results in our sample during the fast phase (0–2 min).

The heart rate recovery increment was only statistically significant in HRV-G. This might be due to the intensity and duration of the previously performed exercise, as the HRV-G performed statistically less high-intensity minutes of total training than did the HIIT-G (36.81% vs 45.73%, respectively), thus conditioning the normalization of the associated metabolic stress, as stated previously [44]. According to authors such as Buchheit et al. [45] or Al Haddad et al. [44], a lower volume of HIIT training is associated with metabolite accumulation in the blood, which favors the inhibition of a postexercise parasympathetic effect caused by elevated sympathetic activity. Other factors that should be taken into account here are the higher resting heart rate and the lower blood pressure in HRV-G. As stated by Al Haddad et al. [44], both factors also determine the impaired restoration of parasympathetic activity following exercise. They reported that complex interactions occur between the sympathetic and vagal systems with respect to HR regulation after exercise. In this regard, measuring heart rate recovery after 2 min and after 5 min in this population could clarify this result. Including blood lactate or plasma epinephrine concentration measurements is also recommended.

The results regarding heart rate variability indicated that the HRV-guided training group had a lower LnrMSSDcv than in the HIIT-G. However, this result was statistically influenced by the baseline LnrMSSDcv, which was lower (although non-significant) in the HRV-G. Thus, a more interesting result found in our study was the significant marked increase in this variable in both exercise groups, which was significantly influenced by age. The existing research offers both positive [24, 42] and negative findings [15] in this regard; however, none used age as a covariable. This LnrMSSDcv increment indicates greater a priori sympathetic activity in both exercise groups at the end of the intervention. This pattern is also seen in other time-domain and frequency-domain outcomes, such as pNN50, HF, or LF/HF. Although the results were not statistically significant, their tendency meant that by the end of the intervention, the parasympathetic activation in the HRV-G was diminished whereas it was maintained or increased in HIIT-G.

In other studies [44, 45], it has been stated that HIIT training improves cardiac parasympathetic function. However, in our case, such results cannot be attributed to the exercise programs but rather to the participants' age. As pointed out by Balasubramanian et al. [46] and Grässler et al. [40], normal aging processes cause impairment in autonomic cardiac control and this manifest reduced parasympathetic modulation of the cardiovascular system. Consequently, long-term interventions are needed to achieve greater autonomic nervous system balance in cardiovascular rehabilitation. On the other hand, the lack of statistical changes in the frequency domains might be due to the measuring time used (60 s) since a period of at least 2 min [31] is recommended to ensure more reliable results. Therefore, standardization of the assessment protocol should be encouraged.

Both training programs presented a safe exercise modality and did not differ in terms of the frequency or magnitude of adverse cardiovascular events, while adherence was similar to that in other studies [24, 36, 41]. No differences in quality of life were found within- or between-groups, according to other studies [12, 41]. However, the significant relationship between quality of life, VO_2max, METS, and HRV suggests that these physiological improvements generate a better subjective perception of the patients' physical, mental, and social ability to carry out day-to-day activities.

Finally, there are certain limitations that should be considered for future research. The heterogeneity of the sample in terms of age makes it difficult to draw conclusions regarding some variables. Therefore, a larger sample size and multicenter intervention is recommended to minimize such bias obtaining a higher sample size and homogenizing the data. A standardized protocol to record heart rate recovery and heart rate variability is suggested to investigate clinical endpoints. In this regard, it is recommended that the heart rate recovery is recorded in a supine position in cardiomyopathy patients after 1', 2', and 5' in order to analyze the sympathetic withdrawal and the heart rate variability. Moreover, a long-term intervention (i.e., 12 weeks) is recommended to obtain better results as well as a multi-factorial intervention composed of individualized exercise training, nutritional and psychological counseling, and cardiovascular risk factor management.

Conclusion

HRV-guided training and HIIT-based traditional training had the same effect in improving VO_2max and METS in cardiomyopathy patients. However, the HRV-guided training had a better effect on the blood pressure and heart rate parameters, increasing the vagal activation at rest and at maximal effort. The heart rate variability decreased in both exercise groups, but age was an interfering factor, so these results are inconclusive. There were no significant differences in quality of life, although it was associated with cardiorespiratory and autonomic improvements. The HIIT-group trained for more minutes at high intensity although both programs were safe and feasible. In our study, we argue that preference should be given to HRV-guided training in cardiac rehabilitation as it shows a better cardioprotective effect with less high-intensity training volume. Nonetheless, longer training interventions are recommended to achieve enhanced performance and age should be considered as a fundamental parameter to include in future research.

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Data availability The data that support the findings of this study will openly available in the University of Almería repository through this link: https://repositorio.ual.es/submissions.

Declarations

Conflict of interest The authors declare no competing interests.

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