



# Exercise-based cardiac rehabilitation for heart failure: effects on echocardiographic parameters and functional capacity: a randomized clinical trial

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**Introduction:** Multiple comorbidities and physiological changes play a role in a range of heart failure (HF) conditions and influence the most effective approach to exercise-based rehabilitation. This research aimed to examine and compare the outcomes of concurrent exercise training, focusing on echocardiographic parameters and functional capacity of patients with heart failure with reduced ejection fraction (HFrEF).

**Methods:** In this randomized control trial, a total of 76 patients (average age:  $68.2 \pm 4.8$  years) with HFrEF were randomly allocated into two groups: intervention group (IG, N = 38) and control group (CG, N = 38) that IG performed an 8-week concurrent exercise training (three aerobic and two resistance exercise sessions/week) and daily breathing exercises. Echocardiographic parameters (left ventricular ejection fraction, left ventricular end-diastolic dimension, left ventricular end-systolic dimension, and functional capacity (6-minute walking test) were assessed before and the end of the study.

**Results:** The comparison of CG and IG showed that 6-min walking test (204.2  $\pm$  28.72 vs. 273  $\pm$  38.37) and ejection fraction (EF) (28.28  $\pm$  4.39 vs. 37.23  $\pm$  6.54) had increased, and left ventricle end-diastolic dimension (53.89  $\pm$  4.73 vs. 46.71  $\pm$  5.35) and left ventricle end-systolic dimension (45.55  $\pm$  4.8 vs. 39  $\pm$  5.26) had decreased after 8 weeks, respectively (P < 0/05).

**Conclusion:** In summary, this study provides compelling evidence that exercise-based cardiac rehabilitation can lead to meaningful improvements in echocardiographic parameters and functional capacity among older adults with HF, advocating for its broader implementation in clinical settings.

Keywords: cardiac rehabilitation, echocardiography, exercise, functional residual capacity, heart failure

#### Introduction

Heart failure (HF) is a global public health issue that affects over 26 million individuals<sup>[1]</sup>. The prevalence of HF is steadily increasing worldwide and is expected to rise significantly due to the aging population<sup>[2]</sup>. Despite significant advancements in treatment, HF continues to be a major cause of hospital admissions, with a 1-year mortality rate of approximately 50% among individuals experiencing symptoms<sup>[3]</sup>.

Heart failure can be categorized into three main types based on ejection fraction: heart failure with reduced ejection fraction (HFrEF): This type of HF occurs when the heart's pumping ability is significantly impaired, resulting in an EF of  $\leq 40\%$ .

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#### **HIGHLIGHTS**

- The findings of this study can help to reduction in morbidity and mortality.
- There is still a difference about the type and severity of endurance and resistance exercises that can have optimal effects on chronic heart failure.

Heart failure with mildly reduced ejection fraction (HFmrEF): In this category, the EF falls within the range of 41%–49%. Heart failure with preserved ejection fraction (HFpEF): HFpEF is characterized by symptoms of HF despite a relatively preserved EF of ≥50%<sup>[4]</sup> Generally, noninvasive parameters are measured by echocardiography to determine heart function and structure. These parameters include left ventricle end-diastolic dimension (LVEDD), left ventricle end-systolic dimension (LVESD), end-diastolic interventricular septum thickness, posterior wall end diastole (PWD), and EF. Also, functional capacity is measured by maximal oxygen uptake (VO2 max) in a direct cardiac assessment or by indirect submaximal exercise tests such as 6-min walking test (6MWT) and is considered a strong predictor factor for determining mortality rate in HF patients<sup>[5,6]</sup>.

Many studies have shown numerous benefits of cardiac rehabilitation (CR) and exercise training in patients with HF, including a reduction in morbidity and mortality<sup>[7,8]</sup>. Exercise training improves the quality of HF patients' life<sup>[9]</sup>. Doing concurrent aerobic-resistance exercise is also a novel training method<sup>[10]</sup>.

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Exercise training increases peripheral vasodilatation and muscle strength, reduces peripheral vascular resistance, reduces inflammation, helps the left ventricle (LV) regeneration<sup>[11]</sup>, reduces stress on LV, and increases left ventricle ejection fraction<sup>[2]</sup>. Additionally, CR programs, an effective tool that can help patients with heart disease improve their physical and mental health, reduce their risk of future cardiac events and avoid hospitalization<sup>[12]</sup>. The results of this study could focus on exercise-based CR, which is a critical intervention aimed at improving outcomes for patients with HF. This emphasizes the role of physical activity in the management of this disease. Given that, there is still a difference in the type and severity of endurance and resistance exercises that can have optimal effects on chronic HF. The aim of this study was to scrutinize the effects of exercise-based CR on echocardiographic parameters and functional capacity in patients with HF.

## Patients and methods Study population

A randomized, two-arm parallel clinical trial was conducted to recruit a total of 76 adult subjects, with HF from individuals who visited the cardiologist at Dr. Heshmat Hospital in Rasht, Iran. After initial ambulatory screening by a cardiologist, patients were systematically allocated into two distinct groups: one group underwent concurrent training, while the other served as the CG. In our open-label study, we employed a 1:1 computer-generated randomization ratio for participant allocation. At the onset of the study, each patient performed 6-min walk tests (6MWTs, and their Borg score was evaluated at the end of each test. Concurrently, echocardiography tests by single cardiologist were conducted to assess various cardiac parameters. These procedures were repeated after an 8-week interval, providing patients' heart function and exercise capacity throughout the study. These training sessions were held in Heshmat Hospital, Rasht by trained nurse. The CG received the usual treatment and care that the hospital received.

The sample size was calculated to be 38 people in each group. This calculation was determined from the study by Ulbrich *et al*<sup>[13]</sup>, which aimed to compare the effects of training with different intensity on physical fitness, hemodynamic performance, and quality of life in 12 weeks of training. Among the comparisons are blood pressure, heart rate, EF, VO2 peak, and 6-min test. The number of samples in the present study was calculated using the following formula, considering the error of  $\alpha = 0.05$ ,  $\beta = 0.10$ , and 10% probability of falling:

$$N = \frac{\left(Z1 - \frac{\alpha}{2} + Z1 - \beta\right) 2(S1^2 + S2^2)}{\left(\mu_1 - \mu_2\right)^2} = 38$$

The following details outline our search strategy:

We systematically searched multiple databases, including PubMed, Scopus, and Web of Science, to ensure a broad coverage of relevant literature. The search utilized specific keywords and phrases such as "exercise-based cardiac rehabilitation," "heart failure," "echocardiographic parameters," "functional capacity," and "aerobic resistance training." Boolean operators (AND, OR) were employed to refine the search results. Studies were included if they focused on adult patients with HF undergoing exercise-based rehabilitation interventions. Excluded studies were those that did not provide relevant outcomes related to echocardiographic parameters or functional capacity. The

literature search was limited to studies published in the last 10 years to ensure that the findings were current and relevant.

#### Inclusion and exclusion criteria

Patients with HF were recruited from the division of Cardiology at Dr. Heshmat Hospital in Rasht and enrolled during an ambulatory visit.

The following terms were applied to the inclusion criteria: adults aged between 40 and 70 years with a medical diagnosis of HF (with the diagnosis of HF according to the classification of the New York Heart Association (NYHA), patients with HF II and III are selected and documented as having HFrEF with EF≤40%) along with the completion of 6MWT.

The exclusion criteria encompass patients with NYHA class IV HF, those experiencing acute HF or a recent acute coronary syndrome, individuals diagnosed with acute myocarditis or cardiomyopathy, patients with severe aortic stenosis, and those with musculoskeletal complications<sup>[14]</sup>. Initially, patients were informed about the study's benefits and drawbacks, and after documenting each patient's information, we obtained their signed consent.

#### The training intervention

Participants engaged in concurrent exercise training that spanned 8 weeks. During this period, they conducted five sessions weekly, which included three aerobic and two resistance sessions. Each of these sessions lasted for a duration of 50-60 min. A minimum rest period of 48 h was ensured between resistance training sessions. Each session began with a 5-min dynamic flexibility routine followed by concurrent exercises. This was followed by aerobic training, which involved walking performed at 60%-75% of the participants' heart rate reserve for a duration of 30–40 min<sup>[15]</sup>. Resistance training was also incorporated, with exercises initiated at 40% of one repetition maximum (1RM) for upper body exercises and 50% of 1RM for lower body exercises. Prior to baseline testing, patients were familiarized with resistance training to ensure correct lifting and breathing techniques and to avoid the Valsalva maneuver<sup>[15,16]</sup>. The resistance was progressively increased by 5%-10% up to 70%. The resistance exercises included lateral raise, chest press, back row, biceps curl, triceps kickbacks, half squat, leg extension, and calf raise, each performed in one set of 12-15 repetitions. Resistance was provided by red, green, and blue theraband, with intensity ranging from low to moderate based on their color and stiffness. Each session concluded with a 5-min static stretching and breathing exercises. Before the start of the program, participants were educated on how to measure their heart rate. In this study, aerobic and resistance exercises were provided by a trained nurse in the form of a booklet along with daily follow-up and control through telephone calls.

#### Measurements

Before and after the 8-week training protocol, both the control and combined training groups underwent the 6MWT and an echocardiography test. For the 6MWT, patients were fully informed about the purpose and procedure of the test. Each patient performed two rounds of the 6MWT, with a rest period

of 30 min between the two tests. This was done at the beginning and after 8 weeks of the training protocol. At the end of each 6-min test, patients' perceived exertion was evaluated using the Borg scale, which ranges from 0 to 10. A 2D echocardiography device (Affinity 50, Philips, USA) was used based on the guidelines of the American Society of Echocardiography to measure LVEDD and LVESD. Then, Simpson's revised method was used for calculation of EF<sup>[17]</sup>.

#### Statistical analysis

Descriptive variables are presented as frequencies (%), and numeric variables are presented as the mean (standard deviation). The demographic characteristics of the participants in both the experimental group and CG were described using chisquare and Fisher's exact tests. For the pre- and post-measurements, a two-way repeated measures ANOVA was used to examine the effect of time (pre vs. post), the effect of the group

(control vs. experimental), and the interaction between time and group. This allowed us to determine whether the changes over time differed between the two groups. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

#### **Results**

Out of 80 patients who were evaluated for eligibility, 76 were selected and the study began. Accordingly, 76 individuals ended the trial, which is depicted comprehensively in Figure 1.

In this study, patients were included (mean age  $68.2 \pm 4.8$  years). For each group, baseline clinical characteristics are presented in Table 1. No statistically significant difference was found between the two intervention group (IG) and CG in terms of age, gender, hypertension, diabetes mellitus, and hyperlipidemia (P < 0.05) (Table 1).

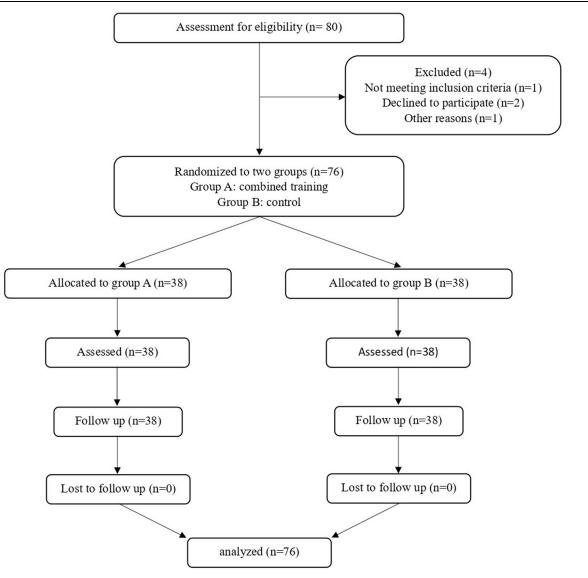


Figure 1. Flow diagram of the studied patients.

Table 1

#### Basic characteristics of participated patient groups.

Variables	Intervention (38 patients)	Control (38 patients)	<i>P</i> -value
Age (years)	$67.42 \pm 5.83$	$69 \pm 3.58$	0.45
Sex (male)	31 (81.6)	30 (78.9)	0.77
Hypertension	12 (34.3)	23 (65.7)	0.55
Diabetes mellitus	11 (57.9)	8 (42.1)	
Hyperlipidemia	12 (31.6)	17 (44.7)	

Multiple pairwise comparisons test (time effect) for outcome variables within each group revealed that there was a significant (P < 0.05) decrease in LVEDD and LVESD at post-intervention compared to pre-intervention within the IG (P = 0.001). This significant decrease in LVEDD and LVESD at post-intervention is in favor of IG, followed by CG. There was significant (P < 0.05) increase in EF and 6MWT at post-intervention compared to pre-intervention within IG (P = 0.0001) and (P = 0.0001), respectively) (Table 2).

#### **Discussion**

The present study implemented an 8-week concurrent exercise program that combined aerobic and resistance training using hand and leg weights, Therabands, and walking exercises, along with daily breathing exercises. Participants completed the program without significant issues or serious side effects. This research introduces a novel approach to CR for patients with HFrEF by integrating both aerobic and resistance exercises, unlike many existing studies that focus on only one type of training<sup>[7,18,19]</sup>. The findings demonstrated significant improvements in echocardiographic parameters, including left

Table 2

Within- and between-group comparisons for outcome variables.

		Groups (Mean ± SD)		
Outcome variables	Items	Intervention	Control	<i>P</i> -value
LVEDD (mm)	Pre-treatment Post-treatment P-value	55.23 ± 4.73 46.71 ± 5.35 0.0001	51.39 ± 4.48 53.89 ± 4.73 0.0001	0.0001
LVESD (mm)	Pre-treatment Post-treatment P-value	49 ± 6 39 ± 5.26 0.0001	41.86 ± 4.91 45.55 ± 4.8 0.0001	0.0001
DIVS (mm)	Pre-treatment Post-treatment P-value	9.51 ± 1.4	$10.34 \pm 0.62$ $10.57 \pm 0.82$ $0.04$	0.22
PWD (mm)	Pre-treatment Post-treatment P-value	9.62 ± 1.42		0.63
LVEF (%)	Pre-treatment Post-treatment P-value	$30.92 \pm 5.3$	31.84 ± 4.41 28.28 ± 4.39 0.0001	0.0001
6MWT(m)	Pre-treatment		214.2 ± 31.16	0.0001

Data are expressed as mean  $\pm$  SD; \*Significant (P < 0.05).

6MWT, 6-min walking test; DIVS, diastolic thickness of the interventricular septum; LVEDD, left ventricle end-diastolic dimension; LVEF, left ventricle ejection fraction; LVESD, left ventricle end-systolic dimension, PWD, pulsed wave Doppler; SD, standard deviation.

ventricular ejection fraction (EF) and functional capacity as measured by the 6MWT, highlighting the effectiveness of this dual-training strategy in enhancing multiple aspects of physical fitness and cardiac function.

Regarding echocardiographic outcomes, it was shown that there was a significant decrease in LVEDD and LVESD at post-treatment compared to pre-treatment within IG. This significant decrease in LVEDD and LVESD at post-treatment is in favor of IG, followed by CG. There was a significant increase in EF and 6MWT at post-treatment compared to pre-treatment within IG.

Abdeen et al. found that the 6MWT significantly increased between the groups<sup>[2]</sup>. Hassanpour Dehkordi study's results showed that there was a significant change in left ventricular diameter and EF after exercise training in the experimental group<sup>[19]</sup>. These two findings are consistent with the current findings of this investigation. In fact, exercise training leads to positive effects, including a reduction in the thickness of the left ventricular wall and an improved EF[2,7,8,11,19]. In scientific investigations, experts contended that a 24-week training program led to substantial enhancements in LVESD, LVEDD, and EF. Specifically, the study revealed a 10% rise in EF and a corresponding 10% reduction in the volume of the  $LV^{[20,21]}$ . The differences in their study were not significant between the experimental group and CG. However, unlike the present study, the EF differences were not significant between these groups. Interestingly, although elderly individuals experience reduced LVESD with exercise, this deficit is offset by an increase in LVEDD during the exercises<sup>[22,23]</sup>.

While many studies have emphasized exercise intensity, only a limited number have investigated the duration and specific types of training. Metabolite buildup in active contractile muscles leads to the expansion of muscular arteries, resulting in up to a 4-fold increase in blood flow to skeletal muscles compared to the resting state. This, in turn, reduces a ortic output impedance. The size and position of muscle groups involved in exercise impact hemodynamic responses differently. Hand exercises, for instance, exhibit variations in sympathetic output, peripheral vasodilation, and venous and metabolic return. These effects are influenced not only by muscle mass but also by the stabilizing muscles engaged during hand exercises<sup>[24]</sup>. The positive outcomes observed in this study can encourage healthcare professionals to focus on holistic treatment approaches that include physical activity as a key component. The results indicate that structured exercise regimens can be effectively implemented within CR programs, potentially leading to reduced rates of hospitalization and improved patient outcomes. This is consistent with findings from other studies that indicate exercise-based rehabilitation reduces rehospitalization rates and enhances health-related quality of life<sup>[25,26]</sup>. Also, the study opens avenues for further research into the long-term effects of exercise-based interventions, particularly regarding sustainability and adherence over time. Understanding how these programs can be maintained or adapted for different populations, including older adults or those with comorbidities, will be crucial for maximizing their benefits.

#### Conclusion

It was determined that the 8-week exercise program appears to yield the most favorable outcomes in enhancing echocardiographic measures and functional capacity among HFrEF patients. In summary, this study provides compelling evidence that exercise-based CR can lead to meaningful improvements in echocardiographic parameters and functional capacity among older adults with HF, advocating for its broader implementation in clinical settings.

#### Limitations

This study had several limitations; one of these limitations was the small sample size, which made it impossible to check the basic characteristics of the patients. The other limitation of this research is that it was conducted at a single center, and the results may not be representative of different healthcare environments or patient populations, which can affect the applicability of the findings.

#### **Suggestions and recommendations**

Although the study included 76 participants, the relatively small sample size may limit the generalizability of the findings to broader populations. It is suggested that larger studies are needed to confirm these results across diverse demographics and clinical settings.

#### **Ethical approval**

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Guilan University of Medical Sciences (IR. GUMS.REC.1396.107). In addition, it is registered with Iranian Registry of Clinical Trials (accessed on 18 July 2017, identifier: IRCT2017070534911N1).

#### Consent

Initially, patients were informed about the study's benefits and drawbacks and after documenting each patient's information, we obtained their signed consent.

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None

#### **Author's contribution**

Z.M. and A.S. contributed to study concept. A.S. and M.G. contributed to design and data collection. Z.A. contributed to data analysis or interpretation. Z.M. and Z.A. contributed to writing the paper.

#### **Conflicts of interest disclosure**

The authors declare that they have no competing interests.

### Research registration unique identifying number (UIN)

None.

#### Guarantor

None.

#### Provenance and peer review

None.

#### **Data availability statement**

The datasets used and analyzed during the current study are available from the corresponding author.

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