Can cardiac rehabilitation programs improve functional capacity and left ventricular diastolic function in patients with mechanical reperfusion after ST elevation myocardial infarction?: A double-blind clinical trial

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Abstract

BACKGROUND: Current guidelines recommend cardiac rehabilitation programs (CRP) as a means to improve functional status of patients after coronary revascularization. However, research supporting this recommendation has been limited and positive effects of CRP on diastolic function are controversial. The aim of this study was to examine the effects of an 8-week CRP on left ventricular diastolic function.

METHODS: This randomized, clinical trial included 29 men with ST elevation myocardial infarction (MI) who had received reperfusion therapy, i.e. coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI). They were randomized to a training group (n = 15; mean age: 54.2 ± 9.04 years old) and a control group (n = 14; mean age: 51.71 ± 6.98 years old). Patients in the training group performed an 8-week CRP with an intensity of 60-85% of maximum heart rate. Exercise sessions lasted 60-90 minutes and were held three times a week. At the start and end of the study, all patients performed symptom-limited exercise test based on Naughton treadmill protocol. Pulsed-wave Doppler echocardiography was also used to determine peak velocity of early (E) and late (A) waves, E/A ratios, and the deceleration time of E (DT).

RESULTS: Left ventricular diastolic indices (E, A, E/A ratio, DT) did not change significantly after the CRP. Compared to baseline, patients in the training group had significant improvements in functional capacity (8.30 ± 1.30 vs. 9.7 ± 1.7) and maximum heart rate (118.50 ± 24.48 vs. 126.85 ± 22.75). Moreover, resting heart rate of the training group was significantly better than the control group at the end of the study (75.36 ± 7.94 vs. 79.80 ± 7.67; P < 0.001).

CONCLUSION: An 8-week CRP in post-MI patients revascularized with PCI or CABG led to improved exercise capacity. However, the CRP failed to enhance diastolic function.

Keywords: Cardiac Rehabilitation, Diastolic Function, Functional Capacity, Post-Myocardial Patients

ARYA Atherosclerosis Journal 2012, 8(3): 125-129

Date of submission: 2 Apr 2012, Date of acceptance: 4 Jul 2012

Introduction

Almost one million Americans experience acute myocardial infarction (MI) every year.1 The increasing incidence of coronary heart diseases has raised mortality rates all over the world and has been ranked among the world's top 10 causes of mortality.2 The benefits of cardiac rehabilitation program (CRP) for patients with a history of MI have been known for many years.3,4 Studies showed that CRP reduces the rate of major adverse cardiac events after coronary artery bypass graft (CABG) surgery4 and percutaneous coronary intervention (PCI).5 In patients with coronary artery disease (CAD), CRP has consistently shown a 15-31% reduction in all cause and cardiac mortality.7 Other advantages of CRP include improvements in lipid profile, blood pressure, functional capacity, and stress levels, weight loss, and probably smoking cessation and thus improved dyspnea.8-11 Despite the expanded use of PCI and CABG, few controlled studies have assessed CRP after these procedures.3 Consequently, there are still many controversies about the effects of exercise.
programs on cardiac function improvement in patients with CAD.\textsuperscript{12-15} Results of several studies have shown that regular exercise can improve functional capacity in cardiac patients without any significant effects on diastolic function.\textsuperscript{14,16} Other studies, however, have reported exercise programs to improve diastolic function.\textsuperscript{12,17-19}

The prevalence of MI is rapidly increasing in Iran.\textsuperscript{2} Considering the necessity of rehabilitation programs as a secondary prevention method and based on different results of previous studies about the positive effect of exercise programs in CAD patients, this study was designed to assess the effect of CRP on diastolic function in patients with ST elevation MI.

**Materials and Methods**

**Study population**

This was a randomized, controlled trial to examine the effects of a 2-month CRP on left ventricular (LV) function in patients following MI. We evaluated 29 male patients who had been treated with primary PCI or CABG. After undergoing baseline testing, the subjects were randomly assigned to training (n = 15; mean age: 54.20 ± 9.04 years) or control (n = 14; mean age: 51.71 ± 6.98 years) groups.

**Study design**

Patients had a history of ST elevation MI and had undergone PCI or CABG. While patients with PCI started the CRP four weeks after the procedure, CABG patients had to wait until the eighth week. All subjects were regularly followed up in the CRP center. The study protocol was reviewed and approved by the Ethics Committee of Isfahan Cardiovascular Research Center (Isfahan, Iran). This study was also registered in the Iranian Registry of Clinical Trials (IRCT201011085136N1).

At the time of admission, a checklist was completed for patients according to their medical history and physical examination by trained general practitioners, physiotherapists, and nurses. To determine functional capacity, patients continued their medications and performed a Naughton exercise test under the supervision of a cardiologist.\textsuperscript{20} Resting systolic and diastolic blood pressure was measured in sitting position before exercise for all persons in the training group.

**CRP**

The CRP comprised 24 sessions of exercise, scheduled over 8 weeks in the Cardiac Rehabilitation Center of Chamran Hospital (Isfahan, Iran). Each session lasted 60-90 minutes and included 10-20 minutes of warm-up followed by 20-40 minutes of aerobic exercise and a 10-minute cool-down. Each session was terminated with 20 minutes of relaxation. According to the determined risk, the intensity of exercise was calculated as 60-85% of maximum heart rate achieved on the exercise test.\textsuperscript{21} The exercise was performed under electrocardiographic monitoring if the patient was at high risk. All patients received psychological, nutritional, and smoking cessation recommendations. Weekly educational sessions were also held during the 8 weeks of CRP for both patients and their families. These sessions provided explanations on cardiovascular diseases, risk factors, diagnostic and treatment approaches, medications and their complications, and stress reduction methods, and advices on healthy lifestyle including smoking cessation, appropriate nutrition, and physical activity. For all patients who completed the whole CRP period, the tests were re-conducted at the end of the study.

**Echocardiography**

Echocardiographic measurements were performed before CRP and after the last session (VIVID3, General Electric). Transmitral flow velocity is correct at the tip of the mitral valve leaflets were obtained using pulsed-wave Doppler echocardiography in apical 4-chamber view. The peak velocity of early (E) and late (A) waves, E/A ratios, and the deceleration time of E (DT) were then determined.

**Statistical analyses**

All data was expressed as mean ± standard deviation (SD). A normal distribution was proven by Kolmogorov-Smirnov test. Paired Student t-test was used to compare significant differences of each variable within each group before and after the CRP period. Differences between the two groups were assessed using analysis of covariance.

All analyses were performed in SPSS\textsuperscript{17} for Windows (SPSS Inc., Chicago, IL, USA) at a significance level of P < 0.05.

**Results**

Baseline characteristics of the subjects are listed in table 1. There were no significant differences in baseline clinical variables or treatment methods between training and control groups. Table 2 summarizes the echocardiographic indices of the groups. No significant differences on diastolic function indices (E, A, E/A ratio, and DT) were caused by CRP. Table 3 compares results of Naughton exercise test. Functional capacity, maximal heart rate, and resting heart rate of patients in the training group improved after the CRP.
Table 1. Baseline characteristics of participants in training and control groups

| Characteristics                     | Training group (n = 15) | Control group (n = 14) |
|-------------------------------------|-------------------------|------------------------|
| Age (yr)                            | 9.04 ± 54.20            | 51.71 ± 6.98           |
| Height (cm)                         | 167.66 ± 4.62           | 172.64 ± 6.58          |
| Weight (kg)                         | 75.16 ± 11.69           | 78.75 ± 10.84          |
| Systolic blood pressure at rest (mmHg) | 131.00 ± 16.80         | 121.78 ± 17.49         |
| Diastolic blood pressure at rest (mmHg) | 76.00 ± 11.80          | 75.71 ± 12.22          |
| Anterior myocardial infarction      | 9                       | 7                      |
| Interior myocardial infarction      | 6                       | 7                      |
| Coronary artery bypass graft        | 8                       | 7                      |
| Percutaneous coronary intervention  | 7                       | 7                      |
| Risk factors                        |                         |                        |
| Hypertension*                       | 2                       | 3                      |
| Hyperlipidemia*                     | 8                       | 9                      |
| Diabetes*                           | 2                       | 3                      |
| Positive family history*            | 7                       | 6                      |
| Medications                         |                         |                        |
| Beta blockers                       | 15                      | 14                     |
| Angiotensin converting enzyme inhibitors | 15                  | 14                     |
| Statins                             | 15                      | 14                     |
| Anticoagulants                      | 15                      | 14                     |
| Smoking                             | 5                       | 6                      |

* Values are expressed as mean ± SD or numbers

Table 2. Echocardiographic indices of left ventricular diastolic function before and after the cardiac rehabilitation program

|                        | Training group | Control group |
|------------------------|----------------|---------------|
|                        | Pretest        | Posttest      | t  | P   | Pretest       | Posttest     | f  | P   |
| E (m/s)                | 0.78 ± 0.18    | 0.80 ± 0.20   | -0.54 | NS | 0.75 ± 0.16  | 0.74 ± 0.19 | 0.59 | NS |
| A (m/s)                | 0.77 ± 0.16    | 0.73 ± 0.14   | 1.56  | NS | 0.72 ± 0.16  | 0.81 ± 0.21 | 2.65 | NS |
| E/A ratio              | 1.01 ± 0.03    | 1.06 ± 0.35   | -0.90 | NS | 1.02 ± 0.45  | 1.03 ± 0.25 | 0.20 | NS |
| DT (ms)                | 282.07 ± 77.60 | 302.71 ± 109.29 | -0.44 | NS | 267.00 ± 61.70 | 308.00 ± 55.80 | 0.23 | NS |

E: Peak velocity of early wave; A: Peak velocity of late wave; DT: Deceleration time of E

Table 3. Comparison of functional capacity between training and control groups

| Variable                | Group | Pretest | Posttest |
|------------------------|-------|---------|----------|
| Functional capacity (Met) | Training | 8.30 ± 1.30 | 9.70 ± 1.70* |
|                        | Control | 8.20 ± 1.80 | 8.60 ± 2.20 |
| Maximum heart rate (beat/minute) | Training | 118.50 ± 24.48 | 126.85 ± 22.75* |
|                        | Control | 119.60 ± 23.65 | 121.80 ± 25.72 |
| Resting heart rate (beat/minute) | Training | 79.71 ± 9.27 | 75.36 ± 7.94**† |
|                        | Control | 79.13 ± 8.69 | 79.80 ± 7.67 |

*Significant difference between values before and after rehabilitation (P ≤ 0.05)
** Significant difference between values before and after rehabilitation (P ≤ 0.001)
† Significant difference with the control group after rehabilitation (P ≤ 0.001)

**Discussion**

The aim of this study was to investigate the effects of CRP on diastolic function and functional capacity of post-MI patients. We found that 8 weeks of CRP could not significantly affect diastolic function indices. Previous studies on patients with CHD and normal diastolic function\(^{12}\) and post-MI patients with preserved LV systolic function and mild diastolic dysfunction\(^{14}\) reported similar results about diastolic function indices. Likewise, aerobic endurance exercise
could not consistently modulate changes caused by physiological aging in healthy men. CRP also failed to have any positive effects on diastolic function in patients with chronic heart failure and hypertrophic cardiomyopathy.

In this study, CRP could positively affect functional capacity and maximal and resting heart rate. Heart rate has a positive correlation with velocity and reverse correlations with E velocity and E/A ratio. Several studies have emphasized on the role of heart rate as an important factor in LV diastolic function. Decreased resting heart rate due to exercise prolongs the relaxation period which in turn increases functional capacity and maximal and resting heart rate. The reason might have been decreased preload that can modify heart rate without significant changes in E velocity and E/A ratio. In contrast, Yu et al. trained 127 post-MI patients with moderate LV diastolic dysfunction for eight weeks and observed significant increases in E and E/A and shortening of DT. Similar results were reported by research on old patients without any cardiovascular disease. The inconsistency between our results and the findings of the two studies above may have been caused by differences in characteristics of study subjects, short duration of intervention, small sample size, and normal diastolic function in our participants. Previous research has reported CRP to be most beneficial in improving functional capacity among patients with CHD, patients with MI, and patients with heart failure after CRP.

The mechanism by which baseline LV diastolic function contributes to exercise tolerance is not clear. It is well known that major factors limiting maximal oxygen consumption are stroke volume and heart rate in response to exercise. We can hypothesize that in our patients with preserved LV systolic function, exercise training improved the stroke volume response to exercise only in those without any abnormalities in the diastolic function. Moreover, it is possible that only some patients performed exercise training appropriately, among whom the dilating capacity of peripheral arteries has been enhanced and muscle function has been improved.

Conclusions
In conclusion, 8 weeks of CRP had no significant effects on diastolic function indices in post-MI patients. Longer exercise is thus suggested for improvement in diastolic function in similar patients. Since functional capacity improved in our participants, supervised CRP can be of value for post-MI patients.

Acknowledgments
This study was supported by Isfahan Cardiovascular Research Institute (Isfahan, Iran). The authors would like to thank the Cardiac Rehabilitation Center of Chamran Hospital (Isfahan, Iran) and the patients who devoted their time to participate in this study.

Conflict of Interests
Authors have no conflict of interests.

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How to cite this article: Golabchi A, Basati F, Kargarfard M, Sadeghi M. Can cardiac rehabilitation programs improve functional capacity and left ventricular diastolic function in patients with mechanical reperfusion after ST elevation myocardial infarction?: A double-blind clinical trial. ARYA Atherosclerosis Journal 2012; 8(3): 125-129.