

The effect of cardiac rehabilitation on plasma levels of cellular adhesion molecules VCAM-1, ICAM-1 in coronary patients after CABG

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Abstract:

Coronary heart disease is one of the leading causes of death in today's society. This disease is associated with exercise. Factors affecting VCAM-1 and ICAM-1 are paths in the treatment of this disease that are reduced by exercise. This study aimed at evaluating the effect of eight weeks of combined aerobic and resistance training on plasma levels of VCAM-1 and ICAM-1 cell adhesion molecules in patients after CABG.

The present study was a quasi-experimental study with pre-test and post-test design. Thirty middle-aged men after coronary artery bypass graft surgery were randomly divided into two groups: combined aerobic and resistance training (15) and control group (15). The experimental group performed combined rehabilitation exercises for eight weeks (3 sessions per week) and the control group received no training during this period. Blood samples were taken 48 hours before and after the training period in order to measure the desired blood indices. Independent t-test was used to analyze the data.

Results: The results showed that there was a significant difference between the two groups in the plasma levels of cell adhesive molecules VCAM-1, ICAM-1, but after the implementation of aerobic training and resistance training protocol, a significant decrease in gene expression of plasma levels of cell adhesive molecules VCAM-1 and ICAM-1 were observed in the experimental group and in comparison with the control group ($p \leq 0.001$). The results of the present study indicated that aerobic and resistance training in middle-aged patients after coronary artery bypass surgery resulted in plasma levels of VCAM-1 and ICAM-1 cell adhesion molecules. It seems that the present training protocol as a combined rehabilitation protocol can be identified as improving cardiovascular function and preventing cardiovascular disease.

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I. Introduction:

Coronary artery disease, which refers to the narrowing or blockage of all or part of the coronary artery due to atherosclerosis, spasm, or clot, resulting in insufficient oxygen supply to the myocardial muscles, lead to Angina pectoris and heart attack. The link between inflammation and atherosclerosis has been established in many studies (Abramson, 2005).

The most important cause of coronary artery disease is atherosclerosis. This disease is characterized by abnormal accumulation of lipids and the formation of atherosclerotic plaques in the endothelial wall of arteries and causes blockage, narrowing of blood vessels and reduced blood flow to the myocardial muscle (Rahmani, 2018). Increased fat mass production causes proinflammatory factors (adiponectin, leptin, IL-6, IL-18, TNF α) and some inflammatory markers that predict cardiovascular disease include fibrinogen, haptoglobin, cytokines, serum amyloid A, CRP, and adhesive molecules cells such as ICAM-1 and VCAM-1, selectins and integrins. Despite this, many studies have identified ICAM-1 and VCAM-1 as new inflammatory markers that independently predict cardiovascular disease (Guilin, 2009).

Decreased secretion of anti-inflammatory factors, which is associated with increased inflammation and inflammatory reactions due to endothelial tissue disorders. In this regard, one of the most sensitive cell markers in identifying the process of formation of atherosclerotic plaques in the endothelial wall of arteries are vascular adhesion molecules (Saxton It, 2008). It is now known that the endothelial wall of the artery plays an important role in vascular homeostasis and its lack of integration and dysfunction is considered as an important indicator in cardiovascular diseases.

In the early stages of the disease, an inflammatory process is formed in which the adhesion of monocytes to the endothelium is mediated by adhesive molecules ICAM- and VCAM-1 and selectins, resulting in the transformation of monocytes into macrophages, spongy cells, and plaques. As a result, some other factors are constantly released into the bloodstream. An increase in these factors indicates the destruction and activation of endothelial cells. Increased adhesion molecules present on the surface of endothelial cells cause inflammation in the cell wall, which in turn is the main cause of heart attacks and subsequent inability of the part of the heart muscle known as heart failure. The available data show that these molecules, in addition to playing an important role in initiating the atherosclerosis process, can also have negative effects on the postoperative treatment process (Rouhani et al., 2017). Therefore, scientists are looking for inflammatory markers to be able to diagnose, predict and control this disease.

One of the most important measures for the effectiveness of heart surgery and reducing its complications is cardiac rehabilitation. Rehabilitation programs aim at improving the social and psychological well-being of patients, limit the physical and psychological effects of cardiovascular disease, reduce the risk of sudden death or recurrent heart attack, and control the symptoms of atherosclerosis and coronary artery disease. Exercise is an integral part of

the cardiac rehabilitation program, the effect of physical activity and exercise on cardiovascular health has been well established.

The beneficial effects of combination exercise in reducing the risk of cardiovascular disease have been shown in numerous studies (Adams et al. 2008, Beck et al. 2012, Carlin et al. 2016, Carvalho et al. 2011, El Misiri et al. 2016, Yuji Naga et al. 2006). In this regard, researchers investigated the effectiveness of resistance and endurance training on basal metabolism, muscle adaptations and cardiovascular function, mitochondrial volume, strength, endurance, etc., as well as the relationship between weight loss and body mass (BMI) with changes in plasma levels of adhesive molecules. (Doye Brom et al., 2017) 1 VCAM-Reports also indicate a positive association between obesity (BMI Pool et al., 2004; Jacobs et al. 2000) with weight loss due to exercise and subsequent decrease in BMI can alter the level of adhesion molecules (Van Darley et al. 2004; Erdman et al. 2007, Hamedinia (Haghighi, 2011). The results indicated that after regular aerobic exercise, inflammatory responses are inhibited due to reduced predictors of cardiovascular disease (Mogharnesi et al., 1398). In a study, the effect of 12 weeks of cycling training on indicators of Peripheral inflammation in patients with chronic heart failure has been studied and it is stated that 30 minutes of daily exercise, 5 days a week on an exercise bike with 70 to 80% of maximum heart rate significantly reduces VCAM-1 levels and thus reduces peripheral inflammatory factors (edemplus et al. (2001).

One of the methods of treatment or prevention for cardiovascular diseases is lifestyle adjustment and it seems that it is possible to prevent the occurrence of such diseases through sports activities and nutrition. Exercise can be effective in many ways, one of which is the intensity of exercise. Exercise can have several benefits, including a reduction in visceral fat, a reduction in ICAM- and VCAM-1 adhesive molecules. 1 VCAM- Therefore, due to some inconsistencies in the studies performed, and considering that most previous studies have been performed on inhuman and animal samples or healthy human samples and few studies in this field have been performed on cardiac bypass patients in our country, there is a need for more controlled studies to review and present a better and more useful cardiac rehabilitation exercise program. So does cardiac rehabilitation affect the levels of ICAM- and VCAM-1 adhesion molecules in coronary patients after CABG?

II. Research Methods:

It was an applied semi-experimental study. For this purpose, the sample was selected according to the conditions of inclusion in the study and were divided into two groups of experimental and control. The statistical population of this study consists of men aged 40 to 60 years living in Mashhad who have undergone coronary artery bypass graft surgery. Statistical samples were selected from the statistical population voluntarily using available sampling according to the inclusion criteria. Thirty men who underwent bypass surgery were selected in the age range of 45-60 years by available sampling method and were randomly divided into two groups of 15 (experimental and control). The participants in the experimental group completed rehabilitation exercises in the rehabilitation ward of Javad Al-A'meh Heart Hospital and the control group did not receive any training or did not have any regular physical

activity. These exercises were performed in phase three of rehabilitation. For the first time, patients performed exercises in this phase.

Exercise program:

In this study, endurance and resistance exercises were performed simultaneously in patients.

Aerobic exercise: Patients exercised three days a week for a period of 24 sessions. Each cardiac rehabilitation session was performed for one to one and a half hour, depending on the assessments (cardiopulmonary status, exercise tolerance test, etc.). The treatment program includes: walking on a treadmill (20 to 30 minutes), pedaling on a stationary bike (10 to 12 minutes), using ergometrics (10 minutes). All members of this group performed the above exercises during each treatment session. In each treatment session, stretching exercises were used to warm up at the beginning and gradually cool down at the end of the exercise program. Exercise began with moderate intensity. Thus, in addition to the rate of fatigue and the occurrence of cardiac symptoms, 60% of the patients' maximum heart rate during the exercise test was considered as the target heart rate for the patients and was adjusted based on the intensity of the exercises. The intensity and duration of the exercises gradually increased according to the patients' abilities, so that in the last 7 to 10 sessions, the patients' maximum heart rate reached 80%.

Resistance training: The specified training movements were performed for eight weeks and three sessions per week, with 8 repetitions in the initial sessions and increasing the number of repetitions of movements to 15 repetitions in subsequent sessions in three sets. The movements included: 1) squat with physioball ball, 2) shoulder flexion, 3) hip flexion, 4) shoulder abduction, 5) hip abduction, 6) elbow flexion, 7) plantar ankle flexion, and 8) dorsi ankle flexion.

The movements were initially performed with eight repetitions using a weak (yellow) traband. Then, in each session, two repetitions were added to each movement to increase the number of repetitions of each movement to 15 repetitions. Then, the strength of the traband (pink) increases and the movements increase again with eight repetitions and gradually up to 15 repetitions in the next sessions. At the end of each session, cool down exercises with stretching movements for 5-10 minutes and relaxation exercises for 5-10 minutes were conducted. The patient's heart rate fluctuations were monitored by the monitoring system at all stages of training. Blood pressure was measured and recorded by rehabilitation nurses after using each device

Laboratory and sampling methods:

The samples were placed at room temperature for 20 minutes for clotting and then the tubes containing the sample were centrifuged with RMP 3000 for 20 minutes and the isolated serum was stored in a separate microtube at -80 ° C for further experiments. Biochemistry and measurement of ICAM-1 and VCAM-1 from ELISA commercial kit of BMS232 and BMS232TEN company made in the Netherlands by Elisa Reader kit made by Casabayo company made in China with sensitivity less than 39.0 ng / ml (Sensitivity > 0.039 ng / ml) and In-group and out-group change coefficients less than 7 were used.

Statistical Methods:

Using the ShapiroWilk test, the normality of the data was determined and after determining the normality of the data distribution, the correlated t-test was used to determine the effect of exercise on dependent variables in each group and the independent t-test was used to compare the effect of exercise on dependent variables between groups. SPSS software version 21 was used to analyze the data at a significant level of $P \leq 0.05$.

III. Research results and findings:

A): A course of combined rehabilitation training affects the plasma levels of ICAM-1 adhesive molecules in CABG patients. Based on the calculations of t-test (two independent samples), the significance of the difference between the plasma levels of ICAM-1 adhesive molecules in CABG patients in pre-test and post-test was investigated.

T test:

Assuming that μ_1 is the mean plasma level of ICAM-1 adhesive molecule in the pretest and μ_2 is the mean plasma level of ICAM-1 adhesive molecule in the post-test, the statistical hypotheses of the test are as follows:

$$\begin{array}{ll} \mu_1 = \mu & H_0 : \\ \mu_1 \neq \mu_2 & H_1 : \end{array}$$

Table 1: Independent t test results to compare the mean of icam1 in pre-test and post-test

p-value	t	df	SD	M	variable
* 0/001	7.94	28	32.39	280.69	pretest
			14.46	207.91	Post-test

According to the information in Table 1, which was performed with the aim of comparing ICAM1 pre-test and post-test scores of CABG patients, because the significant value was equal to 0.001 and less than the alpha value of 0.05, so it can be concluded that the combined rehabilitation training was effective on plasma levels of icam-1 adhesion molecules in CABG patients.

B): A combined rehabilitation training course affects the plasma levels of VCAM-1 adhesive molecules in CABG patients.

Based on the calculations of t-test (two independent samples), the significance of the difference between the plasma levels of VCAM-1 adhesive molecules in CABG patients in pre-test and post-test is investigated.

T test:

Assuming that μ_1 is the mean plasma level of VCAM-1 adhesive molecule in the pretest and μ_2 is the mean plasma level of the VCAM-1 adhesive molecule in the post-test, the statistical hypotheses of the test are as follows:

$$\mu_1 = \mu_2 \quad H_0 :$$

$$\mu_1 \neq \mu_2 \quad H_1 :$$

Table 2: Independent t test results to compare the mean of VCAM-1 in pre-test and post-test

c	t	df	SD	M	variable
* 0/001	6.26	28	21.00	396.41	pretest
			27.61	340.32	Posttest

According to the information in Table 2, which was performed with the aim of comparing the pre-test and post-test scores of VCAM-1 in CABG patients, because the significant value is equal to 0.001 and less than the alpha value of 0.05, so it can be concluded that combined rehabilitation training Plasma levels of VCAM-1 adhesion molecules in CABG patients were affected.

IV. Conclusion:

The index of many diseases in the onset and appearance of symptoms is not hidden from us. In the meantime, considering the role and importance of cell adhesion molecules such as VCAM-1, ICAM-1 as a new predictor of cardiovascular disease, we decided to investigate the effect of combined activities on cardiovascular patients and those at risk. Inflammation has estimated the extent of this factor and its possible decrease or increase. The results of the study showed that there is a significant effect between ICAM-1 index in men after 8 weeks of combined training. Evidence suggests that combination training can improve muscle endurance and cardiovascular endurance due to the physiological adaptations that follow. It can now be said that regular combination exercises probably have protective mechanisms against cardiovascular diseases with several mechanisms. Combined exercise inhibits the release of inflammatory mediators IL-1 β and TNF- α from adipose tissue by decreasing sympathetic stimulation and increasing

anti-inflammatory cytokines (IL-10), thereby reducing the concentration of cellular adhesion molecule (ICAM-1) (Golberg, 2010). Therefore, it can be claimed that regular combined exercise has a significant effect on the ICAM-1 index of cardiovascular patients, which are consistent with the findings of Mogharnasi (2007), Ito (2002), Zicardi (2002), Ponitroli (2004), Parisi (2001), Vogue (2004) and Robert (2006) but contradict the findings of Nassis (2005), Hemmat (2006) and Manning (2008). The findings of the present study on the decrease in the amount of ICAM-1 due to combined exercise are consistent with the findings of Mogharnasi (2007). It seems that the unity of the results is due to training and compatibility with training (Mogharnasi, 2007).

It is also consistent with the findings of Ito (2002) and Zicardi (2002) and Ponitroli (2004). It seems that the reason for the similarity was due to the selection of homogeneous groups in terms of age, sex and body type, and emphasizing that weight loss can be suggested as a suitable method of relieving inflammation to reduce the risk of cardiovascular disease.

However, despite the shorter training duration of Vogue (10 weeks) and Robert (3 weeks), the subjects were unhealthy and performed resistance activity every day and followed a special diet (Nicholas, 2006). The discrepancy between the results of Nassis (2005) and Manning (2008) with this study may be due to the fact that they do not change body weight and fat percentage and their combined exercise program is different. It can be said that the subjects are smokers and their training protocol is different (Donun, 2009). On the other hand, the results of the study showed that there is a significant effect between the level of VCAM-1 index in cardiovascular patients after 8 weeks of combined training. So it can be claimed that combination training has a significant effect on the VCAM-1 index. My claim that such a result is achieved in training may be due to several reasons.

1. Observance of the principle of adaptation to practice. Also, the meetings are held consecutively, but the meetings are held three days a week on a daily basis.

3. Regular meetings, 24 sessions per week and 8 consecutive weeks. The effects of regular combined training on VCAM-1 index are not known due to lack of research background in this field. However, in various articles and researches, the effects of one-session intense endometrial resistance training on VCAM-1 index have been studied, and the results indicated an increase in VCAM-1 values after acute, intense and resistance training. Undoubtedly, the reason for this can be considered as muscle damage, inflammation and high intensity of exercise. In this regard, it contradicts the research of Nemt (2002) and White (2006). They investigated the effects of an intense resistance training session on VCAM-1 cell adhesion molecules and the results showed an increase in this factor (Nicholas, 2006). The results obtained from the study of differences between groups showed that there is no significant difference between the effect of combined mobility training and both groups have a significant difference with the control group.

Among the reasons for achieving such a result are the effectiveness of both training protocols in terms of intensity, duration, compliance with training principles, similarity and homogeneity of subjects in both groups, the same time and place of training and continuous monitoring and control. It can also be concluded that increasing the level of physical fitness of the subjects can be a good reason to reduce the level of VCAM-1 and ICAM-1 adhesive molecules after exercise. This result is similar to the findings of Mills (2006) (Willem, 2008).

We also find from the results of the present study that the decrease in the mean values of ICAM-1 after training in control and combination groups is significant. Other notable results of this study include a significant difference in the inflammatory factor VCAM-1 after exercise in the combination and control groups. What can be said to justify this result is similar to the justifications discussed above. Assuming that both our experimental groups have similar results and the subjects in the resistance group have also experienced a reduction in fat percentage and weight, we conclude that the findings are consistent with the results of Zicardi (2002), Ito (2002), Pontiroli (2004) and Nicholas (2004) and Zupini (2006). (Zicardi, 2008). Therefore, it can be claimed that both aerobic and regular resistance training have a valuable and effective role in preventing cardiovascular diseases, etc., and in practice there is no difference in terms of effect and result.

Based on the results of the present study and related research, aerobic and resistance training, regardless of the intensity and duration of training can be a way to reduce factors 1 ICAM- and VCAM-1 which is an inflammatory factor in the incidence of cardiovascular disease. It should be considered as a non-pharmacological treatment and should be used in many medical centers.

Suggestions for future research:

- 1) It is suggested that a longer period and different intensities of training should be used
- 2) It is suggested that the effect of some supplements and effective vitamins on other inflammatory indicators be used in conjunction with aerobic and resistance training.
- 3) It is suggested that other factors involved in the field of other inflammatory factors, E-selectin, V-selectin, etc., be measured at the same time.
- 4) The study of changes in body composition, including the percentage of body fat and the percentage of fat should also be measured in research

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