**Cardiac Rehabilitation Program with High Intensity Aerobic Exercise Can Reverse Diastolic Impairment in Patients Undergoing Coronary Artery Bypass Surgery**

***Short title:*** Cardiac Rehabilitation and Diastolic Dysfunction

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ABSTRACT

*Background:* Cardiac rehabilitation is known as a powerful non-pharmacological approach for improving functional capacity, and left ventricular systolic function; however some limited data have suggested an attenuation of the decline in diastolic function with this program. This study investigated the effect of high intensity aerobic exercise following coronary artery bypass graft surgery (CABG) on diastolic dysfunction.

*Methods:* Forty four consecutive patients with different levels of diastolic dysfunction who underwent CABG surgery were included. The participants attended the complete cardiac rehabilitation program three times per week for two months (totally 24 sessions). The patients underwent complete transthoracic echocardiographic studies including two-dimensional and spectral Doppler echocardiography immediately before attending rehabilitation program and also after the completion of rehabilitation sessions.

*Results:* There was a significant decrease of isovolumic relaxation time (IVRT) after participating complete cardiac rehabilitation (94.0 to 89.0, p = 0.001). The diastolic function parameters of early diastolic mitral inflow peak velocity to late diastolic mitral inflow peak velocity (E/A) ratio (0.94 to 1.04, p = 0.001), deceleration time of the mitral E wave (DT) (192.7 to 219.0, p = 0.011), and velocity of early diastolic mitral annular motion (Ea) (5.9 to 6.7, p = 0.026) were improved after the rehabilitation, whereas mitral A duration to pulmonary A duration (MAD/PAD) ratio was slightly improved (1.07 to 1.12, p = 0.056) and pulmonary veins systolic flow to pulmonary vein diastolic flow (PVS/PVD) ratio (0.89 to 1.04, p = 0.345) were remained unchanged.

*Conclusion:* A complete cardiac rehabilitation program with high intensity aerobic exercise approach can reverse diastolic impairment in patients undergoing CABG.

KEYWORDS:

Cardiac Rehabilitation; Diastolic Dysfunction; Coronary Artery Bypass Graft Surgery; Doppler Echocardiography

INTRODUCTION

The vital role of cardiac rehabilitation program in both primary and secondary prevention as well as its therapeutic effects, especially after cardiac invasive interventions, has been clearly identified [1-3]. This exercise-based rehabilitation strategy has also been known as a powerful non-pharmacological approach for improving functional capacity, and left ventricular systolic function especially in heart failure patients [4]. In this regards, the ACC/AHA guidelines for the management of heart failure have recommend regular exercise training as an adjunct therapy to improve the clinical status of patients with symptoms of heart failure and reduced left ventricular (LV) ejection fraction (LVEF) [5]. Although this programmed training has a proven impact on the functional status of patients with systolic dysfunction, its role in diastolic dysfunction is already undefined. Some studies have revealed some evidences for improving diastolic function following regular exercise training. Some probable mechanisms of this useful effects include the improvement in peak VO2 and reduction of diastolic wall-stress following exercise training [6-8]. Also, some limited data have suggested an attenuation of the decline in diastolic function with exercise training [9]. However, according to the findings of some others, both short and long-time exercise training had no effect on left ventricular diastolic function [10-12]. Thus, we conducted the current clinical trial study on cardiac rehabilitation following coronary artery bypass surgery (CABG) in diastolic dysfunction to investigate whether rehabilitation program with high intensity aerobic exercise improves diastolic function in these patients.

METHODS

The current study was conducted on patients with different levels of diastolic dysfunction [13] graded as abnormal relaxation (Grade I), pseudonormal (Grade II), and restrictive (Grade III) (Table 1) who had attended the cardiac rehabilitation ward of our heart center in 2011. The participants consisted of 44 consecutive CAD patients who underwent CABG three months ago and referred to the cardiac rehabilitation clinic. Those with atrial fibrillation or other serious cardiac arrhythmias on electrocardiogram at the admission to rehabilitation, left ventricular hypertrophy or valvular heart disease according to echocardiography reports, uncontrolled hypertension (> 140/90 mmHg), cardiomyopathies, or other cardiac interventions, systemic illness or fever, severe renal dysfunction (creatinine >2.0 mg/dL), or severe orthopedic problems that would prohibit exercise were not included into the study. The study was approved by the Ethic Committee of the Kermanshah University of Medical Sciences and all participants gave their written informed consent.

The participants attended the complete cardiac rehabilitation program with high intensity aerobic exercise approach three times per week for two months (totally 24 sessions). Each session was preceded by 5 to 10 minutes warming up, followed by 40 to 45 minutes high intensity aerobic exercise training on a treadmill, bicycle and running, and then 5 to 10 minutes cooling down. Training sessions, performed under continuous electrocardiogram monitoring, were supervised by a physician.

The patients underwent complete transthoracic echocardiographic studies including two-dimensional and spectral Doppler echocardiography before attending rehabilitation program and also after the completion of rehabilitation sessions. Left ventricular ejection fraction (LVEF) was estimated using a modified Simpson’s biplane method. The following parameters were obtained: deceleration time of the mitral E wave (DT), isovolumic relaxation time (IVRT), early diastolic mitral inflow peak velocity (E), late diastolic mitral inflow peak velocity (A), their ratio (E/A), velocity of early diastolic mitral annular motion (Ea), E/Ea ratio, Mitral A duration (MAD), Pulmonary A duration (PAD), Pulmonary veins systolic flow (PVS), Pulmonary vein diastolic flow (PVD), and systolic velocity to diastolic velocity ratio of pulmonary veins (PVS/PVD).

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Changes in study variables after the cardiac rehabilitation were assessed using paired *t* test or Wilcoxon test. Statistical significance was determined as a p value of ≥ 0.05. All statistical analysis was performed using SPSS software (version 20.0, SPSS Inc., Chicago, Illinois).

RESULTS

The mean age of study patients was 59.54 ± 6.27 ranged 44 to 74 years and 31 (70.5%) were men. The overall prevalence of systolic hypertension was 11.5%, and the history of hyperlipidemia and diabetes mellitus was reported in 9.1% and 11.5%, respectively.

There was a significant decrease of IVRT parameters (94.0 to 89.0, p = 0.001) after participating complete cardiac rehabilitation program (Table 2). The diastolic function parameters of E/A ratio (0.94 to 1.04, p = 0.001), DT (192.7 to 219.0, p = 0.011), and Ea (5.9 to 6.7, p = 0.026) were improved after the rehabilitation, whereas MAD/PAD ratio was slightly improved (1.07 to 1.12, p = 0.056) and PVS/PVD (0.89 to 1.04, p = 0.345) as well as E/Ea ratio (10.79 to 10.22, p = 0.316) were remained unchanged. Regarding changes of diastolic dysfunction grading (Figure 1), none of the participants had normal diastolic function and 27.3% of them had grade II to III diastolic dysfunction, while normal diastolic function was revealed in 36.4% of the patients after rehabilitation schedule and grade II to III diastolic dysfunction was observed only in 13.7% after this program.

The improvement in diastolic dysfunction grading was not significantly correlated with general risk profile including female gender, advanced age, systolic hypertension, hyperlipidemia, and diabetes mellitus. There were no serious adverse events during or immediately after the completion of cardiac rehabilitation.

DISCUSSION

It is well known that physical exercise reduces mortality from cardiovascular causes by reducing blood pressure, changing the lipid profile, as well as enhancing the autonomic control of the heart [14,15]. It has been also revealed that the patients undergoing regular exercise training can reach a significantly better glucose balance than the controls. In addition, the systolic blood pressure decrease and VO2max improve significantly following this training [16]. Despite evidences of a beneficial training effect on cardiac systolic function, a few evidences of exercise effect on cardiac left ventricular diastolic function are available. In the present study, a 24-session cardiac rehabilitation program resulted in a 5.0% decrease in IVRT in the study patients. Furthermore, E/A ratio and DT parameter were significantly improved. These findings are in consistent with the study by Alves et al that exercise training decreased E/A ratio and increased DT, while both of which were unchanged after usual care alone [17]. Also, in Brassard et al study, reversal of diastolic dysfunction to a normal function was observed in half of the study participants following exercise training, whereas no change in diastolic function was observed in the control group. They also found that the maximal oxygen uptake increased in the exercise training group following exercise training while there was no change in the control group [18]. Some reports showed that the physical fitness, reductions in abdominal fatness and insulin resistance after exercise training program mediate improving left ventricular diastolic function [19]. The training response may also be due to some various none-cardiac factors include improved oxidative capacity, anaerobic glycolysis of the muscle, improved arteriovenous difference, improved vascular function, and reducing peripheral arterial resistance [20-23]. Another probable factor mediating improvement in diastolic function has been control of blood pressure. Müller-Brunotte et al. [24] showed that blood pressure could explain 20% of the variance associated with IVRT. Baynard [25] also observed that the change in diastolic blood pressure explained about 20% of the variance in IVRT parameter. This relationship may be related to changes in wall tension [26,27] so that elevated diastolic blood pressure is associated with increased wall tension which makes it more difficult for the heart to relax [28] and thus exercise training can control diastolic blood pressure and therefore improve muscle relaxation.

Finally, our data suggest that a complete cardiac rehabilitation program with high intensity aerobic exercise approach can reverse diastolic impairment in patients undergoing CABG. Therefore, these data indicate it may be possible to reverse early diastolic dysfunction following cardiac rehabilitation program with high intensity aerobic exercise in the group with significant cardiovascular disease and undergoing cardiovascular interventions.

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TABLE 1: Diastolic dysfunction grading based on parameters of diastolic dysfunction

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Grade III | Grade II | Grade I | Normal | Grade  |
| <160 | 160-200 | >240 | 160-240 | DT |
| <70 | <90 | >90 | 70-90 | IVRT |
| >1.5 | 1-1.5 | <1 | 1-2 | E/A |
| <1 | <1 | >1 | ≥1 | MAD/PAD |
| <1 | <1 | >1 | ≥1 | PVS/PVD |
| >15 | >8 | <8 | <8 | E/Ea |
| <8 | <8 | <8 | >8 | Ea |

DT: Deceleration time

IVRT: Isovolumic relaxation time

MAD: Mitral A duration

PAD: Pulmonary A duration

PVS: Pulmonary veins systolic flow

PVD: Pulmonary vein diastolic flow

E: Early diastolic transmitral flow velocity

Ea: Velocity of early diastolic mitral annular motion

TABLE 2: Changes in parameters of diastolic function following cardiac rehabilitation

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters  | Before rehabilitation(n=44) | After rehabilitation(n=44) | P-value |
| IVRT | 94.00 ± 26.50 | 89.00 ± 17.00 | 0.001 |
| E/A | 0.94 ± 0.40 | 1.04 ± 0.50 | 0.001 |
| MAD/PVAD | 1.07 ± 0.26 | 1.12 ± 0.32 | 0.056 |
| PVS/PVD | 0.89 ± 0.37 | 1.04 ± 0.30 | 0.345 |
| E/Ea | 10.79 ± 3.78 | 10.22 ± 4.00 | 0.316 |
| DT | 192.71 ± 55.83 | 219.00 ±47.60 | 0.011 |
| Ea | 5.90 ±1.29 | 6.77 ± 1.41 | 0.026 |
| DDG | 1.30 ± 0.41 | 0.88 ±0.74 | 0.001 |
| LVEF | 43.41 ± 8.56 | 45.07±7.96 | 0.001 |

DT: Deceleration time

IVRT: Isovolumic relaxation time

MAD: Mitral A duration

PAD: Pulmonary A duration

PVS: Pulmonary veins systolic flow

PVD: Pulmonary vein diastolic flow

E: Early diastolic transmitral flow velocity

Ea: Velocity of early diastolic mitral annular motion

DDG: Diastolic dysfunction grading

LVEF: Left ventricular ejection fraction



Figure 1: Diastolic dysfunction grading before and after cardiac rehabilitation program