The effects of baseline heart rate recovery normality and exercise training protocol on heart rate recovery in patients with heart failure

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Abstract

Objective: It is unclear which exercise training protocol yields superior heart rate recovery (HRR) improvement in heart failure (HF) patients. Whether baseline HRR normality plays a role in the improvement is unknown. We hypothesized that an exercise training protocol and baseline HRR normality would be factors in altering HRR in HF patients.

Methods: In this prospective, randomized, controlled and 3 group parallel study, 41 stable HF patients were randomly assigned to 3-times-weekly training sessions for 12 weeks, consisting of i) 30 minutes of interval training (IT) (n=17, 63.7±8.8 years old) versus ii) 30 minutes of continuous training (CT) (n=13, 59.6±6.8 years old) versus iii) no training (CON) (n=11, 60.6±9.9 years old). Each patient had cardiopulmonary exercise testing before and after the training program. Maximum heart rates attained during the test and heart rates at 1 and 2 min (HRR1 and HRR2) during the recovery phase were recorded. Paired samples t-test or Wilcoxon signed-rank test was used for comparisons before and after training. One-way ANOVA or Kruskal-Wallis variance analysis was used for comparisons among groups.

Results: HRR1 was unchanged after training. HRR2 improved in the IT group after training, and post-training HRR2 values were significantly faster in the IT group than in controls. Both HRR1 and HRR2 was significantly faster, irrespective of exercise protocol in patients with abnormal baseline values after training.

Conclusion: HRR1 did not improve after training. HRR2 improved only in the IT group. Both HRRs in patients with abnormal baseline values improved after both exercise protocols. IT might be superior to CT in improving HRR2. Baseline HRR might play a role in its response to exercise. *(Anatol J Cardiol 2015; 15: 727-34)*

Keywords: cardiac rehabilitation, autonomic nervous system, cardiopulmonary exercise testing

Introduction

Heart failure (HF), characterized by autonomic imbalance and neurohormonal activation, is a common disorder associated with high rates of morbidity and mortality (1). Autonomic imbalance includes increased activity of the sympathetic system, decreased activity of the parasympathetic system, and depressed heart rate variability (2) and is a common clinical predictor of poor survival in HF (3, 4). Neurohormonal modulation is consequently a cornerstone of modern heart failure treatment (5). Current guidelines recommend that patients in cardiac rehabilitation (CR) programs perform moderate exercise at between 40% and 80% of peak heart rate (6, 7). Many of the effects are exerted by the interplay between the sympathetic and parasympathetic nervous systems. Heart rate at 1 or 2 min of recovery has been validated as a prognostic measurement (8). Heart rate recovery (HRR), as a simple and easily acquired response of autonomic function, has the potential to be an additional marker of training efficacy and risk stratification in patients undergoing CR. There may be an association of abnormal HRR at baseline and at CR exit with all-cause mortality (9). CR may favorably affect HRR (10). Whether baseline HRR normality may play a role in the improvement of HRR is uncertain. CR improves symptoms, quality of life, and functional capacity in patients with HF, mainly by continuous aerobic training. Recent studies have suggested that interval cycle exercise training might also exert favorable effects (11). The data on the beneficial

The abstract has been presented as an oral presentation at 9th International Congress of Update in Cardiology and Cardiovascular Surgery, 21-24 March 2013, Antalya, Turkey.

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Accepted Date: 28.08.2014 **Available Online Date:** 15.10.2014

DOI:10.5152/akd.2014.5710

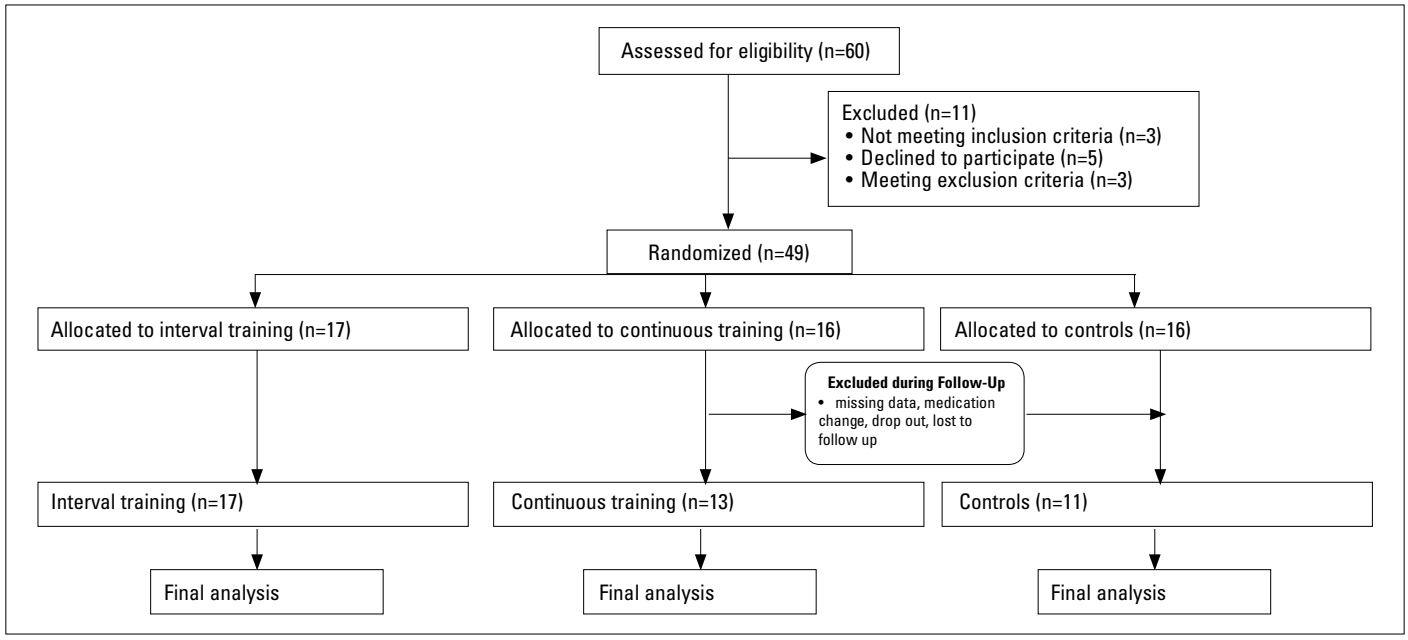

Figure 1. Inclusion of the study population

effects of aerobic exercise training on HRR in HF patients are limited. In addition, the effects of an exercise protocol on HRR are not fully characterized yet. A recent study by Dimopoulos et al. (12) demonstrated that continuous, rather than interval, exercise training improved HRR1. In this prospective, randomized, controlled study, we assessed the effects of baseline HRR normality and interval versus continuous training on HRR in HF patients in order to better determine the influence of the exercise protocol on this prognostic marker.

Methods

Participants

Patients were included in the study as follows: (1) adults of either gender and any age with satisfactory control of New York Heart Association Class II or III heart failure (asymptomatic at rest, mildly symptomatic on exertion, euvolemic, and normal renal functions); (2) any etiology of left ventricular systolic failure except aortic stenosis and hypertrophic cardiomyopathy with significant gradient; (3) left ventricular ejection fraction between 30% and 45%; and (4) stable (>4 weeks) pharmacologic therapy at the discretion of the treating physician. The diagnosis of HF was established by signs, symptoms, and an echocardiographically determined ejection fraction <45%. All participants had at least one previous hospital admission for HF and evidence of left ventricular dysfunction. Individuals with a history of pacemakers, acute coronary syndrome, acute stroke, New York Heart Association Class I and IV heart failure, occurrence of myocardial infarction within the previous 3 months, previous ischemic stroke within the last 3 months, cardiac arrest, sustained arrhythmia, current angina, musculoskeletal or respiratory problems (such as COPD) or another comorbidity in which exercise is contraindicated or maximal effort is not attained, symptoms that prevent exercise, exercise-induced symptomatic or sustained ventricular tachycardia, and blood pressure drop during exercise test were excluded (Fig. 1).

Study design

At the time of CR initiation, a detailed history and physical examination were obtained. Greater than 70% of the study sample underwent cardiac revascularization (percutaneous intervention with angioplasty and stent or coronary artery bypass grafting surgery). None of the participants had revascularization within the 3 months preceding the study. Participants were also followed for routine management of diet, weight, blood pressure, lipids, and diabetes mellitus. We did not make any medication changes. The study was designed as a prospective, randomized, controlled, 3-group parallel study. After a baseline exercise tolerance test (ETT), participants were randomly allocated to an interval training group (IT) (n=17) or a continuous training group (CT) (n=13) or an inactive group (CON) (n=11) by our statistician, who was blinded to the clinical characteristics of the patients, and with the aid of a statistical software package. The training groups exercised for 12 weeks, involving 3 sessions per week under physician supervision. Cycle ergometers (Ergoline, Ergoselect II 100/200/Reha Model 2003, German) were used for aerobic exercise. Each session consisted of a 5-minute warm-up and stretching period, followed by 30 minutes of aerobic exercise with an intensity of 50% to 75% of heart rate reserve, calculated by Karvonen formula, and ended with a 5-min cool-down period (13). Patients in the IT group did aerobic exercise for 30 seconds at 50% to 75% of heart rate reserve, calculated by Karvonen formula, followed by rest intervals of 30 seconds. Those randomized to CT exercised without resting intervals. CON continued with daily living activities.

Table 1. Clinical and laboratory characteristics and medications in all patients and according to type of training

	All patients (n=41)	Controls (n=11)	Patients assigned to interval training (n=17)	Patients assigned to continuous training (n=13)	*P*
Age, years	61.3±8.4	60.6±9.9	63.7±8.8	59.6±6.8	0.407
Male, n (%)	35 (85)	9 (81.8)	13 (76.5)	13 (100)	0.93
BMI, kg/m^2	29.4±4.8	29.3±4.8	28.7±4.9	30.1±5	0.599
Hypertension, n (%)	35 (85)	9 (81.8)	13 (76.5)	13 (100)	0.93
Diabetes mellitus, n (%)	16 (39)	4 (36.4)	6 (35)	6 (46.2)	0.978
Hyperlipidemia, n (%)	27 (65)	7 (63.6)	11 (64.7)	9 (69.2)	0.73
CAD, n (%)	38 (92)	10 (90.9)	13 (76.5)	13 (100)	0.294
Current smoking, n (%)	28 (68)	6 (54.5)	11 (64.7)	11 (84.6)	0.531
Alcohol, n (%)	13 (31)	4 (36.4)	4 (23.5)	5 (38.4)	0.858
Prior MI, n (%)	25 (60)	8 (72.7)	8 (47)	9 (69.2)	0.614
Prior CABG, n (%)	15 (36)	5 (45.5)	4 (23.5)	6 (46.2)	0.05
ACE inhibitors, n (%)	14 (34.1)	3 (27.3)	4 (23.5)	7 (53.8)	0.196
ARB, n (%)	9 (22)	3 (27.3)	5 (29.4)	1 (7.7)	0.270
Diuretics, n (%)	17 (41.5)	6 (54.5)	6 (35)	5 (38.5)	0.498
Beta-blockers, n (%)	21 (51.2)	5 (45.5)	6 (35)	10 (76.9)	0.311
Digitalis, n (%)	2 (4.9)	0	2 (11.8)	0	0.160
Nitrates, n (%)	12 (29.3)	4 (36.4)	5 (29.4)	3 (23)	0.384
Statins, n (%)	20 (48.8)	6 (54.5)	8 (47)	6 (46)	0.664
CCB, n (%)	4 (9.8)	1 (9.1)	2 (11.8)	1 (7.7)	0.929
Oral anti-diabetics, n (%)	11 (26.8)	3 (27.3)	5 (29.4)	3 (23)	0.926
Insulin, n (%)	3 (7.3)	1 (9.1)	1 (5.9)	1 (7.7)	0.949

Values are given as percentages or means±SD. ACE - angiotensin-converting enzyme; ARB - angiotensin receptor blocker; BMI - body mass index; CABG - coronary artery bypass grafting; CAD - coronary artery disease; CCB - calcium channel blocker; MI - myocardial infarction
One way analysis of variance, Chi-square analysis

Maximal cardiopulmonary exercise test

Baseline stress tests were performed right before the initiation of CR, and final stress tests were performed within 1 week of completion of CR. Resting heart rate and blood pressure values were recorded after 5 min of resting. Participants underwent symptom-limited cardiopulmonary exercise testing with a stepwise exercise protocol performed on a bicycle (Technogym, Bike-Med, Italy) with breath measured by breath gas analysis (Masterscreen CPX, CareFusion Germany 234 GmbH, 2011*)*. Pedaling speed was set at 60 revolutions per minute during the entire test. The power was increased by 10 watts starting from 10 watts every minute until the appearance of symptoms. Blood pressure, heart rate, ECG, and symptoms were monitored every 2 min and recorded at each stage. Measured aerobic capacity was expressed as peak O_2 consumption (mL/kg/min). After peak exercise, the participant was required to undergo a 3-minute cool-down period, starting from 30 watts (corresponding to that at 1.5 mph and 2.5% grade on the treadmill, as suggested by previous work) (13) and decreasing 10 watts per min. HRR1 and 2 were defined as the difference between heart rate at peak exercise and exactly 1 and 2 min into the recovery period. HRR1, HRR2, and cardiopulmonary measurements were recorded for each participant during cardiopulmonary exercise testing before and after CR. An HRR1 value less than or equal to 12 bpm was considered abnormal (14, 15). An HRR2 value less than or equal to 22 bpm was considered abnormal (8).

This study protocol was approved by the medical Ethics Review Committee of the participating university and conforms to the ethical guidelines of the 1975 Declaration of Helsinki. All participants gave written informed consent.

Statistical analysis

A statistical software package (SPSS 18.0, Chicago, IL, USA) was used to perform all analyses. Continuous and categorical data are reported as mean±standard deviation and percentages, respectively. Paired samples t-test or Wilcoxon signed-rank test assessed differences in variables at baseline and after CR, where appropriate. Comparisons among groups were assessed using one-way ANOVA or Kruskal-Wallis variance analysis. Tukey and Mann-Whitney U test with Bonferroni correction were used for post hoc comparisons. Differences in categorical data were assessed by chi-square analysis.

Table 2. Comparison of cardiopulmonary exercise testing responses of the study population

	Controls (n=11)			Patients assigned to interval training (n=17)			Patients assigned to continuous training (n=13)			
	Pre-exercise	Post-exercise	*P* within*	Pre-exercise	Post-exercise	*P* within*	Pre-exercise	Post-exercise	*P* within*	*P* between*
Resting heart rate, bpm	76±14	79±11	0.169	78±12	73±11	0.005*	78±13	68±7	0.007*	0.057
Peak heart rate, bpm	120±22	113±16	0.281	118±15	117±16	0.738	119±15	112±14	0.052	0.45
SBP at rest, mm Hg	124±15	127±16	0.146	123±13	117±10	0.01*	121±11	114±9	0.012*	0.022*
DBP at rest, mm Hg	85±8	85±9	0.80	80±9	78±9	0.154	82±6	72±8	0.002*	0.004*
Peak SBP, mm Hg	182±26	182±19	1.00	184±36	169±39	0.05*	184±27	164±15	0.007*	0.104
Peak DBP, mm Hg	97±8	98±6	0.705	103±27	92±11	0.026*	97±6	85±8	0.004*	0.002*
Absolute V O_2, mL/kg/min	1104±479	918±370	0.003*	1214±347	1299±448	0.306	1119±294	1170±261	0.428	0.044*
Peak workload	96±51	83±40	0.077	97±22	116±31	0.002*	93±33	113±28	0.002*	0.031*
VE, mL	38±15	35±12	0.101	40±14	47±15	0.032*	44±10	44±10	0.912	0.077
V CO_2, mL	1019±474	954±401	0.175	1020±297	1210±420	0.032*	1126±301	1193±281	0.119	0.184
Peak absolute V O_2, mL/kg/min	14±6	11±5	0.002*	15±6	17±7	0.281	14±4	14±3	0.399	0.035*
V 'E/V' CO_2	0.04±0.005	0.038±0.004	0.044*	0.06±0.09	0.04±0.005	0.492	0.04±0.004	0.037±0.002	0.016*	0.222
HRR1	13±12	11±9	0.684	9±5	11±6	0.123	16±11	14±4	0.517	0.159
HRR2	22±17	19±16	0.131	17±9	24±8	0.03*	24±9	23±6	0.689	0.045*

Values are given as means±SD. DBP - diastolic blood pressure; HRR - heart rate recovery; SBP - systolic blood pressure; V CO_2 - carbon dioxide output; VE - minute ventilation; V 'E/V' CO_2 - ventilatory equivalent of carbon dioxide; V O_2 - oxygen uptake.
**P* within: *P* value for the within-patient comparison, i.e., pre- vs. post-exercise.
**P* between: *P* value for the between-group (controls vs. interval vs. continuous) comparison of the post-exercise group difference (i.e., systolic blood pressure at rest, controls vs. continuous; diastolic blood pressure at rest, controls vs. continuous; peak diastolic blood pressure, controls vs. continuous; absolute V O_2, controls vs. interval; peak workload - controls vs. interval; peak absolute V O_2, controls vs. interval; HRR2, controls vs. interval)
One way analysis of variance, Kruskal- Wallis variance analysis

Table 3. Differences in key clinical characteristics in the overall group and HRR subgroups

	Overall group	Normal baseline	Abnormal baseline	*P*
HRR1				
Beta-blockers, n (%)	21 (51.2)	14 (87)	7 (28)	0.0001*
HRR2				
Age, years	61±8	56±8	64±8	0.008*
Beta-blockers, n (%)	20 (53)	10 (83)	10 (38)	0.01*

Values are given as percentages or means±SD.
*difference between subgroups
Independent samples t-test, Chi-square analysis

Patients were also grouped as those with normal HRR1, abnormal HRR1, normal HRR2, and abnormal HRR2. Normal and abnormal groups (normal HRR1 vs. abnormal HRR1; normal HRR2 vs. abnormal HRR2) were compared using independent samples t-test, Mann-Whitney U test, or chi-square analysis, where appropriate.

Results

Patients (n=41; New York Heart Association, II-III participants: mildly symptomatic on exertion; age, 61±8 years; 35:6, male:female) with either ischemic or non-ischemic cardiomyopathy were enrolled into the study. The IT group consisted of 17 patients, the CT group consisted of 13 patients, and the controls were 11 patients. The patient groups were well matched for baseline clinical and laboratory characteristics and medications (Table 1). Age, sex, the presence of coronary artery disease (CAD), the risk factors for CAD, the use of alcohol, coronary revascularization, medications for heart failure, and diabetes were all similar among the groups. All participants underwent symptom-limited, maximal exercise tests. All participants complied with the prescribed exercise protocol. We aimed for maximal effort. Tests were stopped largely due to fatigue. In all groups, the participation rates were greater than 90% at the time of follow-up testing, and there was no statistical difference among groups. The cardiopulmonary exercise testing responses of the overall group are demonstrated in Table 2. Significantly more patients with a normal baseline HRR1 were on beta-blockers than those with an abnormal HRR1 (87% vs. 28%, p=0.0001) (Table 3). Significantly more patients with a normal baseline HRR2 were on beta-blockers than those with an abnormal baseline HRR2 (83% vs. 38%, p=0.01). Patients with an abnormal HRR2 were significantly older than those with a normal HRR2 (p=0.008). CR, irrespective of exercise protocol, improved HRR1 only in patients with abnormal baseline HRR1

Table 4. Comparison of cardiopulmonary exercise testing responses of heart rate recovery at 1 min (HRR1) and 2 min (HRR2) according to baseline HRR1 and HRR2 normality

	Normal			Abnormal			
	Pre-exercise	Post-exercise	*P* within*	Pre-exercise	Post-exercise	*P* within*	*P* between*
HRR1	20±9	14±7	0.053	6±3	12±6	0.013*	0.057
HRR2	27±14	23±12	0.144	16±7	21±9	0.03*	0.890

HRR1 is considered normal when >12 and abnormal when ≤12.
HRR2 is considered normal when >22 and abnormal when ≤22.
**P* within: *P* value for the within-patient comparison, i.e., pre- vs. post-exercise.
**P* between: *P* value for the between-group (normal vs.abnormal) comparison of the post-exercise group difference
Independent samples t test

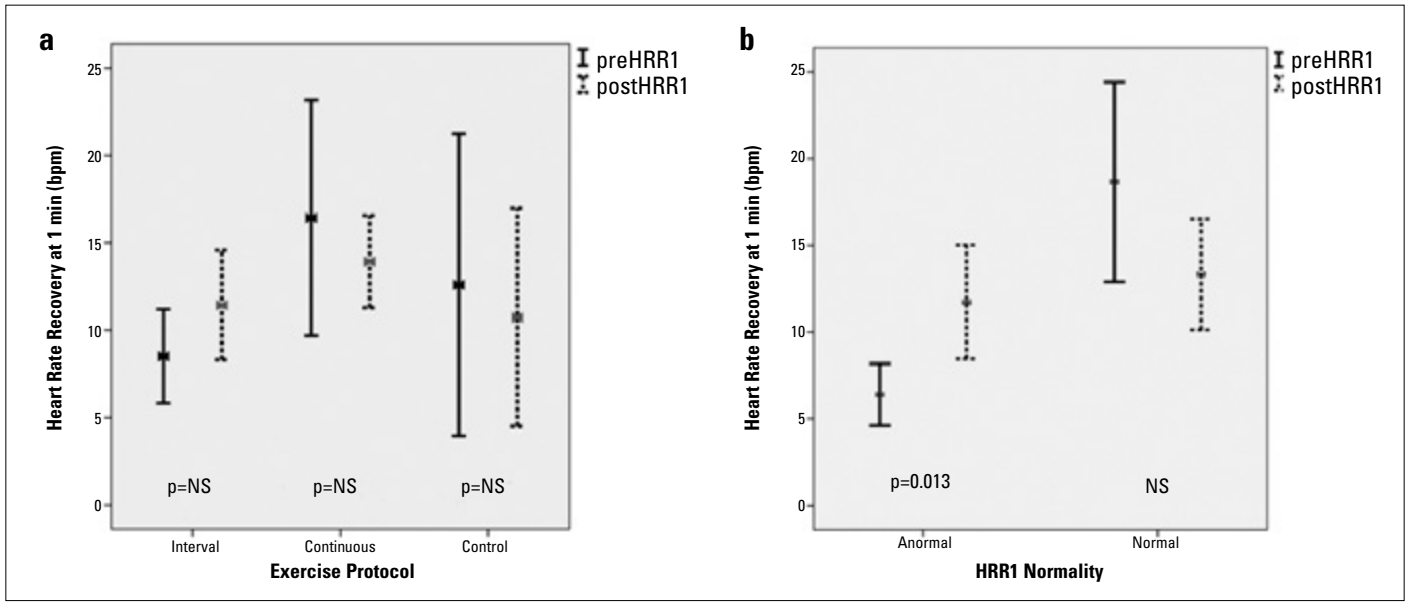

Figure 2. a, b. Heart rate recovery at 1 min (HRR1) of the overall group in the 3 training subgroups pre- and post-rehabilitation (a). HRR1 in the HRR1 subgroups according to baseline normality (b)
Paired samples t-test, Wilcoxon signed-rank test

values (Table 4). Only the IT protocol improved HRR2. HRR1 values were unchanged after exercise training in all groups (Fig. 2A). When only participants with an abnormal baseline HRR1 were analyzed, HRR1 values were significantly faster (6±3 vs. 12±6 bpm, p=0.013). HRR1 in patients with a normal baseline HRR1 were unchanged after CR (Fig. 2B) (Table 4). There was no difference among exercise protocols with respect to the improvement in HRR1 in those patients with an abnormal baseline HRR (p=0.180). HRR2 values were significantly faster only in the IT group after exercise training (17±9 vs. 24±8 bpm, p=0.03) (Fig. 3A). After CR, HRR2 values were significantly faster in the IT group than in controls (19±16 vs. 24±8 bpm, p=0.045) (Table 2). HRR2 in patients with a normal baseline HRR2 were unchanged after CR (Fig. 3B).

Before CR, 41% of the patients had a normal HRR1 versus 59% with an abnormal HRR1. After CR, 51% had a normal HRR1 and 49% had an abnormal HRR1. Before CR, 31.6% of the patients had a normal baseline HRR2 versus 68.4% with an abnormal baseline HRR2. After CR, 47.5% had a normal HRR2 versus 52.5% with an abnormal HRR2. There were no normality group differences among HRR groups when HRR normality considered.

There were no differences in blood pressure, heart rate, or VO_2 values among normal and abnormal HRR1 groups. The normal HRR2 group had significantly higher peak absolute $V0_2$, VE, V CO_2, V 'E/V' CO_2, and peak workload than the abnormal HRR2 group (p<0.05).

There were 13 patients with an abnormal HRR1 in the IT group; 4 patients with an abnormal HRR1 in the CT group; and 7 patients with an abnormal HRR1 in the CON group (p: 0.026). There were 13 patients with an abnormal HRR2 in the IT group; 7 patients with an abnormal HRR2 in the CT group; and 6 patients with an abnormal HRR2 in the CON group (0.334). Regarding, HRR1 changes, there were no differences among the groups (IT, p=0.688; CT, p=1.00; CON, p=1.00). Regarding, HRR2 changes, there were no differences among the groups (IT, p=0.125; CT, p=0.453; CON, p=1.00).

Discussion

The main finding of the current study was that HRR1 did not improve after CR; however, HRR1 improved in only patients with abnormal baseline HRR1 values, irrespective of exercise proto-

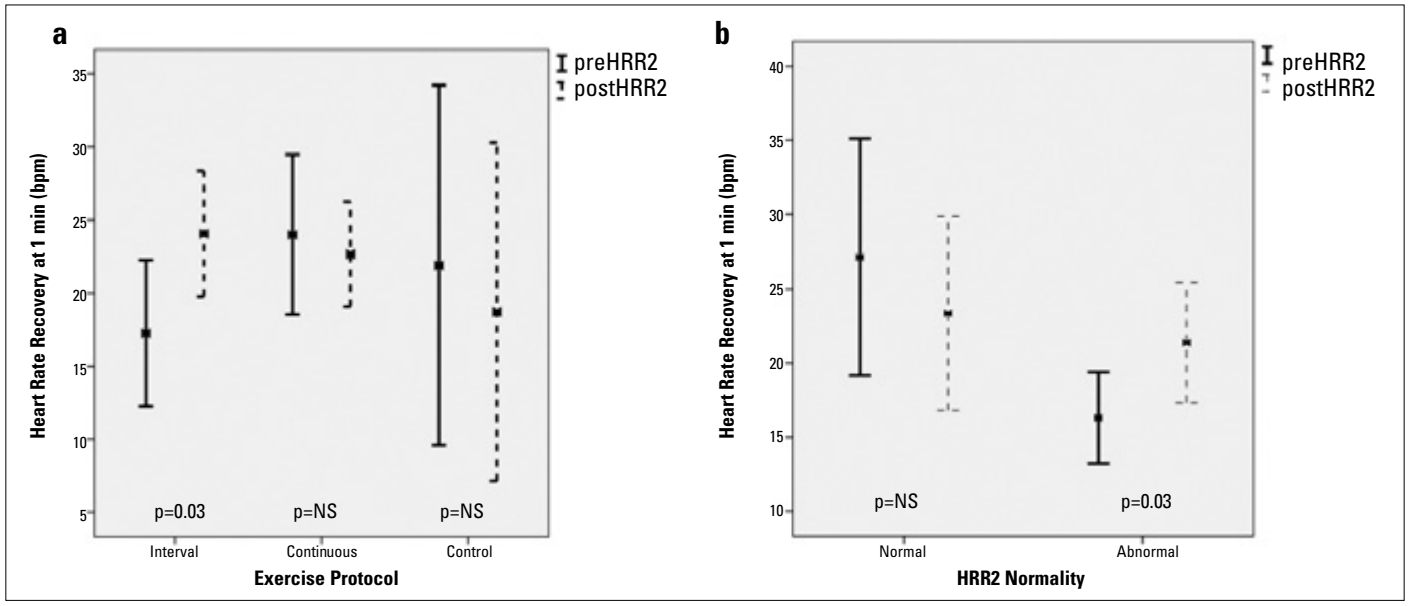

Figure 3. a, b. Heart rate recovery at 2 min (HRR2) of the overall group in the 3 training subgroups pre- and post-rehabilitation (a). HRR2 in the HRR2 subgroups according to baseline normality (b)

Paired samples t-test, Wilcoxon signed-rank test

col. The current study is the first to our knowledge to show that HRR2 improved after CR. Our results indicate that HF patients with abnormal baseline HRR1 (less than or equal to 12 bpm) can improve their HRR1 after the completion of a 12-week aerobic interval or continuous CR program. However, the interval CR program might be superior to the continuous CR program in improving HRR2, which is a better predictor of mortality (8). The results in the current study require confirmation by larger randomized trials.

A growing body of evidence in recent years has shown that HRR is associated with all-cause and cardiovascular mortality, particularly in patients with abnormal baseline HRR (16-21). Previous studies have shown that heart rate reduction plays a critical role in the improvement of clinical outcomes in heart failure. Numerous investigators have observed that exercise training in patients with cardiovascular disease increases HRV (22, 23). Training may have a considerable effect on outcomes in patients with HF via altered vagal modulation. In this study, a significant improvement was observed among those with abnormal baseline HRR1. The response was similar in both the interval and continuous training groups, despite that the 2 exercise protocols are not isocaloric. This is in accordance with Streuber et al. (24), who reported that abnormal baseline HRR1 was the primary factor in determining whether exercise training would improve HRR1 in HF patients. In this study, HRR2 improved only in the IT group, which was in line with the significant improvements in fitness levels of the group (Table 2). This can be considered an extension of previous studies, in that IT might be superior to CT in improving HRR2. Especially, HRR2 was found to be superior to all other time periods as a mortality predictor (8).

A few studies demonstrated that different exercise protocols, including walking on a treadmill or unsupervised walking, improved HRR in HF patients (25, 26). Although we observed improvements in some parasympathetic parameters, such as resting heart rates, systolic blood pressures at rest and exercise, and diastolic blood pressures at rest and exercise, a significant number of our patients did not improve their HRR1. It is unclear why training, irrespective of exercise protocol, failed to improve HRR in our patients, especially in those with normal baseline HRR responses. Perhaps vagal tone in this patient group was relatively unimpaired compared with those with abnormal baseline HRR responses; thus, there was not enough room for parasympathetic activity to improve further. Those patients with normal baseline HRR responses might have required a greater training stimulus to improve their HRR, because HRR improvement in HF patients with higher initial exercise capacities may require greater training intensities. We used cycle ergometry for training, which might have led to lower exercise stimulus due to leg fatigue. Absolute peak oxygen uptake did not improve, regardless of baseline HRR1 or HRR2 normality, which can also be explained by the fact that the patients might have exercised at 50% of their heart rate reserve, although we asked for maximal effort. We allowed them to exercise at 50% to 75% of their reserve, as they tolerated. The improvement of autonomic responsiveness by exercise training in HF patients, assessed by HRR improvement, could require longer exercise program duration. Nonetheless, Tsarouhas et al. (25) suggested in their report that the potential favorable effects of exercise, irrespective of baseline HRR1 values, on endothelial and musculoskeletal metabolism led to HRR1 improvement in their patients. HRR2 normalized in more patients with abnormal baseline values than HRR1. Whereas HRR1 can be considered a marker of cardiac parasympathetic outflow, HRR2 is thought to be related to the gradual with-

drawal of sympathetic activity (27). A CR program, especially IT, might be more effective in the withdrawal of sympathetic activity.

The current study confirms the benefits of both exercise protocols in HF patients with abnormal baseline HRR1. Our findings are consistent with those of Streuber et al. (24), who also observed that short-term aerobic training can favorably modify HRR1 in HF patients with low exercise capacity. In contrast, Dimopoulos et al. (12) recently reported that HRR1 improved only among subjects in the continuous training group, although they did not mention what percentage of patients had an abnormal baseline HRR. Whether patients largely had an abnormal baseline HRR or the recovery protocol, the training stimulus that was used may explain the differences between our study and that study. Their study also lacked a control group. In the current study, HRR2 improved only among subjects in the IT group. Given the differences in methods, direct comparisons between the 2 studies are not possible, but our study showed that HRR2, as a superior predictor, was significantly faster after IT compared to controls.

More recently published data showed significant improvements in fitness levels following high-intensity interval and moderate-intensity endurance exercise training in patients with coronary artery disease. However, they demonstrated no change in HRR and heart rate variability. Their pre-training HRR values were in a low-risk range; thus, they suggested that training-induced improvements may only be achievable in populations with attenuated pre-training values (28). The observed differences in HRR between studies may be due to differences in clinical characteristics, exercise protocols, the recovery protocol, and weight-bearing status. The recovery protocols employed in studies that have examined HRR vary. In the current study, participants underwent a 3-minute cool-down period, starting from 30 watts [corresponding to that used in the study by Cole et al. (14)] and decreasing 10 watts per min.

In contrary to the common assumption that high-exertion exercise increases diagnostic sensitivity, Cahalin et al. (29) just recently demonstrated that the prognostic significance of HRR does not depend upon maximal effort. In view of this, the recommendation for HF patients to exercise as maximally as possible may be unnecessary when examining HRR for prognostic purposes. Thus, our study is relevant, as we aimed to achieve 80% of maximum heart rate or anaerobic threshold limited by symptoms during the cycle ergometry exercise. HRR1 reflects the recovery of parasympathetic activity after maximal exercise. In this study, only a small number of patients normalized their HRR1 after CR. This is in line with the previously mentioned findings of some investigators (9, 12, 24, 30). One of the possibilities is that parasympathetic recovery may remain impaired in some HF patients, despite CR. Another potential explanation for the lack of HRR improvement may be the presence of some clinical characteristics, including older age, peripheral arterial disease, diabetes mellitus, and the use of nitrates, as suggested by Jolly et al. (9). Yet, another possibility is that 36% of the overall group had CABG operation, and the cardiac innervations might have been affected. In addition, the compliance with medications for the overall group, especially those with abnormal HRR values, is unacceptably low. None of the patients had a hospitalization for HF or revascularization in the 3 months preceding the study. Therefore, the lack of improvement in HRR may also be attributed to the time at which the training was initiated, as suggested by Currie et al. (28).

Study limitations

We had to exclude several participants because of medication change and missing data, and we also experienced several dropouts during the training intervention; therefore, our sample was smaller than desired. Our study largely included patients with HF with an ischemic etiology after MI; thus, the results may not be applicable to the wider population of HF patients. Thirty-six percent of our patients had undergone CABG, in whom both afferent and efferent cardiac innervations might have been impaired. The rate of evidence-based medication use is unacceptable. However, the power of the current study comes from its prospective nature, as the majority of large studies examining HRR after exercise has been retrospective.

Conclusion

Training in HF patients with abnormal baseline HRR resulted in improvements in this prognostic marker, more so in HRR2 than HRR1. Both exercise protocols (i.e., interval or continuous) are suitable for HRR1 improvement. IT might be superior to CT in improving HRR2. However, HRR remains unimproved in a significant number of patients, which corroborates prior studies that have shown similar results. Further research should focus on optimizing the most efficient protocol of exercise and the length of the rehabilitation program with respect to HRR improvement and identifying appropriate HF patient groups to target.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - Y.T.Y., G.F., S.K.; Design - G.F., S.K., H.Ş.; Supervision - G.F., Y.T.Y., S.K.; Resource - G.F., S.K.; Data collection &/or processing - G.F., Y.T.Y., S.K., M.Y., H.Ş.; Analysis &/or interpretation - G.F., Y.T.Y., S.K., M.Y., H.Ş.; Literature search - G.F., Y.T.Y., S.K., M.Y.; Writing - Y.T.Y., G.F., M.Y., S.K.; Critical review - Y.T.Y., G.F., M.Y., S.K., H.Ş.

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