

Autonomic function change following a supervised exercise program in patients with congestive heart failure

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Original Article

Abstract

BACKGROUND: Few studies have investigated changes in autonomic function after training in patients with cardiovascular diseases, particularly patients with congestive heart failure (CHF). Heart rate recovery (HRR) is a strong predictor of mortality in coronary artery disease (CAD) patients. The aim of this study was to determine the effect of 8 weeks of supervised exercise training on autonomic function, which were assessed by heart rate, systolic blood pressure (SBP), and rate-pressure product (RPP) in CHF patients.

METHODS: 65 patients aged 57-82 years with CHF were assigned to two groups randomly. The first group received a supervised 8-week aerobic training program of 30-45 min sessions, 3 days per week on alternate days, while controls received standard medical care and were followed up. Body weight, body mass index, functional capacity, resting heart rate, HRR, resting systolic blood pressure, peak heart rate, peak systolic blood pressure, and RPP were measured before and after the study period. Medications and diet recommendations remained unchanged in both groups during the study period.

RESULTS: The exercise group consisted of 33 patients with mean age of 61.54 ± 5.89 years and the controls were 32 patients with mean age of 60.94 ± 5.03 years. One-way analysis of variance (ANOVA) with repeated measures revealed a statistically significant difference in the exercise group compared to the control group regarding body mass index, resting heart rate, heart rate recover, functional capacity, peak heart rate, peak systolic blood pressure, peak RPP after 8 weeks ($P \leq 0.05$).

CONCLUSION: In conclusion, a multidisciplinary CR program with supervised exercise training support significantly improves functional capacity and autonomic function in CHF patients. Therefore, a supervised and guided exercise training program is safe and beneficial for patients with CHF with different etiologies.

Keywords: Aerobic Exercise, Cardiorespiratory Fitness, Hemodynamics, Autonomic Function, CHF

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Introduction

Cardiovascular diseases, particularly congestive heart failure (CHF), are the most common cause of human deaths in the world.¹ According to WHO estimates, in 2002, 16.7 million people in the world die of cardiovascular diseases each year.² According to previous studies 46% of deaths in Iran each year are from cardiovascular disease.³⁻⁴ Autonomic nervous system dysfunction appears to be involved in the pathophysiology of coronary artery disease and is associated with an increased risk of death.⁵⁻⁷

Autonomic function can be appraised by measuring resting heart rate, heart rate variability, or heart rate recovery (HRR) following exercise.⁶⁻⁷

Physical activity and function capacity improvement is critical in primary and secondary prevention of cardiovascular disease.⁸ Regular aerobic exercise training and cardiac rehabilitation has been shown to reduce the rate of mortality, improve functional capacity, and control the risk factors in myocardial infarction patients.⁹⁻¹²

The term cardiac rehabilitation refers to

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coordinated, multifaceted interventions designed to optimize a cardiac patient's physical, psychological, and social functioning, in addition to stabilizing, slowing, or even reversing the progression of the underlying atherosclerotic processes, thereby reducing morbidity and mortality.¹³⁻¹⁴

Exercise in the outpatient setting is performed under the supervision of health care providers with monitoring based on exercise tolerance test results. Moreover, patients are typically advised to complete a period of supervised aerobic exercise training as adherence to these programs is usually insufficient.¹⁵

The evaluation of the cardiovascular response to various modes of aerobic exercise is critical to the clinician supervising and prescribing exercise programs. Although an acute period of aerobic exercise can cause critical cardiovascular changes, there are few and controversial published data on the effect of different exercise intensities on blood pressure, heart rate, and rate pressure product (RPP), an index of myocardial oxygen consumption, which is calculated by multiplying the heart rate (HR) and the SBP).^{16,17} Other studies have used RPP to estimate changes in myocardial oxygen consumption during physical training of individuals with myocardial infarction disease. Ribeiro et al. observed a significant decrease in resting heart rate, while they found no significant change in systolic and diastolic blood pressure, and rate-pressure product at rest and following exercise sessions in patients after a first acute myocardial infarction.¹⁸ Robinson and Collier et al. found that effort angina pectoris (angina threshold) was reproducible at fixed levels of the RPP.^{19,20} May and Nagle reported that the RPP of patients with coronary artery disease significantly increased during maximal exercise, and decreased significantly during submaximal exercise.²¹ De Backer et al. reported a significant decrease in RPP during each of the three submaximal work loads in the experimental group with anterior myocardial infarctions.²² Kargarfard et al. found an increase in cardiac function and no changes in diastolic indices during 8 weeks of aerobic exercise training in myocardial patients.²³ Due to the importance of cardiac rehabilitation for the performance of many daily activities, we were interested in evaluating the effects of an 8-week aerobic exercise program on BP, HR, and RPP in patients with congestive heart failure (CHF).

Materials and Methods

Subjects

The current study was approved by the Ethics

Committee of Isfahan Cardiovascular Research institute (ICRI, a WHO collaborating center) and the University of Isfahan, before the study was launched.

Male and female patients who were referred to ICRI with a history of myocardial infarction and a diagnosis of CHF between June 2010 and December 2011 were invited to take part in this study.

The inclusion criteria were: being residents of Isfahan; aged over 50 years; currently not taking part in regular physical activities; having heart failure for at least three months; having a left ventricular ejection fraction of $\leq 35\%$ on echocardiogram and have been in functional class (FC) II according to the New York Heart Association (NYHA) in the previous 2 years. Patients should be referred by a cardiologist. The exclusion criteria included NYHA FC, acute myocardial infarction, or revascularization within the past 4 months, hypotension, unstable angina, ventricular or symptomatic arrhythmias, obstructive aortic valve disease, chronic obstructive pulmonary disease, hypertrophic obstructive cardiomyopathy, severe musculoskeletal problems preventing exercise, and case-note reported dementia or current severe psychiatric disorder.

Sixty-five male and female patients with CHF agreed to participate in the study. They were assigned randomly to two groups of exercise ($n = 33$) and control ($n = 32$). Participants signed a written informed consent after being informed of the details of the study.

There was no alteration in the prescribed medications and diet in both groups throughout the study. All subjects underwent comprehensive medical screening prior to participation, including medical history, physical examination, and stress testing. The patients did not participate in an exercise program for at least 3 months prior to the study; they were instructed to avoid any extra exercise not included in the study training program.

Experimental design

All patients followed a familiarization training period of 2 weeks. Thereafter, each patient underwent anthropometric evaluation, physiological evaluation, and exercise stress testing using the Naughton protocol. Afterwards, they participated in a supervised and systematic exercise program of aerobic training three times per week for 8 weeks. The training program was arranged to provide an alternative day for the replacement of a possible lost session during the week. The baseline assessment was repeated after 8 weeks of training.

Aerobic training program

Aerobic exercise consisted of walking/jogging on

the treadmill three times per week. Each session lasted about 45-60 min including a warm-up period (5-10 min), stretching exercises (10 min), the main program with treadmill exercise (15-30 min), and a cool-down period (15 min including stretching). During the first 4 weeks, the intensity of aerobic exercise was 60-70% of maximum heart rate (HRmax) achieved during stress testing. Thereafter, training intensity was increased to 70-80% HRmax according to the individual adaptation observed during training sessions.

Testing procedures

Demographic measures and medical history

A detailed medical history was obtained from each participant. The medical history addressed all of the aforementioned exclusion criteria, as well as history of hyperlipidemia, dyspnea, diabetes hypertension or other symptoms of CHF.

Height was measured using a stadiometer, with the measurement taken to the nearest 0.1 cm. Weight was measured using a balance scale, with the measurement taken to the nearest 0.1 kg. Height and weight measurements were then used to calculate body mass index (BMI); $BMI = (\text{weight in kilograms})/(\text{height in meters}^2)$. Waist-to-hip ratio was measured with a measuring tape, with a horizontal measure at both the waist and hip sites, taken to the nearest 0.1 cm. Blood pressure and heart rate were measured with a sphygmomanometer following 30 minutes of rest.

Exercise stress testing

All patients underwent a symptom-limited exercise test on the treadmill with electrocardiogram (ECG) monitoring according to the modified Naughton protocol. The Naughton protocol is a submaximal study which is used for high-risk patients. It uses 10 3-min exercise periods. The modified Naughton protocol has 2-min stages and starts at a lower metabolic equivalent (MET) workload increasing by patients stop because of either fatigue or dyspnea. It contains a 4-min warm-up and a set speed of 2.0 miles per hour (mph). The grade increases 3.5% every 2 min until maximum effort is achieved. This approach allows for a better tolerated gradual progression in exercise. Moreover, it is a more accurate assessment of functional capacity. During aerobic exercise sessions in these patients, exertion levels are often evaluated by the Borg Rating of Perceived Exertion Scale, because the rate of perceived exertion and heart rate (HR) are linearly concerned with each other and work intensity.^{24,25}

Resting HR and peak HR were measured using a 12-lead electrocardiograph with an automatic ST-segment analysis, while blood pressure was recorded

manually at rest and then at 3-min intervals during the stress test.

Peak HR was considered the highest mean 10-s value achieved during the test. Blood pressure was measured with a mercury sphygmomanometer at rest, during the last 15 seconds of exercise near the end of the test. Peak systolic and diastolic blood pressures were recorded as the highest value achieved during the test. PRR product was computed by multiplying peak HR by peak systolic blood pressure. HRR was determined by calculating the difference between HR at peak exercise and HR 1 min after completion of exercise.¹⁰ Patients were instructed to sit after ending the test, and there was no cool-down period until after HRR was recorded.¹¹ There was then a 4-min cool-down period that consisted of light walking at 2 km/h on a flat treadmill (0% grade).

Statistical analysis

All data are expressed as means \pm SD. Student's t-test was used to compare the baseline characteristics of exercise and control groups. Paired t-tests were performed on continuous variables to determine differences in cardiorespiratory fitness and hemodynamic measurements in the exercise and control groups. Finally, one-way ANOVA with repeated measures was performed on cardiorespiratory fitness and hemodynamic variables to determine differences between the two groups after 8 weeks. SPSS for Windows (version 18; SPSS Inc., Chicago, IL., USA) was used to analyze all data. Statistical significance was assumed for P values $<$ 0.05.

Results

A total of 70 eligible patients with CHF were recruited from June 2010 to December 2011, but only 65 (33 exercise and 32 controls) patients completed the study within 8 weeks. Five of the 70 patients, 2 in the exercise group and 3 in the control group, were not able to complete the study for non-medical reasons and were not included in the data analysis.

Table 1 lists the baseline data (mean \pm SD) for age, height, body weight, body mass index, resting heart rate, heart rate recovery, resting diastolic blood pressure, resting systolic blood pressure, peak functional capacity, peak heart rate, and peak rate pressure product between cases and controls.

The patients had a mean age of 61.25 ± 5.45 years, mean height of 167.12 ± 7.94 cm, mean weight of 73.06 ± 7.80 kg, and mean BMI of 26.11 ± 1.45 kg/m². There were no significant differences in all characteristics of the cardiorespiratory fitness and hemodynamics

between exercise and control groups at baseline ($P > 0.05$; Table 1).

At the initial exercise stress testing, before physical rehabilitation, there was no significant difference between groups in regard to functional capacity; which were 5.11 ± 0.93 METs in exercise group and 5.19 ± 0.83 METs in control group.

Physical training was prescribed on the basis of initial exercise capacity and exercise tolerance, and the first part of rehabilitation was performed as a physical rehabilitation. At the end of the rehabilitation phase, the functional capacity was assessed again by the same exercise stress protocol

as the initial one.

Table 2 lists the mean \pm SD values for all of cardiorespiratory fitness and hemodynamics parameters for each group before and after the 8-week study. It also shows the differences in all outcomes included in the study from the baseline to eight weeks, within and between the exercise and control groups. Patients in the exercise group have shown statistically significant improvement in resting heart rate, heart rate recovery, resting systolic blood pressure, peak functional capacity, peak heart rate, and peak RPP except for the body weight, body mass index and resting diastolic blood pressure.

Table 1. Baseline characteristics of cardiorespiratory fitness and hemodynamics in heart failure patients before the study

Characteristics	Exercise training group (n = 33)	Control group (n = 32)	P
Age (year)	61.54 \pm 5.89	60.94 \pm 5.03	0.66
Gender (male: female)	22: 11	17: 15	> 0.05
Weight (kg)	73.54 \pm 7.54	72.56 \pm 8.16	0.62
Height (cm)	168.30 \pm 7.94	165.91 \pm 7.88	0.23
BMI (kg/h ²)	25.93 \pm 1.44	26.30 \pm 1.46	0.32
FC (METs)	5.11 \pm 0.93	5.19 \pm 0.83	0.70
RHR (beats/min)	87.03 \pm 4.50	86.19 \pm 3.75	0.42
RSBP (mmHg)	151.50 \pm 6.51	148.41 \pm 6.79	0.18
RDBP (mmHg)	85.06 \pm 11.96	90.06 \pm 9.92	0.07
Peak HR (beats/min)	130.01 \pm 4.05	130.46 \pm 3.13	0.61
HRR (beats/min)	21.13 \pm 4.44	20.66 \pm 4.93	0.69
Peak SBP (mmHg)	162.45 \pm 5.93	159.34 \pm 6.53	0.18
Peak DBP (mmHg)	99.52 \pm 5.85	98.31 \pm 5.81	0.41
Peak RPP (mmHg \times bpm)	21117.54 \pm 958.89	20789.98 \pm 1013.88	0.19

Note: BMI: body mass index; RHR: resting heart rate; HRR: heart rate recovery; RDBP: resting diastolic blood pressure; RSBP: resting systolic blood pressure; Peak FC: Peak Functional Capacity; Peak HR: Peak heart rate; Peak RPP: Peak rate pressure product; derived from independent Student t-tests

Table 2. Comparison of cardiorespiratory fitness and hemodynamics of exercise and control group patients before and after the study

Characteristics	Exercise (n = 33)			Control (n = 32)			P**
	Before	After	P*	Before	After	P*	
Weight (kg)	73.54 \pm 7.54	73.14 \pm 7.32	0.12	72.56 \pm 8.16	73.98 \pm 8.64	0.02	0.97
BMI (kg/h ²)	25.93 \pm 1.44	25.79 \pm 1.41	0.14	26.30 \pm 1.46	26.86 \pm 1.44	0.01	0.04
EF (%)	32.30 \pm 3.87	37.94 \pm 5.33	0.000	31.44 \pm 3.61	30.62 \pm 3.22	0.11	0.000
FC (METs)	5.11 \pm 0.93	6.44 \pm 1.22	0.000	5.19 \pm 0.83	4.85 \pm 0.84	0.02	0.001
RHR (beats/min)	87.03 \pm 4.50	83.33 \pm 5.04	0.000	86.19 \pm 3.75	88.22 \pm 4.67	0.05	0.03
RSBP (mmHg)	152.45 \pm 5.93	150.24 \pm 6.35	0.02	149.34 \pm 6.53	149.03 \pm 7.83	0.82	0.14
RDBP (mmHg)	85.06 \pm 11.96	83.54 \pm 10.44	0.10	90.06 \pm 9.92	90.97 \pm 10.15	0.22	0.02
Peak HR (beats/min)	130.01 \pm 4.05	141.64 \pm 4.61	0.000	130.46 \pm 3.13	132.99 \pm 4.35	0.01	0.000
HRR (beats/min)	21.13 \pm 4.44	25.97 \pm 6.34	0.000	20.66 \pm 4.93	19.62 \pm 4.27	0.02	0.003
Peak SBP (mmHg)	162.45 \pm 5.93	173.00 \pm 7.81	0.000	159.34 \pm 6.53	162.03 \pm 7.83	0.06	0.000
Peak DBP (mmHg)	99.52 \pm 5.85	97.70 \pm 4.87	0.003	98.31 \pm 5.81	99.78 \pm 6.08	0.03	0.74
Peak RPP (mmHg \times bpm)	21117.54 \pm 958.89	24513.64 \pm 1527.60	0.001	20790.98 \pm 1013.88	21553.12 \pm 1333.38	0.005	0.000

Note: BMI: body mass index; EF: ejection fraction; RHR: resting heart rate; HRR: heart rate recovery; RDBP: resting diastolic blood pressure; RSBP: resting systolic blood pressure; FC: functional capacity; Peak HR: Peak heart rate; Peak SBP: peak systolic blood pressure; Peak DBP: peak diastolic blood pressure; Peak RPP: Peak rate pressure product; * significant difference between before and after the intervention in each group; ** significant difference between exercise and control groups at the 8th week

Functional capacity and ejection fraction were increased in the exercise group from 5.11 ± 0.93 METs to 6.44 ± 1.22 METs, and 32.30 ± 3.87 to 37.94 ± 5.33 , respectively ($P < 0.001$). However, they were decreased in the control group ($P < 0.001$).

At the end of the rehabilitation phase, at the same sub maximal exercise level, the resting HR and resting SBP were significantly reduced in the exercise group ($P < 0.01$), when compared with pre-training values (Table 2). Moreover, the resting HR increased significantly in the control group ($P < 0.05$).

One-way analysis of variances (ANOVA) with repeated measures revealed a statistically significant difference in the exercise group compared with control group in their body mass index, resting heart rate, heart rate recovery, functional capacity, peak heart rate, peak systolic blood pressure, and peak rate pressure product ($P \leq 0.05$; Table 2).

Discussion

Most interventional studies evaluated the efficacy of aerobic exercise in lowering BP and HR. Information regarding the efficacy of aerobic exercise training on autonomic function factors is limited.

The present study aimed to evaluate the effects of 8 weeks aerobic exercise training on RPP, maximal and rest heart rates, and blood pressure in patients with CHF. To define the effect of exercise training per se, other important variables were controlled such as medications use and diet. The main finding of our investigation is that cardiac rehabilitation independently improves cardiac autonomic function.

In this study, we found that an 8 week aerobic exercise program improved resting heart rate, heart rate recovery, resting systolic blood pressure, peak functional capacity, peak heart rate, and RPP significantly ($P < 0.05$). While the body weight, body mass index, and resting diastolic blood pressure in the exercise group did not show any significant changes. At the end of the rehabilitation, exercise capacity and ejection fraction were increased significantly in the exercise group, while they were decreased in the control group ($P < 0.001$).

At the end of the rehabilitation phase, at the same sub maximal exercise level, the resting HR and resting SBP were significantly reduced in the exercise group ($P < 0.01$), when compared with pre-training values (Table 2). However, there was a

significant increase in the resting HR in the control group ($P < 0.05$).

Furthermore, in comparison with baseline data, the exercise group showed significantly higher scores in functional capacity, heart rate recovery, peak heart rate, peak systolic blood pressure, peak diastolic blood pressure, and peak RPP following the 8-week exercise-training program.

One-way analysis of variances (ANOVA) with repeated measures revealed a statistically significant difference between the exercise group and the control group in body mass index, resting heart rate, heart rate recovery, functional capacity, peak heart rate, peak systolic blood pressure, and peak rate pressure product ($P \leq 0.05$).

Previous studies have reported that autonomic nervous system dysfunction appears to be involved in the pathophysiology of coronary artery disease and is associated with an increased risk of death.⁵⁻⁷ Autonomic function can be appraised by measuring resting heart rate, heart rate variability, or heart rate recovery (HRR) following exercise.⁶⁻⁷ Thus, the positive effect of cardiac rehabilitation on cardiac autonomic nervous system is important. Following the rehabilitation program in the present study, all factors in the training group had a significant improvement.

These positive effects on the autonomic nervous system suggested that the results of the current study are supported by decreasing RPP, maximal and resting heart rates, and blood pressure (systolic, mean, and diastolic) observed in the exercise-training group.

In healthy subjects and athletes, heart rate rapidly decreased after exercise. However, during exercise due to the withdrawal of parasympathetic tone and increased sympathetic tone, heart rate increases. Immediately after exercise, heart rate decreases due to rapid reactivation of the parasympathetic nervous system. The ability of the heart rate to recover after exercise is related to the capacity of the cardiovascular system to inverse the autonomic nervous system and baroreceptors adaptation, which is often called vagal reactivation.²⁶

A study by Wu TY et al. (2007) showed that both systolic and diastolic blood pressures at rest and after 8 weeks of exercise were significantly decreased in the training group. However, changes in blood pressure were not significantly different between the training and control groups. This may be due to the relatively low number of patients ($n = 18$ per group) to achieve statistical significance.²⁷

Another study performed by Ribeiro et al. showed that resting heart rate decreased by 5 beats per minute in the exercise group. However, there was no change observed in systolic and diastolic blood pressures, and RPP at rest and peak; this finding is inconsistent with the results of this research.¹⁸ The results of the present study is consistent with Forjaz et al., May and Nagle and MacMasters et al.^{16,21,28}

Adams et al. showed that the mean RPP during clinical training sessions on the treadmill was far below the clinically safe rate for the training group.²⁹ In the study by Kim et al., no significant differences were observed in both groups after a 6-week rehabilitation program regarding rest and peak systolic and diastolic blood pressures, resting heart rate, and maximal pressure produced. However, maximum heart rate and submaximal RPP were significantly different.³⁰ Ahn et al. reported that in comparison to the exercise group, there was no significant difference in the RPP of the control group. Such significant progression can be credited to cardiac rehabilitation by improving exercise tolerance and exercise duration, as well as increasing heart rate and systolic blood pressure.³¹ The Asian Department of Cardiovascular Prevention and Rehabilitation (2011) reported that aerobic exercise has a moderate effect on resting heart rate, caused no changes in systolic and diastolic blood pressure, and has a strong effect on submaximal RPP.³² However, the results of this study support previously mentioned studies.

In conclusion, a multidisciplinary CR program with supervised exercise training support significantly improves functional capacity and hemodynamics parameters in CHF patients. Therefore, a supervised and guided exercise training program is safe and beneficial for patients with CHF with different etiologies.

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Conflict of Interests

Authors have no conflict of interests.

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