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Original Article

Effect of Strengthening Exercises on Serum C-Reactive Protein after Coronary Artery Bypass Grafts

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Abstract

Background: Strengthening exercises are not favored in the rehabilitation of patients after coronary artery bypass grafts (CABG) for concerns over potential adverse effects. However, patients often present with weakened skeletal muscles post CABG due to disuse.

Methods: We studied the effects of aerobic and strengthening exercises on the serum C-reactive protein (CRP) levels and blood pressure in 79 post CABG patients aged 40-60 years. Patients were randomly assigned to one of four programs five days per week, consisting of either aerobic exercises alone (controls) or combined with strengthening exercises (experimentals) at moderate intensity. The serum CRP levels were quantified at the beginning, 12th and 24th sessions, and at 3-month follow-up. Patients' blood pressure was measured before and after each exercise session. Patients were re-evaluated at 3-month follow-up.

Results: There was a mild but significant increase in the CRP levels at 12th session in all groups. Patients systolic blood pressures declined by 2%-7% at 12th and 24th sessions, respectively. There was no significant difference in changes of blood pressure among the groups.

Conclusion: The results suggest that the four exercise programs were equally safe in low-risk, post CABG patients. Exercises did not promote a systemic inflammatory response. These beneficial effects were still evident at 3-month follow-up.

Keywords: *C-reactive protein, Aerobic & strengthening exercises, Coronary artery bypass*

Introduction

It is now widely accepted that atherosclerosis is an inflammatory disease and the pathogenesis is more complex than the accumulation of lipids in the arterial walls (1-5). Recent clinical evidence demonstrates that CRP is the strongest predictor of impending myocardial infarction and stroke (6, 7). The relationship between cardioprotective interventions and the serum CRP levels has been examined by several studies (1-4). In addition, certain biological events such as changes in endothelial nitric oxide release, regulation of adhesion molecules and proliferation of vascular smooth muscle cells are believed to be associated with variations in the serum CRP levels (4).

In addition to treatment with vastatins, studies have suggested exercise as another clinical modality for lowering CRP levels and blood pressure in cardiac patients rehabilitating from coronary artery bypass grafts (CABG) procedures (8). It has been suggested that the anti-inflammatory effect of aerobic exercise plays a role in lowering the CRP levels (9). In addition, low to moderate intensity strengthening exercises may be safely included in the cardiac rehabilitation programs, since cardiac patients benefit from improved muscle strength for activities of daily living. While Strength training exercise improves skeletal muscle strength in low-risk male MI patients, the risk of angina, arrhythmia and increased blood pressure are not common (10). In this context, data are lacking on the effect of combined aerobic and strengthening exercise on CRP levels in CABG patients in various ethnicities.

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The purpose of this study was to determine the effects of strength and aerobic exercise programs in phase II cardiac rehabilitation on the serum levels of CRP in Iranian patients who underwent CABG procedures at Tehran Heart Center (THC) between November 2005 and September 2006. The rationale was that these patients often had difficulty with their daily activities due to weakened skeletal muscles secondary to low physical activities following the bypass surgery.

Materials and Methods

This study was approved by the Research Ethics Committees from both the Faculty of Rehabilitation and the THC affiliated with Tehran University of Medical Sciences. These standing committees are similarly authorized to review the human safety and ethical aspects of research projects conducted by the faculty and students on the respective premises.

Subjects & Inclusion Criteria: The study population was chosen from patients referred to the Cardiac Rehabilitation Department, THC from November 2005 to September 2006. These patients had undergone CABG procedure four to five weeks earlier and were considered low risk subjects by objective criteria, such as ejection fraction (≥ % 50), functional capacity (>5 METs) and exercise tolerance test (negative). Seventy nine (53 males, 26 females) post CABG patients at ages of 40 to 60 yr old (mean age= 52.4±5.9 yr) participated voluntarily in this study. Other inclusion criteria were having a systolic blood pressure of ≤ 160 mmHg, diastolic blood pressure of ≤ 105 mmHg, and no uncontrolled dysrhythmia or hypertension. A physician specialized in cardiac rehabilitation determined the risk stratification of the patients.

Monitoring All patients were connected to a telemetric cardiac monitoring system and supervised by the principal investigator, cardiac rehab nurses and staff throughout their attendance. All data and continuous electrocardiograms from each patient were recorded on a computer system (COGNIMED software, MEDSET, Germany). Patients' blood pressure and heart rates were recorded before and after each exercise session, using above mentioned system and wrist digital units (OMRON 637IT, Intellisense, Japan).

Exercise Programs Before starting the program, patients were given an orientation about the equipment, screening and exercise routines. All patients performed identical exercise protocols, depending on their respective group. Patients in combined programs performed strengthening exercises three days per week (on alternate days) following an aerobic exercise program and a 5-minute break. They performed only aerobic exercises in the other two days of the week. All patients completed 24 sessions of exercise over 5 d a week. Each patient was randomly placed in one of the following four exercise groups:

1. Controls: These patients (N=22) performed an aerobic exercise program only. See below for details of all exercise programs.
2. Combined Exercise Program- ST40: These patients (N=18) performed aerobic exercises combined with strengthening exercises at 40% of a 2-repetition maximum test (2RM).
3. Combined Exercise Program- ST60: These patients (N=21) performed a similar exercise program as in group 2 with the strengthening exercise intensity set at 60% of a 2RM test.
4. Combined Exercise Program- ST80: These patients (N=18) performed a similar exercise program as in group 2 with the strengthening exercise intensity set at 80% of a 2RM test.

Details of Exercise Protocols Two-repetition Maximum Test (2RM): The 2RM test represents a near 90% of maximal voluntary contraction (11, 12). This method has provided an acceptable representation of the one repetition maximal strength performance reduces musculoskeletal injury and has been used by investigators in cardiac rehabilitation studies (11, 13). The procedure begins with performing four movements against a light-weight resistance. The patient then performs sets of four repetitions.

If the patient was able to complete the task at least in two repetitions correctly, the resistance was progressively increased. A one-minute rest is given between each set of movements, and

the procedure is continued until patients cannot perform more than two repetitions correctly.

Aerobic Exercises These consisted of brisk walk on treadmill (10-15 min) and paddling a stationary cycle (10-12 min) followed by cranking an arm ergometer (8-10 min). The exercise intensity at each step was set at moderate intensity, according to the patients' heart rate, fatigue level and cardiac symptoms.

Strengthening Exercises These included five different exercises as follows: a) knee extension; b) knee flexions; c) arms crossing across chest; d) elbow extension; and e) elbow flexion.

Patients performed each exercise in a circuit manner in two sets of 10-12 repetitions per session. To avoid isometric contractions and Valsalva maneuver, patients were instructed to keep their exercise motions smoothly and continuously while assuming an appropriate posture. In ST40, ST60 and ST80 groups, the initial workload was set at 40%, 60% or 80% of 2RM test, respectively. When patients were able to complete 12 repetitions for both sets of each exercise, the resistance was increased by about 10%.

Short breaks were given between exercises. One set of 10-12 repetitions was performed for each exercise, with patients going from one to the next motion in a circuit manner, before performing a second set. A 30 seconds rest was given between each set of exercises. Exercises were performed in a random sequence. A cool-down period was included after completing the circuits. The entire strengthening exercise routine took each patient approximately 15 minutes per session.

Three-month Follow-up At the 24^{th} session in each exercise program, each patient was encouraged to include as many exercises as possible in their daily activities during the following three months. Each patient was notified near the due date and was scheduled for a follow-up session, at which patients completed a questionnaire.

Blood Analyses The serum's C-reactive protein (CRP) of all patients was measured at four points in time: a) immediately prior to the study, b) at the middle of program, c) at the study's completion and, d) at 3-month follow up after the completion of the study. These analyses were performed at diagnostic precision level by the Department of Clinical Laboratory Science, Tehran Heart Center.

Statistical Analyses The statistical analyses were performed using SPSS version 13.0. Two-way repeated measurement method was used to analyze the data for all patients in four different exercise groups: aerobic, ST40, ST60 and ST80, as described earlier.

Results

Patients' Homogeneity, Compliance and Safety The patient population was relatively homogeneous based on age, low risk, cardiac ejection fraction, functional capacity, blood pressure, absence of uncontrolled dysrhythmia, exercise tolerance and CABG procedure. Based on continuous observation and documentation of the principal investigator and self-report, all patients tolerated the exercise protocol well. Specifically, there was no untoward or unsafe incident during or after any of exercise sessions throughout the study.

Body Mass Index versus Serum CRP Levels: Based on the data collected before and throughout the study, there was no correlation between the patients' body mass index (BMI) and the mean serum CRP levels. Table 1 represents patients' BMI and the mean serum CRP levels throughout the study period.

Serum CRP Levels between Groups In general, the patients' mean serum CRP levels both prior to and throughout the study, remained within the normal range as established for healthy adults (0-10 mg/L). There was no significant difference in the mean CRP levels among the four patient groups. However, there were mild but significant variations in the mean CRP levels, as measured immediately before the study, at middle and final sessions into the study, and at 3-month follow-up (P= 0.005), regardless of the patient groups. Statistical analyses of the marginal means of the CRP levels indicated a significant difference in the four groups before the study and sessions 12 and 24. At middle session the mean

CRP levels showed a significant increase but at the end session, the mean CRP levels had decreased significantly (P= 0.005). There was no significant difference between the mean CRP levels before the study and at the 3-month follow-up (P= 1.00). The highest and lowest mean CRP levels were noted at 12th and 24th sessions into the study, with the corresponding values being 8.2 mg/L and 4.6 mg/L, respectively. Figure 1 represents the marginal means for the serum CRP levels, irrespective of the patient grouping. Variations in the mean CRP levels were also analyzed between groups. The mean CRP level was the highest in ST40 group (6.3 mg/L) and the lowest in ST80 group (5.5 mg/L). The values for the mean CRP levels in exercise patient groups are shown in Figure 2. The highest mean CRP level was noted at middle session for ST40 group (9.09 mg/L) and the lowest CRP levels noted at the end session (4.2 mg/L) and 3-month follow-up (3.9 mg/L) in ST80 group, respectively. The lowest mean CRP level was seen in ST60 group (7.4 mg/L) at middle session into the study. The mean serum CRP levels in the aerobic and ST40 exercise group were fairly similar (6.1 versus 6.3 mg/L).

Effect of Exercise on Blood Pressure There was a relative homogeneity in the initial blood pressure levels of the patients before the start of the study. Performing the exercise programs caused a mild decrease in blood pressure, regardless of the exercise grouping. Specifically, the systolic blood pressure readings at middle and end sessions showed a decrease, ranging from 2% to 7%, compared with those recorded for Day 1 of the study. The diastolic measurements were less consistent, varying from 4% decrease to 2% increase. Interestingly, there were no significant differences in blood pressure readings between the aerobic and combined exercise groups. Variations in the heart rates were mild and insignificant across the exercise groups (data not shown), essentially similar to noted those blood pressure readings. Table 2 represents the mean blood pressure readings and the percentage of differences at middle and end sessions for the four exercise groups.

Table 1: Patients' BMI and mean Serum CRP Levels

Patients' BMI	**CRP Level (mg/L)**			
	First Session	**Middle Session**	**End Session**	**Follow-up**
Less than 25 (Normal; N=25)	5.44	7.86	4.4	5.15
25-29.9 (Overweight; N=48)	5.79	8.33	4.75	5.25
30 or greater (Obese; N=6)	4.42	6.8	3.73	4.7
Average (Total N=79)	5.57±2.3	8.07±3.8	4.56±1.8	5.13±2.1

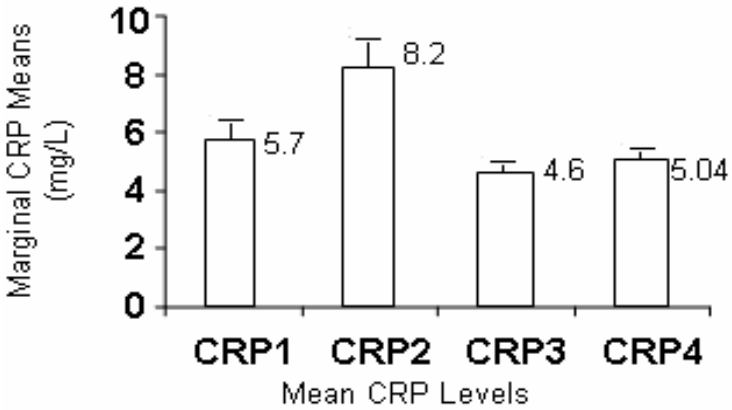

Fig. 1: Estimated marginal means of serum CRP levels before and after study.

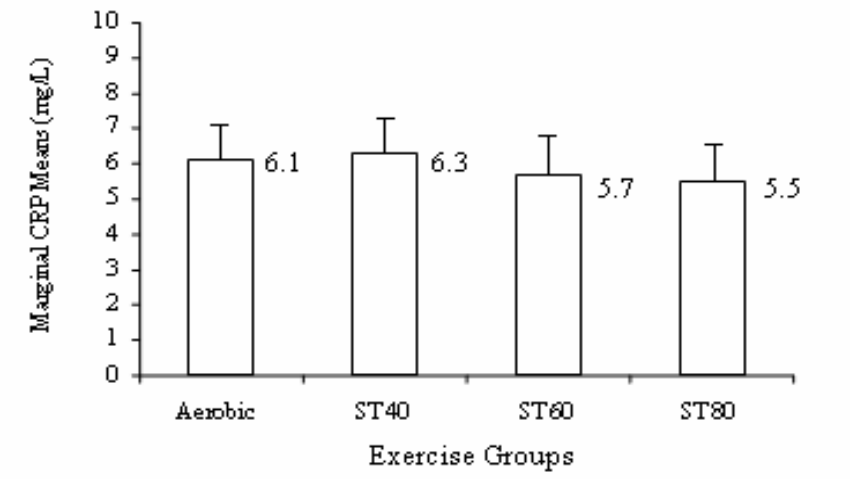

Fig. 2: Marginal means of serum CRP levels in exercise groups.

Table 2: Effect of Exercise Programs on Patients' Mean Blood Pressure

Exercise Group	Day 1*	Session 12*	% Diff.	Session 24*	% Diff.
Aerobic	113 / 69	108 / 70	-5 / +1	110 / 70	-3 / +1
Combined: ST40	112 / 70	107 / 68	-5 / -3	105 / 67	-7 / -4
Combined: ST60	116 / 70	112 / 70	-3 / 0	113 /7 2	-2 / +2
Combined: ST80	122 / 76	115 / 75	-6 / -1	119 / 77	-2 / +2

Notes: Blood pressures taken five minutes after the completion of exercise sessions. Decimals are not shown in the table for clarity.

Discussion

We examined the serum CRP levels and patients' blood pressure before, during and three months after completion of 4 exercise programs. In principle, the results suggest that the exercise programs were safe and useful, as reflected by the findings discussed below.

Safety and Exercise Tolerance The fact that all of the patients completed the study and none of them developed any cardiopulmonary adverse effect, during the study and 3 months thereafter, strongly suggests that the aerobic and strengthening exercise programs were safe and tolerable to the patients. This supports our initial assumption that the patients were indeed low risk individuals for this study. Strengthening exercises have been conducted previously by few researchers on cardiac patients following CABG procedures. The findings of this study provide evidence that combined aerobic and strengthening exercises can be equally safe as aerobics alone in low risk post CABG patients. Further, our observations regarding aerobic exercises are compatible with similar findings reported by previous studies (10, 14).

Serum CRP Levels, BMI and Statins: Based on the data presented in Table 1, there was no correlation between BMI and the mean serum CRP levels in any of the groups. This finding suggests that the slight variations in the CRP levels might be linked to other factors, such as the exercise programs or statin medications. Our patients had been taking fixed doses (20mg) of either Atorvastatin or Lovastatin per day since more than four to five weeks prior to and throughout this study. It is unlikely that the temporary rise in

serum CRP be related to the drugs, since this occurred consistently at or around 12th exercise session and returned to pre-study levels thereafter in all groups. Elucidation of the exact role that statins might have played in the transient rise in the serum CRP levels awaits future research.

Serum CRP Levels and Exercise Programs

The transient and statistically significant increase in the patients' mean serum CRP levels (approx. 3-4 mg/L) compared to those documented at the beginning and end of the study in all groups, is likely to be caused by the exercise programs. This suggestion is based on the assumption that the skeletal muscles involved in the exercise could have been deconditioned; therefore, they showed a mild and transient inflammatory response to the exercises. It can also be suggested that all of the exercise programs, regardless of the type, helped in reconditioning of the skeletal muscles, such that the inflammatory response subsided after the 12th session and the serum CRP returned to pre-exercise levels (Fig. 2). This assumption is backed by the fact that the patients generally had a sedentary life style prior to the bypass surgery, and had been on bed rest after the procedure for 4-5 wk before entering the study. Further support for our findings in this context comes from previous studies that demonstrated a reduction in serum CRP was associated with a decline in general inflammatory response after CABG procedures and an improvement in the health status of patients who participated in cardiac rehabilitation programs (1, 8, 9).

Serum CRP Levels and Exercise Groups: The mean of serum CRP levels in the aerobic and ST40 exercise groups (Fig. 2) were similar (6.1 vs. 6.3 mg/L), suggesting that the two exercise protocols may have elicited essentially similar inflammatory responses. In ST60 and ST80 exercise groups, the mean CRP levels (5.7 vs. 5.5 mg/L) were even lower than those of the aerobic were and ST40 groups and the decline had an inverse relationship with the magnitude of exercise resistance. These findings suggest that adding moderate resistance to the exercise program was advantageous over using aerobic exercise alone in the cardiac rehabilitation of low risk patients following CABG procedure. These further suggest that a combined aerobic and strengthening exercise program at moderate intensity is more efficient in keeping the serum CRP levels low while leading to greater muscle strength for the patients' daily activities, compared with those observed for the aerobic program alone. Lack of a more pronounced statistical difference between the mean serum CRP levels of patients in the aerobic and ST80 exercise group may in part be due to the small number of subjects in this study. Future, large-scale studies may provide greater statistical differences in similar patient populations. The effect of exercise programs used in this study cannot be generalized to post-CABG patients in intermediate or high-risk population. To elucidate these effects, specifically designed studies are required.

Effect of Exercise on Blood Pressure and Heart Rate The observation that exercise programs, regardless of the type, consistently caused a mild decrease in the systolic blood pressure of the patients, suggests that these exercises were similarly protective in keeping the blood pressure within a safe and normal range. It may be argued that patients' blood pressure was being controlled by the anti-hypertensive medications they were taking. While this argument holds truth, the present findings clearly demonstrate that the exercise programs did not cancel or reverse the effect of the drugs, hence this accounts for another protective effect of the exercises. A similar argument may be made in support of the protective effect of the exercises in this study on the patients' heart rate. Other researchers have reported similar effects on blood pressure following performance of aerobic exercises in healthy adults and cardiac patients (15, 16, 17, 18).

Long-term Effects of Exercise Programs: Considering that the mean serum CRP levels at 3-month follow-up remained below the levels for controls in all exercise groups, suggests the anti-inflammatory effect of the exercise programs may last for several months. To ensure this effect, patients need to follow the recommendations pre-

scribed to them at the end of their cardiac rehabilitation program. Lastly, information from the interview and survey of the patients at 3-month follow-up suggests that patients had improved significantly in activities of daily living. The results of this study are of clinical significance, since they provide evidence in support of safety and application of combined aerobic and strengthening exercises in low-risk cardiac patients.

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The authors declare that they have no Conflict of Interests.

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