



## The effects of aerobic exercise program on ICAM-1, leptin serum, LDL/HDL ratio and BMI in middle-aged women

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**Abstract: Background:** In regards to the increased prevalence of cardiovascular diseases (CVDs), various factors, including intercellular adhesion molecule-1 (ICAM-1), leptin, lipid profile, and body mass index (BMI) can be considered as major risk factors of these diseases. The purpose of this study was to investigate the effect of an 8-week aerobic exercise on ICAM-1 levels, serum leptin levels, HDL/LDL ratio, and BMI in middle-aged women.

**Materials and Methods:** Twenty-five healthy women in the age range of  $\pm 3.25$  to 42.26 with no past history of diseases participated in this quasi-experimental study. Further, 13 subjects were assigned as experimental group and 12 as control group. The experimental group had 40-min cumulative aerobic exercise sessions three times a week for 8 weeks. The exercises were aimed to raise their heart rate between 60 to 75% of their maximum heart rate. ICAM-1 levels, serum leptin levels, HDL/LDL ratio and BMI were measured both before and after the exercises. **Results:** The result showed a significant decrease in ICAM-1 levels ( $p = 0.005$ ), serum leptin ( $p = 0.008$ ), HDL/LDL ratio and BMI ( $p = 0.001$ ). An independent t-test was used to analyze the data. **Discussions.:** As the body ages the risk for cardiovascular disease and atherosclerosis increases, so regular aerobic exercise with its significant impact on the cardiovascular risk factor reduction can be a suitable tool for preventing the progression of these diseases, especially in the middle aged.

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### Introduction

The inflammation in artery walls and the migration of monocytes into these areas are the most important factors of initiation and development of the processes of atheroma formation (1, 2, 3, and 4). Since the calling of leukocytes until the final development of atherosclerotic plaque, cellular adhesion molecules and inflammatory mediators play a pivotal role in the development of coronary artery disease (4, 5). Today, the positive correlation between the plasma concentrations of ICAM-1 which causes vascular inflammation with obesity, particularly central obesity (abdominal obesity), and triglycerides, as well as its negative correlation with plasma HDL cholesterol concentrations have been founded (6). Studies have also shown that exercise can significantly change these factors (7, 8). Some studies have reported 45 to 60% blockage in coronary arteries nourishing the heart even in young people. Thus, the process of atherosclerotic plaques in the inner lining of blood vessels grows at an annual rate of 0.86% (9, 10). About the effect of endurance

training on lipid profile, some studies have reported the significant decrease in the blood lipid and lipoprotein levels (11, 12, and 12), and some others have reported the insignificant reduction of them (14, 15). Therefore, perhaps more precise factors at cellular level, along with lipid factor, may better reveal the effect of exercises. One of the most sensitive cell markers for detecting the atherosclerotic plaque formation process in the endothelial cells is cell adhesion molecule (16, 17). Although lipid profile has long been considered an indicator of cardiovascular disease, reports suggest that some people with normal LDL-C and HDL-C had cardiovascular diseases (4).

Increased LDL and decreased HDL cholesterol levels play an important role in the cardiovascular diseases, however evidence is accumulating that other factors such as cell adhesion molecules and proinflammatory cytokines which cause the endothelial function have been introduced as the new inflammatory markers playing a role in the cardiovascular diseases (19, 20). Atherosclerosis can be considered a chronic

inflammatory disease. The build-up of fatty deposits and other substances on the artery walls causes the arteries to become narrow, obstructing blood flow. The condition is called atherosclerosis. Improper eating habits, sedentary lifestyle, smoking and stimulants abuse are factors that contribute, at least in part, to atherosclerosis (21).

Encoded by the obese (ob) gene, leptin is mainly secreted from adipose tissues and plays a key role in regulating body weight (22). High serum leptin level is one of the characteristics of obese people (23). As an independent risk factor for coronary heart diseases, elevated serum leptin is associated with poor performance of vascular wall (24).

Recent evidence suggests that serum leptin is associated with the development of cardiovascular diseases, since it is in connection with defective fibrinogen, blood pressure, and calcification of blood vessel cells. Furthermore, (elevated) serum leptin concentration is connected with an increased risk of heart problems (25). Leptin serum also affects central nervous system, particularly the hypothalamus, decreases food intake, and stimulates increased energy consumption (26). It has been observed that leptin serum is positively correlated with indicators of obesity such as body fat mass (BFM) and body mass index (BMI). Food consumption can influence the leptin serum secretion as well (27). Since exercise is a tool for reducing obesity and its complications, if serum leptin levels are influenced by exercise, it may help justify the effect of exercises on obesity (27).

Dunstan examined the effect of three-month and six-month aerobic exercise training with the intensity of 50 to 60% of maximum heart rate in obese men. Dunstan observed no change in serum lipoproteins (TC, LDL, and HDL) and cholesterol levels at either 3 or 6-months exercise programs, though he found a reduction in body mass index (BMI) and waist-hip ratio (WHR) (29). Koumas (2003) also did a research on the middle-aged men and women. He classified the participants into three groups of high, medium, and low physical activity. Koumas, finally, observed that reduction in total cholesterol, LDL cholesterol, and triglyceride levels occurred in the active individuals, while their serum HDL cholesterol level was elevated (30).

In relation to the effects of aerobic exercises on the levels of adhesion molecules ICAM-1, Wegg & et al. (2004) have conducted a research on postmenopausal women at risk for coronary artery disease. Subjects performed a 10-week exercise program, and ultimately their ICAM-1 level has been significantly reduced (31). In contrast, Marsh & et al. (2005) found no significant changes in adhesion molecules when they conducted a research on healthy men and

women (32). Sabatier & et al. (2008) also carried out a research on healthy women assessing the changes in ICAM-1 and VCAM-1 levels after a 14-week aerobic exercise program. The study found no significant change in the (research) variables (33).

In another study by Christopher & et al. (2006), men and women who smoked cigarettes participated in a 12-week aerobic exercise program, and finally their plasma ICAM-1 levels and CPR significantly decreased (34). One of the researches on the changes in serum leptin levels was performed by Okazaki & et al. (1999). Their study investigated the effect of 12 weeks of aerobic exercises (at 50% of maximal oxygen uptake) on lean and obese inactive women. The study observed reduction in body fat mass, body mass index (BMI), and leptin levels (35). In this regard, boghrabadi & et al. (2012) examined 12 weeks of aerobic exercises on serum leptin levels in diabetic patients, and observed a significant reduction caused by these exercises (36).

On the one hand, the increasing risk of cardiovascular disease with aging, on the other hand, the role of exercise in the prevention of atherosclerosis and progression of cardiovascular diseases, led the researchers to examine this subject whether or not 2 months of aerobic exercise training has effect on ICAM-1 levels, serum leptin, HDL/LDL ratio and BMI in middle-aged women.

## Material and Methods

### Statistical population and the subjects

The current research is a quasi-experimental and applied study. Statistical population of the research includes inactive middle-aged women at Mashhad University in the age range of  $\pm 3.25$  to 42.26. Twenty five volunteers were randomly selected and divided into two groups, i.e., experimental (13 individuals) and control (12 individuals). It should be noted here that the subjects had no history or symptoms of specific diseases, such as diabetes, high blood pressure, cardiovascular diseases, and they also lacked a regular exercise.

### Exercise protocol

The group that was subject of the experiment participated in a eight weeks program (3sessions a week and on average 40 minutes per session, with 60 to 75 percent intensity of maximal heart rate) in aerobic exercises on Treadmill. The exercise intensity was controlled using polar heart rate monitor device (s625x). The control group was advised to avoid participating in any type of sports exercises during the eight weeks of the experiment. During training period, both group had their normal nutrition .

### Blood factors measurements

All subjects in both groups were referred to the laboratory at the same point in the day (8-10 a.m.), where the subjects had been fasting for 12 hours and had undertaken no physical activity 24 hours before the testing. In the laboratory, 20 ml. of blood was taken from each subject's elbow vein. The samplings were conducted similarly before and after the exercises. The leptin concentrations measurement was performed by radio-immunoassay (RIA) method, using a diagnostic **BioVendor** kit made in Czech. For measuring ICAM-1 levels, the same method was used – a Gama counter device together with the eBioscience company made in the Australia. The measurement of lipid profiles levels was conducted through an auto analyzer biochemistry Selectra device, built by Mann Company that used the enzymatic method.

### Measuring the body mass index (BMI)

The body composition analysis device, Tanita B\_C418 model, was used for measuring body mass index and weight of the subjects.

### Statistical Analysis

Research data was processed with the help of SPSS software, version 18 (SPSS Inc. Chicago Illinois, United States). The central trend indices and dispersion indices were shown through descriptive statistics. The Kolmogorov-Smirnov test was used to review the data distribution types. For survey the effect of exercise training on selected factors on each group dependent t test was used and to compare pretest and post-test data means in each group, the statistical independent t test was used. All the statistical tests were performed at the 95 percent confidence level ( $p < 0.05$ ).

## Results

**Table 1: The effect of aerobic exercise training on selected factor's on both group**

Factor	Control	p	Exercise	p
ICAM-1 (Pg/ml)	Pre test: 48/17±17/6	0.742	Pre test: 54/36±10/45	<b>0.000</b>
	Post test: 49/49±17/74		Post test: 41/76±10/97	
leptin (pg/ml)	Pre test: 39/05±12/7	0.731	Pre test: 36/09±12/53	<b>0.000</b>
	Post test: 38/16±14/87		Post test: 26/73±10/89	
LDL/HDL (ml/dl)	Pre test: 2/85±1/08	0.276	Pre test: 2/85±1/08	<b>0.000</b>
	Post test: 3/02±1/34		Post test: 3/02±1/34	
Body mass index (Kg/m <sup>2</sup> )	Pre test: 27/53±5/41	0.124	Pre test: 29/17±2/59	<b>0.005</b>
	Post test: 27/29±5/44		Post test: 27/71±2/63	

\* Significance level ( $p < 0.05$ )

According to the type of study and in order to examine the impact of exercise on each of these factors in the two groups, paired sample t-test was used. Table 1 shows that the two-month exercise program had no significant effect on the control group who had no regular physical activity. While a two-month training program in experimental group caused a significant reduction in all the considered factors.

**Table 2: compartment of the aerobic exercise training between control and experimental group**

variable	F	P covariance	Mean differences	t	p
ICAM-1 (Pg/ml)	5.642	0.026	13.912	3.46	0.005
leptin (pg/ml)	0.761	0.421	8.467	2.907	0.008
(ml/dl) LDL/HDL	0.007	0.934	0.633	4.72	0.001
Body mass index (Kg/m <sup>2</sup> )	0.036	0.431	1.22	3.25	0.001

According to the results of table 1, independent t-test was used to compare the effects of regular exercise program between the two groups of control and experiment. Results of the table 2 have shown that exercise has caused significant differences in all factors between the two groups. In other words, the experimental group who undertook regular aerobic exercise for 8 weeks had a significant reduction in cardiovascular diseases as compared with control participants.

### Discussion

In recent years, the relationship between vascular inflammation factors and coronary heart failure has been known. Adhesion molecules cause adhesion between cells and proteins and they are effective in the development of atherosclerotic plaque. An elevated level of intercellular adhesion is known to increase the risk of coronary artery disease (5). Research evidence suggests that less mobility is the major factor in the development of weight gain and obesity, and that an exercise program can bring major changes in weight and body composition (29). The results of this study showed that eight weeks of cumulative aerobic training program significantly reduced the ICAM-1 level, leptin serum, and HDL/LDL ratio. Adamopoulos & et al. (2001) have reported that endurance exercises (70 - 80% of maximum heart rate) leads to significant decrease in the levels of ICAM-1 (2). It should be pointed out here that aerobic exercises with such intensity can effectively reduce the impact of this factor.

Zoppini (2006) observed decrease in this factor after 6 months of moderate intensity exercise training program. After performing exercises at different intensities, Simpson (2006) concluded that trainings with 60% maximal heart rate optimally reduced ICAM-1 levels (38). The research of Marsh reported no change in the levels of intercellular adhesion molecule-1 (ICAM-1) (32). The medium or low

intensity could be the reason. Besides, the study was conducted on healthy men and women. Hemmat (2006) also reported no change (39). He has done his research on men and women who smoked cigarettes, while it has been noted in researches that smoking cigarettes increase ICAM-1 level and other inflammatory factors (21). It can be stated that despite doing exercises, the inflammatory factor does not decrease as smoking cigarettes elevates it. Sabatier (2008) likewise observed no changes in the level of ICAM-1 in his subjects after 14 weeks of aerobic exercises (33). He presumed that the intensity of the exercises was not enough to exert a significant impact.

One of the most important results of this study is the significant reduction ( $p = 0.008$ ) of leptin levels in the aerobic exercise group, compared to the control group. Considering the duration and intensity of performed exercises, the results of this study were consistent with many researchers, including Kumru et al (2005) (40), boghrabadi et al (36) and Oliveet al. (2001)(41). This would seem to imply that long-term exercise with moderate intensity leads to significantly decreased serum leptin concentrations. Despite the results obtained in this study, when Kraemer (2003)(42) reviewed the influence of intermittent exercises for progressive intensity effects on the leptin levels of individuals, no significant changes were observed. On the other hand, Zaccaria et al (2002) (43) studied the effects of three endurance races on the leptin concentrations of 45 males, each of whom had participated in one of the three races. The results showed that only long-term endurance exercises, that required large energy consumption, were causing significantly reduced serum leptin levels, and no significant decrease was observed in half-marathon running and Nordic skiing.

Since the serum leptin concentrations may be a reflection of the size of fat cells (44), some

researches have indicated that the change in leptin levels is an indirect result of exercise, which can be obtained by reducing body fat mass (45).

Because of the significant decrease in leptin levels as a result of these exercises, it can be concluded that reducing adipose tissues by doing aerobic exercises causes low leptin levels, resulting in dropped serum leptin concentrations. Ultimately, the changes in leptin concentration mostly focus on its original manufacturer cell, namely adipose tissue, while one of the reasons for increased serum leptin concentrations is inability of leptin to pass through the blood-brain barrier to reach the hypothalamus (46). After 8 weeks of aerobic exercise program, LDL declined, while HDL increased. LDL/HDL ratio also decreased. The increase in HDL after the exercise training program was very significant. Thus, with the increase in HDL, the above ratio has been reduced. The influence of exercises was mostly on HDL in this research, and the increase in HDL was greater than the decrease in LDL. The significant reduction of LDL in this research is probably due to the lack of control on the subjects' diet. This factor is one of the limitations of the study. It can be said that in order to decrease LDL, the low-fat diet is also important along with the exercises and physical activity.

### Conclusion

Aerobic exercises can be a suitable method to reduce body weight and fat. It reduces LDL/HDL ratio, the increase of which is one of the causes of cardiovascular diseases. Furthermore, these exercises decrease ICAM-1 level, which is one of the risk factors for cardiovascular disease. Aerobic exercises increase muscle capacity to use fat, which has also a crucial role on the regulation of leptin levels. All these factors contribute greatly to the development and progression of cardiovascular diseases.

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