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# The Acute Effects of 2 Different Intensities of Resistance Exercise on Autonomic Function in Heart Failure Patients: A Randomized Controlled Trial

#### ABSTRACT

**Background:** Although a wide spectrum of resistance exercise intensities was recommended in the guidelines, none of them investigated the acute effects of different intensities of the resistance exercise on cardiac autonomic function in patients with chronic heart failure. This study aimed to investigate the acute effects of the low and high intensities of the resistance exercise on heart rate variability in chronic heart failure.

**Methods:** This randomized controlled trial was performed between October 2019 and December 2020. Fifty-seven patients with chronic heart failure (New York Heart Association class II and class III) underwent hemodynamic, functional capacity, and heart rate variability (time and frequency domains) assessments. They were randomly divided into R1, R2, and control groups. The intervention consisted of performing a short aerobic exercise including 15 minutes of walking at an intensity of 50% reserved heart rate for all 3 groups and additional resistance exercise with the intensity of 50% 1-repetition maximum and 75% 1-repetition maximum for R1 and R2 groups, respectively.

**Results:** The standard deviation of normal to normal intervals and standard deviation of average NN intervals became significantly lower in R2 (P=.031), and both high-frequency power and low-frequency power were significantly higher in R1 (P=.039 and P=.004, respectively) after the intervention. No significant changes were observed in the control group. Between-group changes were not significant for hemodynamics and functional capacity after treatment. The between-group comparison demonstrated a significant increase in root mean square of successive differences of the NN intervals in R1 in comparison to the control (P=.035).

**Conclusions:** These findings indicate that resistance exercise in 50% 1-repetition maximum in comparison to 75% 1-repetition maximum had more favorable effects on the heart rate variability in chronic heart failure.

Keywords: Heart failure, resistance exercise, heart rate variability, autonomic function

## INTRODUCTION

Chronic heart failure (CHF) is one of the important reasons for morbidity and mortality with a prevalence of 1%-2%.<sup>1</sup> Muscle weakness impairs the patient's functional capacity and manifests in their walking ability evidenced by a reduction of muscle power and a 6-minute walking test (6MWT).<sup>2,3</sup>

The autonomic nervous system adjusts cardiovascular homeostasis during and after exercise. However, in heart failure, exercise may represent different autonomic cardiac responses and make this population more vulnerable to complications. Resistance exercise (RE) training assists those with chronic diseases associated with autonomic dysfunction.<sup>4</sup> However, an increase in resistance may decrease vagal activity and increase sympathetic drive.

While aerobic exercise training improved the heart rate variability (HRV) in older patients with CHF,  $^{\rm 5}$  little is known about RE in CHF.  $^{\rm 6-8}$ 

It was reported that an acute bout of RE may have a significant impact on autonomic modulation and could decrease parasympathetic activity.<sup>8</sup> It implies that



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## **ORIGINAL INVESTIGATION**

Marzieh Saeidi<sup>1</sup> Roya Ravanbod<sup>1</sup> Mohammad Hossein Pourgharib-Shahi<sup>2</sup> Hosein Navid<sup>3</sup> Babak Goosheh<sup>4</sup> Abdolvahab Baradaran<sup>5</sup>

Giti Torkaman<sup>1</sup>

<sup>1</sup>Department of Physiotherapy, School of Medical Sciences, Tarbiat Modares University, Tehran, Iran <sup>2</sup>Sport Medicine Research Center. Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran <sup>3</sup>Department of Heart Failure and Heart Transplantation, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran <sup>4</sup>Department of Clinical Sciences, School of Rehabilitation Sciences, Rofeideh Rehabilitation Hospital, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran <sup>5</sup>Department of Cardiology, School of Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

#### Corresponding author:

Roya Ravanbod ravanbod@modares.ac.ir

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high-intensity RE increases the possibility of cardiac complications.<sup>9,10</sup> Therefore, a safe intensity of RE, for both acute bout and training programs, should be considered to prevent the risks of cardiovascular complications during or after RE in CHF.<sup>9,10</sup> Although some studies investigated the acute effects of RE on HRV in patients with hypertension<sup>11,12</sup> and coronary artery disease,<sup>13</sup> there is a lack of literature regarding the acute effects of RE on HRV in patients with CHF. Moreover, a wide spectrum of the intensity of RE has been recommended in the previous studies<sup>14,15</sup> and guidelines have mentioned the intensity from 30% to 80% of the 1-repetition maximum (1-RM) with no clear evidence that which exact intensity is safer and would have more positive impacts.<sup>16,17</sup>

Therefore, this study aimed to investigate and compare the acute effects of RE with low (50% 1-RM) and high (75% 1-RM) intensities on hemodynamic function and HRV in CHF patients.

#### **METHODS**

## Study Design

This study was a single-blind, randomized controlled clinical trial that was performed at a heart failure clinic between October 2019 and December 2020. Every subject who agreed to participate in the study signed a written informed consent, and all procedures were conducted according to the Declaration of Helsinki.

## Subjects

Fifty-seven patients with CHF participated in this study. The inclusion criteria consisted of an established clinical diagnosis of CHF, New York Heart Association (NYHA) classification II and III, optimal medical management for at least 3 months according to American Heart Association (AHA), ejection fraction <40%, age between 45 and 75 years, body mass index (BMI) between 25 and 32 kg/m<sup>2</sup>, and stable hemodynamic condition.

Exclusion criteria consisted of high-risk patients with unstable angina, complex ventricular arrhythmia, recent myocardial infarction, having a pacemaker, and a history of cardiac intervention during the last 6 months.

## HIGHLIGHTS

- The hemodynamic response to exercise was more favorable in the 50% 1-repetition maximum (1-RM) group than the 75% 1-RM group.
- The decrease in standard deviation (SD) of NN intervals and SD of average NN intervals in the 75% 1-RM group and the increase in low-frequency power and highfrequency power in the 50% 1-RM group indicated the more desirable response of the cardiac autonomic system to resistance exercise in the 50% 1-RM group compared to the 75% 1-RM group.
- The physical performance of the patients (6-minute walking test) was increased by the same amount regardless of the type and intensity of exercise in the 3 groups.

#### **Sample Size**

The sample size was calculated by G-power software<sup>18</sup> and was based on the mean difference (533.9) and standard deviation (SD) (572.3) of low-frequency power (LF) (effect size = 0.9) obtained from the Andrade<sup>19</sup> study in 2020 using an alpha level of 0.05 and power of 95%, and 19 cases in each group were considered.

#### **Experimental Protocol**

Demographic information and disease history including age, BMI, duration of CHF, medications, comorbidities, and left ventricular ejection fraction was collected.

### Hemodynamic and Heart Rate Variability Measurement

For hemodynamic assessment, according to the AHA protocol,<sup>20</sup> after 30 minutes of rest, heart rate (HR) and blood pressure (BP) were measured through a digital sphygmomanometer (Omron M3, HEALTHCARE CO., Ltd, Kyoto, Japan). The patients were requested to avoid caffeinated and alcoholic drinks, heavy meals, and heavy activities the night before and on the day of data collection. The experiments were performed at a temperature of 22°C-24°C and a humidity of 50%-60%. Data were collected between 8:00 AM and 12:00 AM to avoid circadian disparities.

For HRV measurement, patients underwent a 45-minute electrocardiogram (ECG) recording at a supine rest position by a Holter monitoring device (My-patch, Model mps-IDTC, DMS-service Inc. 11845-W. Olympic Blvd, STE 880 LA, CA 90064, Los Angeles, USA).<sup>21</sup> Heart rate variability data were saved and analyzed for indices by the special software of the device. The data were obtained through the linear method in both the time and frequency domains. The amount of variability of the inter-beat interval time is quantified by the time-domain indices. Time-domain metrics included the SD of NN intervals (SDNN), the SD of average NN intervals (SDANN), the mean of the SDs of all the NN intervals for each 5-minute segment (SDNN index), root mean square of successive differences of the NN intervals (RMSSD), and the number of interval differences of successive NN intervals greater than 50 ms (pNN50). Frequency-domain metrics included total power, very-low-frequency power, LF, highfrequency power (HF), normalized-LF, normalized-HF, and LF/HF ratio. These data were obtained from the software related to the above-mentioned device.

## **Muscle Strength Measurement**

Muscle strength measurement was performed for ankle dorsi and plantar flexors, knee flexors and extensors, hip flexors, extensors, abductors, wrist flexors and extensors, elbow flexor and extensors, and shoulder abductors using digital dynamometry (Hand-held dynamometer, model 01165SC, Lafayette Instrument Company, Lafayette, Ind, USA)<sup>22</sup> according to the Kendal protocol.<sup>23</sup> The patients were asked to inhale during the concentric phase and exhale during the eccentric phase of contraction to avoid the Valsalva maneuver.<sup>24</sup>

## Functional Capacity (6-Minute Walking Test)

The patients were asked to perform a standard  $6MWT^{25}$ . Before and immediately after the end of the test, BP, HR, and the rate of perceived exertion (Borg scale 1-10)<sup>26</sup> were recorded. The distance covered was recorded in meters. A wireless ECG monitor system (QardioCore, Model C100-1AW, Qardio, California, San Francisco, USA)<sup>27</sup> was used for monitoring the patients during the test.

#### **Myocardial Stress**

Myocardial stress or double product (DP) was calculated by multiplying HR and systolic blood pressure (SBP) at rest and immediately after the end of the exercise session.<sup>28</sup>

## **1-Repetition Maximum Test**

For the 1-RM test, the patient was asked to perform elbow flexion and knee extension with maximum strength in a full range of motion, and then 1-RM was calculated by the following formula (1-RM=W0+w1). W0 is a load that can be lifted at least for 7-8 repetitions and w1 is calculated by w1=W0 ×  $0.025 \times r$  (r=number of repetitions by that load).<sup>29</sup>

#### **Group Assignment**

The patients were randomly allocated to 3 groups by using concealed envelopes (restricted randomization without replacement by a physiotherapist). The study groups included R1 (n = 19), R2 (n = 19), and control (n = 19). The intensity of RE was 50% and 75% of 1-RM for groups R1 and R2, respectively, based on the results of the 1-RM test. Participants were blinded to the group assignment.

#### Intervention

The patients were requested to perform a single session of exercise including 5 minutes warm-up consisting of gentle aerobic and stretching exercises. Then, they were asked to perform 15 minutes of walking with an intensity of 50% of the HR reserve.<sup>30</sup> The experimental groups (R1 and R2) performed additional 32 minutes of RE including 2 sets of 6-8 repetitions of 11 exercises by using free weights with an intensity of 50% or 75% 1-RM. All the subjects performed a 5-minute cooldown consisting of aerobic and stretching exercises at the end of the exercise session.

Resistance exercise program for R1 and R2 groups consisted of exercise with free weights for the evaluated muscle groups. One-minute rest was considered between each set of exercises.<sup>31</sup> During exercise sessions, patients' ECG was monitored using the QardioCore system. Heart rate, BP, and Borg scale were measured at the beginning and the end of the exercise session. All the assessments were repeated immediately after the intervention by a trained physiotherapist.

## **Statistical Analysis**

Data were analyzed using IBM Statistical Package for Social Sciences statistics 24 software. The Shapiro–Wilk test was used to evaluate the normal distribution of the data. For data with normal distribution, the paired *t*-test was used for within-group comparisons and analysis of variance (ANOVA), and the post hoc Tukey's honestly significant difference test for between-group comparisons. In the case of abnormal distribution of data, Wilcoxon signed-rank test was used for within-group comparison and the Kruskal–Wallis *H* test for between-group comparison. The interaction of time and group was analyzed by using 2-way ANOVA and Friedman test for non-normally distributed data. The level of significance was set at P < .05 for all statistical tests. The results were analyzed by an assessor blinded to the group allocation.

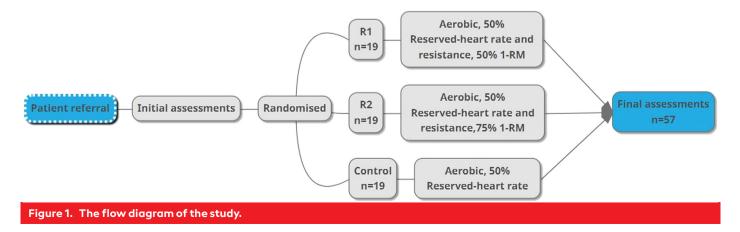
#### RESULTS

Fifty-seven patients were randomized to each of the 3 groups, and all of them were included in the analysis. Participants completed the study without any adverse events. The flow diagram of the study is shown in Figure 1.

The baseline characteristics of the patients are presented in Tables 1 and 2.

Hemodynamic variables were elevated in all exercise groups compared with the baseline (Table 3). However, there was no significant difference between the 3 groups for hemodynamic parameters after the intervention except for HR. Resting HR increased significantly in the control group (P=.048) and HR at the end of 6MWT increased in R1(P=.035) (Table 3).

Within-group comparisons showed that SDNN and SDANN became significantly lower in the R2 group after the intervention (P=.031). Low-frequency power and HF were both significantly risen in R1 after the exercise program (P=.004 and P=.039, respectively) (Figure 2). No significant changes were observed in the control group after the exercise (Table 3).



able 1. Baseline Characteristics of the Study Population								
Groups		R1 (n = 19)	R2 (n = 19)	Control (n = 19)	Р			
Variables								
Age (years)		$62.00 \pm 13.07$	$58.00 \pm 8.45$	62.79 ± 10.43	.350			
BMI (kg/m²)		25.59 <u>+</u> 3.90	$28.04 \pm 5.26$	27.87 <u>+</u> 5.46	.241			
Gender	Male	73.7	68.4	73.7	.917			
	Female	26.3	31.6	26.3				
Education	Primary	52.6	57.9	57.9	.401			
	Secondary	15.8	10.5	10.5				
	Diploma	5.3	26.3	10.5				
	University	26.3	5.3	21.1				
Medications	β-blocker	84.2	68.4	78.9	.498			
	ACEI	89.5	89.5	78.9	.559			
	Diuretics	100	100	100				
	Vasodilators	10.5	31.6	26.3	.274			
	Digitalis	26.3	10.5	5.3	.151			
NYHA class	II	47.4	63.2	47.4	.531			
	111	52.6	36.8	52.6				
EF (%)		26.05 ± 9.06	25.79 <u>+</u> 8.21	26.05 ± 9.06	.981			
Heart failure durc	ition (years)	28.72 <u>+</u> 20.57	26.22 <u>+</u> 16.63	28.22 ± 19.61	.917			
Hemoglobin		14.10 ± 1.61	13.67 <u>+</u> 1.58	13.58 <u>+</u> 1.80	.593			
1-RM (kg)	Elbow flexors	$5.62 \pm 2.02$	5.52 <u>+</u> 2.10	5.15 <u>+</u> 2.60	.772			
	Knee extensors	$5.70 \pm 2.05$	6.48 ± 2.12	5.76 ± 2.60	.501			
FSS (score)		45.11 ± 9.32	40.84 ± 11.62	47.37 ± 9.48	.315			
MMRCDS (score)		$3.21 \pm 0.71$	2.84 ± 0.96	3.32 ± 1.25	.466			
MLHF (score)		56.00 ± 23.31	47.42 ± 17.48	53.74 <u>+</u> 24.65	.466			

Data are presented as mean  $\pm$  SD or (%), level of significance: P < .05.

1-RM, 1-repetition maximum; ACEI, Angiotensin-converting enzyme inhibitors; BMI, body mass index; EF, ejection fraction; FSS, fatigue severity scale; MLHF, Minnesota living with heart failure; MMRCDS, modified Medical Research Council dyspnea scale; NYHA, New York Heart Association; R1, 50% 1-RM; R2, 75% 1-RM.

Between-group comparisons showed that RMSSD increased significantly in R1 in comparison to the control (P=.035) (Table 3).

The results showed that there was no significant difference between groups for functional capacity (distance in 6MWT) after intervention (P=.574) (Table 3). The results of 6MWT showed that the walking distance increased in all 3 groups, but it was significant only for R2 (P=.017). The Borg scale increased significantly in all 3 groups (Table 3).

The interaction effect between time and group was not significant for any variable except for the Borg scale (P = .010) and maximum heart rate (MHR) at the end of 6MWT (P = .026).

#### DISCUSSION

The present study aimed to investigate the acute effects of RE (50% and 75% 1-RM) on hemodynamic changes, functional capacity, and HRV in patients with CHF.

The latest meta-analysis regarding the impact of RE on CHF reported that these patients are underrepresented in RE trials, and further investigations are needed to optimize their inclusion.<sup>32</sup> There are also very limited studies investigating the effects of RE on cardiac autonomic function<sup>7,33</sup> and a lack of evidence for the acute bouts of RE on cardiac autonomic function in CHF. This highlights the importance of the present study as the first study to explore the influence of acute bouts of different intensities of RE on cardiac autonomic modulation in patients with CHF.

The results of this study showed that after a single session of RE, HR, SBP and diastolic BP (DBP), and DP at rest and the end of 6MWT increased in all groups. However, while HR at the end of 6MWT was significantly increased in all groups, SBP was just significantly increased in R1. All other hemodynamic parameters were also significantly increased in R1 except for DBP at rest. It is well established that increasing exercise intensity induces more afferent feedback from muscle metaboreceptors and ergoreceptors that triggers further cardiac parasympathetic withdrawal and sympathetic activation, leading to an increase in both HR and BP response.<sup>34,35</sup> Failure to increase SBP in R2 shows that performing the higher intensity exercise (75% 1-RM) in comparison to 50% 1-RM might impose high stress on the function of a heart with failure in a way that was not able to increase the BP needed to meet the metabolic demands of the working muscles.

Accordingly, SDNN and SDANN were also significantly decreased in R2. The gold standard parameter of the HRV

Table 2. Hemodynamics, Functional State, and HRV Before Intervention
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Groups	R1 (n = 19)	R2 (n = 19)	Control (n = 19)	Р
Variables				
Rest HR (beats/minute)	69.47 <u>+</u> 8.82	72.11 ± 9.32	65.68 <u>+</u> 9.43	.106
HR at the end of 6MWT (beats/minute)	82.37 <u>+</u> 12.82	84.05 ± 13.93	77.05 <u>+</u> 11.18	.217
Rest SBP (mmHg)	113.79 <u>+</u> 14.03	113.79 <u>+</u> 10.95	112.16 ± 15.05	.911
Rest DBP (mmHg)	73.26 ± 9.83	73.58 <u>+</u> 9.03	73.89 <u>+</u> 10.39	.980
SBP at the end of 6MWT (mm Hg)	120.79 ± 14.21	121.47 ± 14.70	118.68 ± 18.27	.852
DBP at the end of 6MWT (mm Hg)	78.37 ± 9.72	76.58 ± 11.08	75.79 <u>+</u> 9.13	.719
Rest double product (mm Hg beats/minute)	7955.26 <u>+</u> 1663.45	8188.42 <u>+</u> 1221.63	7371.74 <u>+</u> 1466.27	.217
Double product at the end of 6MWT (mm Hg beats/minute)	$10\ 003.11\pm 2282.69$	10 267.21 ± 2383.60	$9128.68 \pm 1818.33$	.249
SDNN (ms)	47.72 ± 21.80	45.07 ± 13.42	47.13 <u>+</u> 13.87	.906
SDANN	19.11 <u>+</u> 15.09	25.53 <u>+</u> 21.28	23.75 ± 10.27	.172
SDNN index	40.61 ± 19.76	35.21 <u>+</u> 17.11	38.94 ± 14.41	.627
RMSSD (ms)	41.89 <u>+</u> 24.75	30.00 ± 23.51	35.50 <u>+</u> 22.06	.137
PNN50	16.33 ± 19.03	9.74 <u>+</u> 15.18	13.17 <u>+</u> 16.13	.239
TP (ms²)	1190.18 <u>+</u> 884.45	1164.74 <u>+</u> 983.96	1483.36 <u>+</u> 1035.76	.566
VLF (ms²)	994.76 <u>+</u> 1009.23	671.68 <u>+</u> 606.57	1116.03 <u>+</u> 1069.80	.578
LF (ms²)	292.78 <u>+</u> 354.27	299.96 <u>+</u> 280.61	357.61 <u>+</u> 339.82	.816
HF (ms²)	141.63 <u>+</u> 107.88	79.96 <u>+</u> 65.93	169.17 <u>+</u> 128.03	.060
LFnu (ms²)	56.60 ± 17.13	61.63 <u>+</u> 19.37	57.70 <u>+</u> 20.43	.719
HFnu (ms²)	34.87 ± 12.72	29.22 ± 16.60	32.20 ± 15.19	.560
LF/HF	2.27 ± 2.10	3.52 <u>+</u> 4.01	2.66 ± 2.11	.172
6MWT(m)	298.95 ± 108.26	366.84 <u>+</u> 126.01	293.89 <u>+</u> 172.51	.202
Borg (score)	4.47 ± 1.35	4.58 ± 1.64	4.79 ± 1.62	.814

Data are presented as mean  $\pm$  SD.

1-RM, 1-repetition maximum; 6MWT, 6-minute walking test; DBP, diastolic blood pressure; HF, high-frequency power; HFnu, high-frequency power normalized unit; HR, heart rate; HRV, heart rate variability; LF, low-frequency power; LFnu, low-frequency power normalized unit; PNN50, the number of interval differences of successive NN intervals greater than 50 ms; R1, 50% 1-RM; R2, 75% 1-RM; RMSSD, root mean square of successive differences of NN intervals; SBP, systolic blood pressure; SDANN, SD of average NN intervals; SDNN, SD of NN intervals; SDNN index, SDNN index, mean of the SDs of all the NN intervals for each 5-minute segment of a 24-h HRV recording; TP, total power; VLF, very-low-frequency power.

for medical stratification of cardiac risk is SDNN when recorded over a 24-hour period. Values <50 ms are considered unhealthy and between 50 and 100 ms are considered as compromised health.<sup>36</sup> While baseline values of the SDNN in the 3 groups were around 50 ms, it decreased significantly just in R2 after the intervention. On the other hand, RMSSD which is an indicator of parasympathetic activity increased more in R1 than in other groups. Murad et al<sup>5</sup> reported a significant increase in SDNN and RMSSD after cycling and walking in patients with CHF. This is probably because their training intensity started with 40%-50% of the HR reserved for the first 2 weeks and gradually increased to 60%-70% of the HR reserved over the further 14 weeks.<sup>6</sup> The results of our study that was in favor of R1 were comparable with their study in that their training was started with the low intensity of 40%-60% of the HR reserved. The mean difference of the intra-group comparisons after the intervention revealed a significant improvement in cardiac autonomic balance, which means higher HF and LF occurred in R1 (P < .04) (Table 3). Moreover, between-group comparisons (2-way ANOVA analysis) which demonstrated a higher increase in RMSSD in R1 confirmed the improvement in cardiac autonomic balance in R1 (P=.035). Consequently, according to Murad et al<sup>5</sup> and the present study, it could be concluded that introducing low-intensity training protocols could have a more beneficial effect on cardiac autonomic function in CHF. As mentioned before, frequency-domain analysis showed that both HF and LF were significantly increased in R1. Reduced HRV in CHF is believed to be related to the attenuation of cardiac vagal tone.<sup>37</sup> Considering RMSSD and HF represent parasympathetic and LF reflects both sympathetic and parasympathetic activity and baroreflex sensitivity,<sup>38</sup> an increase in HRV indices indicates improvement in the overall variability that happened in the R1 (50% 1-RM) group. It should be mentioned that according to Nunan et al's<sup>39</sup> findings, all HRV results were in the normal data range.

Selig et al<sup>7</sup> reported no changes in the time-domain parameters of the HRV after 8 weeks of moderate-intensity RE based on HR monitoring with no clear exercise prescription guideline in patients with CHF. Moreover, the patients performed just 7 minutes of RE which is not compatible with routine daily activities.<sup>6</sup>

In our study, after a single exercise session, higher resistance resulted in decreasing HRV, while lower resistance was accompanied by a better response to autonomic function

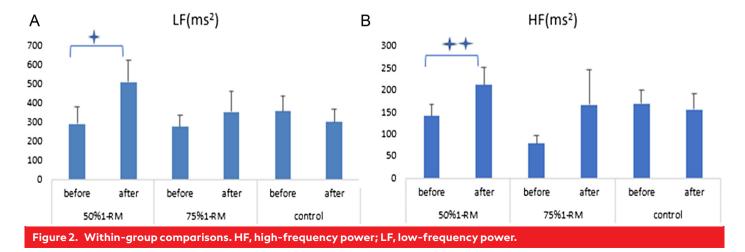
Group	R1 (n = 19)	Р	R2 (n=19)	Р	Control (n=19)	Р	<i>P</i> -Value/ Between Groups	P-Value (Time× Group)
Variables								
Rest HR (beats/minute)	2.58 <u>+</u> 2.91	.001	1.05 <u>+</u> 3.78	.240	3.26 ± 2.51	<.001	.048	.160
HR at the end of 6MWT (beats/ minute)	6.63 ± 4.81	<.001	6.11 ± 4.33	<.001	5.63 ± 5.51	<.001	.035	.026
Rest SBP (mm Hg)	1.63 <u>+</u> 2.79	.020	2.79 <u>+</u> 2.07	<.001	2.26 <u>+</u> 3.59	.010	.815	.247
Rest DBP (mm Hg)	0.47 ± 2.27	.375	1.21 ± 3.29	.126	1.53 <u>+</u> 2.04	.004	.858	.980
SBP at the end of 6MWT (mmHg)	$5.00 \pm 4.85$	<.001	1.63 <u>+</u> 8.90	.434	4.58 ± 13.76	.164	.842	.866
DBP at the end of 6MWT (mm Hg)	2.74 <u>+</u> 5.40	.039	2.16 <u>+</u> 8.10	.261	3.00 ± 5.93	.041	.506	.642
Rest double product (mm Hg beats/minute)	422.37 ± 422.5	<.001	338.11 ± 512.42	.010	527.68 ± 478.57	<.001	.102	.237
Double product at the end of 6MWT (mm Hg beats/minute)	1279.89 <u>+</u> 865.56	<.001	869.37 <u>+</u> 1154.31	.004	1081.37 ± 1210.88	.007	.107	.073
SDNN (ms)	1.76 <u>+</u> 18.59	.410	-6.36 <u>+</u> 13.84	.035	-2.20 <u>+</u> 23.76	.396	.604	.935
SDANN (ms)	0.12 ± 15.93	1.000	-7.27 <u>+</u> 28.72	.031	-5.81±14.98	.098	.757	.551
SDNN index	5.00 <u>+</u> 16.23	.123	3.37 <u>+</u> 19.12	.883	-1.36 ± 17.31	.432	.098	.181
RMSSD (ms)	4.31 ± 17.94	.082	3.89 <u>+</u> 18.84	.938	$-3.33 \pm 21.34$	1.000	.035	.153
PNN50	1.59 <u>+</u> 14.13	.131	$-0.58 \pm 14.13$	.455	$-4.89 \pm 14.43$	.379	.053	.237
TP (ms²)	415.05 <u>+</u> 1039.57	.069	218.14 <u>+</u> 1557.64	.616	-201.07 ± 849.12	.234	.514	.292
VLF (ms²)	$512.74 \pm 1701.86$	.121	$105.25 \pm 992.69$	.586	-362.93 ± 1117.64	.687	.226	.344
LF (ms²)	153.87 <u>+</u> 295.54	.004	80.14 ± 477.99	.813	$-81.26 \pm 283.67$	.227	.609	.501
HF (ms²)	61.53 ± 108.96	.030	$88.74 \pm 306.59$	.245	$-18.41 \pm 130.87$	.215	.827	.246
LFnu (ms²)	0.24 ± 16.00	.864	2.16 ± 11.53	.442	3.05 ± 13.16	.472	.433	.817
HFnu (ms²)	$-3.45 \pm 11.54$	.190	$-0.10 \pm 9.07$	.979	$-0.85 \pm 9.96$	.759	.919	.870
LF/HF	$0.36 \pm 1.41$	.281	$-0.85\pm3.54$	.776	$-0.005 \pm 2.38$	.981	.216	.401
6MWT(m)	$16.84 \pm 61.84$	.252	29.58 <u>+</u> 33.97	.001	$10.11 \pm 30.74$	.169	.017	.118
Borg (score)	1.26 ± 0.73	<.001	1.37 ± 0.68	<.001	0.84 ± 0.69	<.001	.906	.010

#### Table 3. The Changes of Hemodynamics, Functional State, and HRV After the Intervention

Data are presented as mean  $\pm$  SD.

1-RM, 1-repetition maximum; 6MWT, 6-minute walking test; DBP, diastolic blood pressure; HF, high-frequency power; HFnu, high-frequency power normalized unit; HR, heart rate; HRV, heart rate variability; LF, low-frequency power; LFnu, low-frequency power normalized unit; PNN50, the number of interval differences of successive NN intervals greater than 50 ms; R1, 50% 1-RM; R2, 75% 1-RM; RMSSD, root mean square of successive differences of NN intervals; SBP, systolic blood pressure; SDANN, SD of average NN intervals; SDNN, SD of NN intervals; SDNN index, SDNN index, mean of the SDs of all the NN intervals for each 5-minute segment of a 24-h HRV recording; TP, total power; VLF, very-low-frequency power.

in patients with heart failure. Although the most important difference between the 2 studies was the duration of the intervention which was 1 session in the present study and 8 weeks (24 sessions) in the study by Selig et al,<sup>7</sup> other methodological differences such as exercise prescription and the intensity of the RE as well as adding 15 minutes walking in



the present study may explain the different results of these 2 studies.

Ricca-Mallada et al<sup>8</sup> also used circuit resistance training (RT), but they reported positive changes in both time and frequency domains of the HRV as they started with 50% and increased to 80% of the peak workload after 24 weeks in CHF. The results of present study are consistent with their findings according to the reasonable response of the autonomic system to RE, since the exercise intensity at the beginning of the training was the same as R1 group in our study and gradually increased during the rest of the sessions, it can be implied that this intensity is suitable for the first sessions of rehabilitation of these patients.

More distance covered in the higher-intensity group of R2 in 6MWT shows that although this intensity did not have much favorable impact on HRV in 1 acute session, it could be considered for improving functional capacity in CHF in the forthcoming sessions of cardiac rehabilitation programs (Table 3).

A single exercise session is neither a limitation nor enough to achive a training physiological response which needs around 6 weeks.18 However, as a bigining day of any training program where both the clinicians and patients need as much information as possible about its safety. Nevertheless, in the guidelines for CHF patients, a wide range of training intensities are recommended,<sup>18</sup> and we wanted to emphasize that the upper limit of these recommended training intensities might be harmful (at least in some aspects) for, in particular, CHF patients. The results of the present study confirmed our hypothesis that although higher intensity exercise like 75% 1-RM increased 6MWT but imposed unfavorable impacts on the HRV as a precise criteria of neurocardiac function, in comparison to functional outcomes.

#### **Study Limitations**

The plausible limitations of this study were the inability to have a group with RE alone and the performing 24-hour data acquisition of the HRV.

## CONCLUSION

Increasing the BP and improvement of frequency-domain parameters of the HRV showed the favorable impacts of the acute bout of 50% 1-RM RE in comparison to 75% 1-RM RE in CHF. Increasing 6MWT distance in the 75% 1-RM group reveals that higher exercise intensities should also be considered in cardiac rehabilitation programs but not in first sessions.

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of the Tarbiat Modares University (IR. MODARES.REC.1398.071) on 2019.6.16, and the trial has been registered in the Iranian registry of clinical trials (IRCT20190605043821N1).

**Informed Consent:** Written informed consent was obtained from all participants who participated in this study.

**Peer-review:** Externally peer-reviewed.

Author Contributions: M.S. and R.R. participated in the design of the study and contributed to data collection and data reduction/analysis and interpretation of results; M.H.P.S. and H.N. contributed to data collection; and B.G., A.B., and G.T. participated in the design of the study. All authors contributed to the manuscript writing. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

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