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Mai H. Hassan  
NHI

Mohamad El Bordy  
NHI, mohamedbrdy@yahoo.com

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# Efficacy of moderate exercise training on heart rate variability and left ventricular remodeling after myocardial infarction

Mohamad El Bordy<sup>a</sup>, Mai H. Hassan<sup>b</sup>

Departments of <sup>a</sup>Cardiology and <sup>b</sup>Physical Therapy, NHI, Cairo, Egypt

## Abstract

### Background

After myocardial infarction (MI), elevated sympathetic activity and/or reduced parasympathetic activity are observed. As a result, these patients have a decreased heart rate variability (HRV), which has been linked to an elevated risk of adverse effects and death. Following MI, the remodeling of the left ventricle (LV) is a complex and multifactorial mechanism, with therapeutic and prognostic consequences. Medications that reduced LV improved survival and standard of living.

### Aim

We aimed to evaluate the effect of continuous exercise remodeling training on HRV, function capacity [6-min walk test (6MWT)], and LV remodeling in patients who had experienced MI.

### Patients and methods

One month after having MI, 40 eligible male patients aged 45–55 years old were recruited. Patients underwent a supervised intensive CR recovery program consisting of continuous aerobic exercise. Evaluation of the effect of this program was done by clinical examination, transthoracic echocardiography to calculate ejection fraction, 6MWT, and Holter ECG 24 h to measure different HRV parameters. All patients received 36 training sessions (three times/week for 12 weeks). The results of these procedures were compared before and after this program.

### Results

According to the current results, the mean pretreatment and posttreatment 6MWT values were  $208.65 \pm 24.62$  and  $360.98 \pm 109.78$ , respectively, with an improvement percentage of 55.79%. Irrespective of time or frequency domain, HRV parameters were markedly improved after treatment compared with pretreatment values. Ejection fraction % was significantly improved by 14.82%.

### Conclusion

Exercise training tends to be a beneficial clinical technique for patients with MI who have an unbalanced autonomic function, which is manifested by improvement of HRV parameters. Exercise training improves blood pressure and resting heart rate. Improvement of 6MWT parameters occurred after exercise training.

**Keywords:** Exercise training, heart rate variability, left ventricle remodeling, myocardial infarction

## INTRODUCTION

Cardiovascular disease is one of the world's most well-known health problems. Patients after myocardial infarction (MI) have an imbalanced autonomic cardiac function, with the sympathetic activity predominating at the expense of the parasympathetic one. This can be seen in the decreased heart rate variability (HRV), which is linked to cardiovascular event risk in these patients, such as malignant ventricular arrhythmias and subsequent sudden death [1,2].

Exercise training has been suggested as a beneficial complement to current medical therapy in patients who have experienced MI along with left ventricular (LV) systolic dysfunction not only

**Correspondence to:** Mohamed El Bordy, MD Cardiology, Department of Cardiology, National Heart Institute, Cairo 11461, Egypt  
Tel: +01124224861;  
E-mail: mohamedbrdy@yahoo.com

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to avoid the worsening of LV dysfunction and its associated morbidity and mortality but also to achieve symptomatic and functional change. Substantial changes in exercise ability were observed in patients with moderate to extreme LV dysfunction without significant adverse events. In these patients, post-MI training increases maximum cardiac output, corrects skeletal muscle metabolic defects, and improves the quality of life. Other studies have shown that exercise can mitigate and even reverse ventricular remodeling following a recent acute MI with systolic dysfunction [3,4].

One of the straightforward, inexpensive, accurate, and reliable methods for assessing functional capacity is the 6-min walk test (6MWT). This test, which is commonly used in the management of heart disease, is also critical for initiating cardiac rehabilitation early, which is associated with reduced mortality and increased quality of life. The 6MWT may be a safe and feasible choice for assessing functional capacity early after acute MI. It is a self-regulated effort measure that can accurately represent the level of daily living activities [5].

### Aim

In patients who experienced MI, we aimed to evaluate the effect of continuous exercise training on HRV, function capacity (6MWT), and LV remodeling.

## PATIENTS AND METHODS

The Ethical Review Board of the General Health Organization of Teaching Hospitals and Institutes (GOTHI) approved the study. Each patient signed a written consent form.

### Patients

A total of 40 eligible male patients aged 45–55 years old were recruited from National Heart Institute 1 month after having MI. They were receiving optimal medical care during the study, with no significant changes to their treatment plan. Sinus rhythm, blood pressure, diabetes, and New York Heart Association classes II–III were controlled.

Exclusion criteria were patients with decompensated heart failure; history of pulmonary disease; severe functional mitral regurgitation; inability for exercise training owing to angina or peripheral arterial occlusive disease; advanced liver, kidney, or musculoskeletal disease; and poorly controlled or exercise-induced cardiac arrhythmias. All participants were informed about the nature and effects of the trial. An informed written consent form (documented by the ethical committee) was taken from each patient before the study.

### Evaluative procedures

#### *Symptom-limited exercise test*

It was done to record maximum heart rate and resting heart rate, which were used in exercise training. For 1 min and at a work rate of 30 W, the patients pedaled with no added load. The work rate was raised by 30 W/3 min before the patients became symptomatic. During the final 15 s of each stage third minute, the maximum heart rate was measured. At the start, the resting heart rate was registered. At the end and for a brief

time, the patients used the bicycle against zero resistance in a cool-down stage [6].

### *Echocardiographic evaluation*

An ultrasound device was used to conduct M-mode, two-dimensional pulsed Doppler echocardiography examinations; a two-dimensional mechanical sector scanner was used to perform the examinations (2.5-MHz imaging transducer connected to Hewlett-Packard Sons Doppler flow analyzer). According to the American Society of Echocardiography guidelines, patients were evaluated in supine and left lateral position [7]. Using the two-dimensional view, ejection fraction (EF %) was calculated.

### *24-h Holter ECG*

It is used to determine HRV before and after 3 months of the training program. ECG signals were processed and stored concurrently for verification purposes. A computer was used to acquire, store, and process the signals. Using the computer algorithm, each QRS complex was identified, and each noise or ventricular premature complex was rejected, based on its likelihood in a standard QRS template.

HRV indices:

- (1) Time domain.  
SDNN is the standard deviation of all normal RR intervals, and SDANN is the standard deviation of the averages of NN intervals in all 5-min segments of the entire recording.
- (2) Frequency-domain analysis of LF: low-frequency power HF, high-frequency power, and LF/HF ratio (2017).

### *Six-min walk test*

At least for 10 min before the procedure, the patient sat on a chair near the starting spot. During this time, checks were done for contraindications, pulse and blood pressure, and suitable clothing and footwear. Then, the patient stood, and the Borg scale was used to rate the baseline dyspnea and overall exhaustion. The patient was instructed to walk for 6 min as far as possible. Slowing down, pausing, and resting were allowed as needed, but the patient must resume walking as soon as possible. The patient was instructed to refrain from running or jogging and avoid conversing with others during the walk. After the test, we reported Borg dyspnea and fatigue levels following the walk and asked if anything prevented the patient from walking further. We recorded the total distance walked on the worksheet, rounding to the nearest meter [8].

### Training procedure

#### *Moderate continuous aerobic training*

- (1) The session started with warming up exercise in the form of slow-cycling exercise or quiet walking for 5 min. Each patient performed a supervised individual training program based on the result of symptom-limited exercise tests.
- (2) Mode of exercise: bicycle ergometer and treadmill.
- (3) Intensity of exercise: 30 min of moderate-intensity aerobic training was done at 60–75% of maximum heart rate [9].

- (4) Duration of exercise: 40-min session (5 min of warming up, 30 min of conditioning phase, and 5 min of cooling down).
- (5) Cooling down was applied for all patients after finishing the rehabilitation session for 5 min.
- (6) Intensity and duration of the exercise program were progressively increased throughout the 3 months program, as individual tolerance and according to maximum heart rate.
- (7) Frequency of exercise: three times/week for 3 months.
- (8) All participants were closely monitored using ECG telemetry to control exercise intensity. We used the Borg scale of the rate of perceived exertion (RPE) to monitor the exercise intensity progression in patients exercising at 11–13 RPE in the absence of symptoms.
- (9) Patient monitoring included RPE, preactivity and postactivity tracking of symptoms, heart rate, blood pressure, and continuous ECG monitoring. To ensure that the study outcomes were not influenced, patients taking beta-blockers or other rate-lowering medications maintained their current dose during the study period.

### Statistical analysis

The statistical analysis was done using SPSS, version 22 (SPSS Inc., Chicago, Illinois, USA) for Microsoft Windows. To describe numerical variables, means and SDs or medians with interquartile ranges were used according to data normality. To present categorical variables, frequencies with percentages were used. For comparing normally or non-normally distributed quantitative data, unpaired (independent) *t* test or Mann–Whitney *U* test was used, respectively. Comparison of the categorical data was done using  $\chi^2$  test. Survival curves were constructed with Kaplan–Meier estimates and compared using the methods described by Klein and Moeschberger. The level of significance is set at less than 0.05.

## RESULTS

This research was done on 40 male patients after 1 month of experiencing acute MI. The mean age of the participants was  $53.70 \pm 5.79$  years (Table 1).

### Six-min walk test

Table 2 shows the mean pre-6MWT and post-6MWT values of within the study group. The mean pre-6MWT and post-6MWT values were  $208.65 \pm 24.62$  and  $360.98 \pm 109.78$  min, respectively, with an improvement percentage of 73.01%. There was a significant ( $P = 0.0001$ ;  $P < 0.05$ ) increase in 6MWT value at posttreatment period compared with pretreatment period within the study group.

### EF%

Improvement of EF% was noted after treatment, as shown in Table 3.

### Heart rate variability

Irrespective of time domain or frequency domain, HRV parameters showed significant improvement after exercise training, as illustrated in Table 4.

**Table 1: Baseline aspects of the participants**

Variable	Value
Age (years)	53.70±5.79
Weight (kg)	82.0±12.8
BMI (kg/m <sup>2</sup> )	32.01±1.98
EF (%)	49.32±5.12
Culprit lesion artery (%)	
LAD	67.5% ( 27 patients)
LCX	27.5% (11 patients)
RCA	27.5% (11 patients)
Cardiovascular risk factors (%)	
Hypertension	40% (16 patients)
Dyslipidemia	20% (8 patients)
Diabetes mellitus	27.5% (11 patients)
Family history	30% (12 patients)
Current smokers	52.5% (21 patients)
Medical therapy (%)	
Antithrombotic agent	100
$\beta$ -blocker	82.5
ACEI or ARB	87.5
Statin	96
Diuretics	25

EF, ejection fraction; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary; ACEI, Angiotensin converting enzyme inhibitors; ARB, Angiotensin receptor blockers.

**Table 2: Comparison between pretreatment and posttreatment values of 6-min walk test in study group**

Items	6MWT (mean±SD)
Before treatment	208.65±24.62
After treatment	360.98±109.78
Change	152.33
Improvement percentage	73.01
<i>t</i> value	9.123
<i>P</i>	0.0001
Significance ( $P < 0.05$ )	S

6MWT, 6-min walk test. S, significant ( $P < 0.05$ ).

## DISCUSSION

The current thesis was done to assess continuous moderate exercise training effect on HRV, function capacity (6MWT), and LV remodeling in patients who had experienced MI. According to the result of this study, posttreatment assessment revealed high efficacy of the intervention in the measurement of HRV, function capacity (6MWT), and LV remodeling.

For echocardiography, the present study findings indicated a substantial improvement in EF; this improvement could be owing to LV decline in internal dimensions and rise in wall thickness with a greater contractile reserve, and a decrease in total peripheral resistance, as inferred from the present study declines in resting and maximum heart rates. In patients who had experienced MI, exercise training early in life improved their ventricular remodeling, exercise tolerance, and autonomic balance [10]. Batista *et al.* [10], on the contrary, showed that delayed exercise could have a greater effect than early exercise.

**Table 3: Comparison between pretreatment and posttreatment EF%**

	Mean ± SD		MD	% of change	t	P
	Pretreatment	Posttreatment				
EF	49.32±5.12	56.63±5.49	7.31	14.82	9.153	0.0001**

EF, ejection fraction; MD, mean difference. \*\*Significant.

**Table 4: Comparison of heart rate variability parameters before and after exercise**

Variables	Before exercise	After exercise	P	Significance
SDNN	104.9±16.3	121.7±26.8	<0.05	S
SDANN	89.4±17.4	106.9±82.5	<0.05	S
HF	82.5±56.2	131.1±99.8	<0.05	S
LF	321.75	327.75	<0.05	S
LF/HF	3.9±2.2	2.5±1.3	<0.05	S

SDNN, the standard deviation of all normal RR intervals, SDANN, the standard deviation of the averages of NN intervals in all 5-min segments of the entire recording, LF, low-frequency power, HF, high-frequency power, LF/HF, ratio of LF to HF.

As a result, the appropriate amount of exercise time needs further investigation to offer a rational guidance to patients with MI.

After MI, the effects of exercise on myocardial function and LV remodeling are still controversial. Kubo *et al.* [11] hypothesized that after MI, exercise worsens cardiac function further owing to increased stress on the region of infarction, infarct expansion, decrease in EF, or aneurysm formation. Otsuka *et al.* [12] refuted these results, claiming that exercise has no effect on ventricular parameters regardless of training intensity. Giallauria *et al.* [13] and Wisløff *et al.* [14] reported that exercise could delay and even reverse ventricular remodeling following a recent acute MI with systolic dysfunction.

In agreement with our findings, Haddadzadeh *et al.* [15] recorded a substantial LVEF increase (46.9–61.5%) in patients after acute coronary syndrome (ACS) who completed a 12-week center-based or home-based exercise program as opposed to the control group (47.9–47.6%) ( $P = 0.001$ ). No significant difference was reported between the home-based and center-based groups. Additionally, and in agreement with the current research, Xu *et al.* [16] demonstrated that in patients who experienced MI, early HBCR was correlated with LVEF substantial changes at the 4-week follow-up as compared with the control group.

In the literature, there is a consensus that following MI, exercise improves cardiac function and remodeling through a variety of methods: improved endothelial function, decreased preload, decreased systemic vascular resistance, autonomic system adjustment, heart rate, and blood pressure decrease at rest and under submaximal loads, and decrease in LV wall tension [13,17].

Our findings are consistent with Rebecca and Sturek [18], who assessed 458 patients, after a major cardiac incident,

participating in cardiac rehabilitation and exercise programs. Patients showed significant improvements in exercise capacity after cardiac rehabilitation (+40%,  $P < 0.001$ ) as compared with the baseline (6 weeks after the cardiac event and before rehabilitation).

In our study, all HRV parameters improved after exercise training as compared with their value before exercise. These findings corroborate those of Iellamo *et al.* [19], who used, in 45 patients with and without prior MI, a comparable exercise program. After training for 2 weeks, the exercise group's resting RR interval and SDNN rose by 7 and 26%, respectively, in MI and non-MI patients. Moreover, Stahle *et al.* [20] also indicated that the exercise group had significantly higher HRV values (daytime SDNN and SDANN) following a 3-month training cycle. Similarly, on heterogeneous CAD patients, with at least half of them having previously experienced MI, another study was performed [21]. After exercise training for 8 weeks, the exercise group demonstrated an elevation in HF strength and RR intervals mean by 10 and 5%, respectively, compared with the control group. Additionally, more elevations in HRV indices were observed in patients with acute MI than those who did not have acute MI.

In 25 patients who had experienced MI, the time and frequency domain HRV (short-term, 30 min) were measured by Duru *et al.* [22] Before and after a cycling/walking exercise program for 8 weeks, at ~70% of their HR reserve or after receiving only normal medical treatment. They discovered no variations in HRV indices. The mechanisms underlying enhanced cardiac vagal regulation following exercise training include decreased beta-adrenergic receptor density, angiotensin II, and catecholamine levels, and increased bioavailability of nitric oxide [23].

## CONCLUSIONS

Exercise treatment is an important tool for reducing MI behavioral risk factors, increasing exercise ability, and improving the quality of life of patients with MI. Even brief exercise is considered a healthy and convenient way for patients who have experienced MI to boost functional ability, ventricular remodeling, autonomic nerve balance, and exercise tolerance. To help patients with MI, this type of treatment should be standardized and widely used in clinics around the world.

## Limitations

The small sample size is one of the study limitations. Moreover, a comparison of the exercise training effect is needed between patients with and without MI. Furthermore, long-term follow-up is needed.

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**Conflicts of interest**

There are no conflicts of interest.

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