

# The Effect of 12-Week of Aerobic Training on Homocysteine, Lipoprotein A and Lipid Profile Levels in Sedentary Middle-aged Men

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#### ABSTRACT

**Background:** The purpose of this study was to investigate the effect of 12-week of aerobic training on homocysteine, lipoprotein A and lipid profile levels in sedentary middle-age men.

**Methods:** This was a quasi-experimental study. Subjects of the study were 24 men (age 40-60) who participated is the study voluntarily and were randomly assigned in aerobic (n = 12) and control (n = 12) groups. The subjects participated in progressive aerobic training on treadmill 3 times a week (20 min/session (60% maximum heart rate) to 60 min (75% maximum heart rate). Homocysteine, lipoprotein A, triglyceride (TG), cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) were measured before and after 12-week. Data were analyzed using paired *t*-test and independent *t*-test statistical methods.

**Results:** Research findings showed a significant decrease in homocysteine (P = 0.002), lipoprotein A (P = 0.003), TG (P = 0.008), cholesterol (P = 0.024) and LDL (P = 0.019), significant increase in HDL (P = 0.017) in posttest compared to pretest. Furthermore, research findings showed that homocysteine (P = 0.005), lipoprotein A (P = 0.001), TG (P = 0.006), cholesterol (P = 0.015), LDL (P = 0.022), and HDL (P = 0.004) levels between the two groups.

**Conclusions:** These findings reveal the 3 sessions/week of aerobic training cause reduction of homocysteine, lipoprotein A, and lipid profile levels in sedentary middle-aged men and can be recommended for prevention of cardiovascular disease.

Keywords: Aerobic training, homocysteine, lipid profile, lipoprotein A, middle-aged men

### **INTRODUCTION**

Chronic diseases such as heart disease are spreading out worldwide. Sometimes, cardiovascular diseases occur in individuals with no disease background.<sup>[1,2]</sup> Recently, a large number of cardiovascular risk factors have been detected, but the role of new risk factors added to traditional ones in predicting or preventing cardiovascular diseases and mortality is still unknown.<sup>[3,4]</sup> Homocysteine and lipoprotein A are two new risk factors of heart diseases and may cause plaque formation on vessel walls.<sup>[5,6]</sup> However, the pathogenic role of these risk factors in the developing cardiovascular disease is still debating.<sup>[7,8]</sup>

Homocysteine is a nonessential sulfur-containing amino acid mediating metabolic path of nonessential methionine amino acid. It is well-documented that in humans and animals an encoding in homocysteine metabolism gene enzyme results in increased homocysteine and causes several metabolic disorders such as atherosclerosis, clotting in vessels and endothelial malfunctions.<sup>[9,10]</sup> Epidemiological studies have proved the positive relationship between homocysteine concentration and risk of cardiovascular disease.<sup>[11,12]</sup> Decreasing homocysteine concentration is associated with reduced cardiovascular disease risk. Plasma homocysteine concentration increases with age and is higher in men compared to women.<sup>[13]</sup> Randeva et al. examined the effect of a 6-month exercise program on homocysteine levels. Results indicated that exercise can reduce homocysteine levels.<sup>[14]</sup> Duncan et al. examined the effect of severity and frequency of exercise sessions per week on homocysteine levels in middle-age and observed a small increase in homocysteine levels.<sup>[15]</sup>

Lipoprotein A is one of cholesterol derivatives that exist in human plasma. It exacerbates atherosclerosis and its structure is similar to low-density lipoprotein (LDL), but with a glycoprotein called apoprotein an attached to it and its concentration being genetically determined. Research findings indicate that increased lipoprotein A <30 mg/d lit increases cardiovascular diseases risk 3-10 times-depending on the existence of other factors.<sup>[16,17]</sup> There are two mechanisms, which may explain the relationship between lipoprotein A and cardiovascular disease. First, it is argued that lipoprotein A, like LDL, plays a role in initiating the progression of atheromatous plaque as a particle. Second, it is suggested that this particle competes with the plasminogen particles in preventing thrombolytic process.<sup>[18]</sup> Zafari examined the effects of regular exercise on lipoprotein A levels in middle-age men and observed that lipoprotein A levels in active and sedentary individuals are less than coronary artery disease patients.<sup>[19]</sup> Almeida *et al.* studied the effects of 12-week of aerobic and strength training on rats and found no significant differences in lipoprotein A levels.<sup>[17]</sup> Firozeh *et al.* surveyed the effect of 8-week walking on lipoprotein A levels in women and observed no significant difference.<sup>[16]</sup>

Physical fitness reduces cardiovascular risk up to 50% in middle-aged and is accompanied by preventing the developments of triglyceride (TG), cholesterol and LDL risk factors and increasing high-density lipoprotein (HDL) levels.<sup>[20-22]</sup> From general health point of view, aerobic training is one the most effective ways to reduce the risk of cardiovascular diseases. Aerobic training is a key factor either alone or in combination with appropriate lifestyle in improving blood lipid profile. One of the main challenges to maintain health is active life style.<sup>[23-25]</sup> Aerobic training is recommended for improving lipid and lipoprotein levels as a low-cost way for middle-age. Researches have reported significant improvements in lipid profile and lipoprotein levels as a result of aerobic training positive. However, several paradoxes have been reported.<sup>[26-28]</sup> Martin et al. indicated the effect of 16-week of progressive aerobic training with moderate-intensity on lipid profile in middle-aged men.<sup>[29]</sup> As research shows, significant improvements will be observed in TG, cholesterol, LDL and HDL levels after aerobic training. Akcakoyun investigated the changes in lipid profile after moderate-intensity training programs in middle-aged men.<sup>[26]</sup> Experimental group subjects participated in a 2-month training program. The results showed that levels of serum TG decreased, and HDL increased in the experimental group after the training program. In a study Banitalebi et al. investigated the effects of 12-week of progressive aerobic exercise on blood lipids and lipoproteins in 23-49 years old men.<sup>[30]</sup> No significant changes in levels of TG, cholesterol, LDL and HDL after 12-week were observed between the two groups.

Long-term studies show that physical inactivity in middle-aged increases the risk of cardiovascular diseases up to 50%,<sup>[31-33]</sup> in this study, we examined the effect of 12-week of aerobic training on homocysteine, lipoprotein A, and lipid profile levels in sedentary middle-age men. Regarding controversies in previous studies findings and limitation of study about the influence of aerobic training on homocysteine and other lipoproteins this study seem necessary.

## **METHODS**

Subjects' physical characteristics are presented in Table 1. Objectives, procedure, as well as possible risks of training programs were described to the subjects and their written consents were obtained. Subjects were selected according to their age, >30 body mass index, physical health, not attending in regular exercises since 6-month before the study, normal lipid profile status and lack of a specific diet, medication, and smoking. The primary criterion for evaluating subjects' health was to check the physical examination done by a physician and review the health questionnaire. None of the subjects were affected to chronic autoimmune, systemic, cardiovascular, hepatic or other diseases, which can continuously change the lipid status. Also at the preliminary session the participants were asked not to change their diet and lifestyle during the 12-week. Qualified individuals were randomly assigned into two aerobic (n = 12) and control (n = 12) groups.

# Aerobic training program and measurement of research variables

The subjects performed training sessions using a treadmill 3 times a week (on nonconsecutive days) and 20 min/session (60% of maximum heart rate) to 60 min (75% of maximum heart rate). Heart rate was also accounted by Karonen's formula.

Subjects' height and weight were recorded using a medical scale with stadiometer (Seca: 220, Germany). Body compositions were measured using a body composition analyzer (Inbody 3.0, South Korea). Blood samples were collected after 12 h fasting at pretest and 48 h after the last training session

Table 1: Participant characteristics of the aerobic training
and control group

Parameter	Mean (SD)		
	Aerobic training	Control group	
Age (year)	48.16 (5.68)	46.50 (4.37)	
Height (cm)	175.51 (9.72)	175.03 (8.43)	
Body weight (kg)	72.89 (7.99)	74.16 (8.77)	
BMI (kg/m <sup>2</sup> )	26.54 (2.11)	24.50 (3.47)	
Body fat (%)	26.94 (3.50)	26.79 (3.68)	
Lean body mass (kg)	53.53 (8.11)	56.30 (7.66)	

SD=Standard deviation, BMI=Body mass index

at posttest. After collecting blood samples at each step, 10 cc of blood was obtained from the left hand in a sitting position. Axis Homocysteine EIA Reagent kit (Axis-shield co., Dundee, UK). kit (made in England) was used to measure homocysteine levels and DRG ELISA Total Human Lipoprotein (A) (DRG International Inc., USA). to measure lipoprotein A levels. Pars Azmoon kit (Pars Azmoon Co., Tehran, Iran) and enzymatic method were used for the measurement of plasma levels of TG, total cholesterol and HDL; and LDL was calculated by Friedwald equation (LDL = TC – (HDL + TG/5) in terms of milligrams per deciliter.

#### Statistical analysis

Statistical analysis was performed using SPSS for Windows software, version 18 (SPSS Inc., Chicago, IL, USA). Data normality was determined by Kolmogorov–Smirnov test. Paired *t*-test was used for within-group comparison and independent *t*-test was used for between-groups comparison. The significance level of the test was also considered  $P \le 0.05$ .

# **RESULTS**

Comparison of within-group differences of research variables are presented in Table 2. Research findings indicate that there were statistically significant differences in the levels of homocysteine, lipoprotein A, TG, cholesterol, LDL and HDL in posttest compared to pretest (P = 0.002, 0.003, 0.008, 0.024, 0.019, and 0.017, respectively). There was no significant change in the values of variables in the control group. Table 3 shows the comparison of the variables between the aerobic training and control groups following 12-week. The table's results show significant differences between the values of homocysteine, lipoprotein A, TG, cholesterol, LDL and HDL between the two groups (P = 0.005, 0.001, 0.006, 0.015, 0.022 and 0.004, respectively).

### **DISCUSSION**

This study was designed to investigate the effect of 12-week of aerobic training on homocysteine, lipoprotein A and lipid profile levels of sedentary middle-age men. The findings revealed that there was a significant decrease in homocysteine levels at posttest compared to pretest, and following 12-week Mohammadi, et al.: Aerobic training on homocysteine, lipoprotein A and lipid profile and sedantary middle-aged men

Variable	Phase	Aerobic training	P value	Control group	P value
Homocysteine (mmol/l)	Pre	12.47 (2.00)	0.002	11.86 (3.20)	0.837
	Post	10.98 (1.69)		11.93 (3.31)	
Lipoprotein A (mg/dl)	Pre	26.31 (2.20)	0.003	25.88 (2.88)	0.287
	Post	23.40 (2.46)		26.33 (2.96)	
Triglyceride (mg/dl)	Pre	139.17 (26.99)	0.008	167.17 (52.92)	0.818
	Post	131.42 (26.55)		167.42 (53.01)	
Cholesterol (mg/dl)	Pre	191.75 (27.15)	0.024	195.92 (24.78)	0.53
	Post	174.33 (22.82)		198.00 (28.49)	
LDL (mg/dl)	Pre	114.92 (27.00)	0.019	106.42 (15.88)	0.635
	Post	99.67 (11.34)		105.58 (15.00)	
HDL (mg/dl)	Pre	61.08 (6.69)	0.017	59.67 (4.67)	0.127
	Post	66.00 (4.06)		57.50 (4.94)	

Table 2: The results of paired t test in aerobic training and control group before and after the intervention

LDL=Low-density lipoprotein, HDL=High-density lipoprotein

**Table 3:** Comparison of changes in measured variables

 following 12-week in two groups

8	<i>8</i> - <i>1</i>		
Variable	Aerobic	Control	P value
	group	group	
Homocysteine	-1.48 (1.30)	0.06 (1.11)	0.005
(mmol/l)			
Lipoprotein A (mg/dl)	-2.91 (2.65)	0.45 (1.41)	0.001
Triglyceride (mg/dl)	-7.75 (8.36)	0.25 (3.67)	0.006
Cholesterol (mg/dl)	-17.41 (22.98)	2.08 (11.13)	0.015
LDL (mg/dl)	-15.25 (19.30)	-0.83 (5.92)	0.022
HDL (mg/dl)	4.91 (6.03)	-2.16 (4.54)	0.004

LDL=Low-density lipoprotein, HDL=High-density lipoprotein

of aerobic training significant differences between aerobic and control groups. These results were consistent with Randeva et al.[14] and Taghian et al.<sup>[34]</sup> but did not match Duncan et al.<sup>[15]</sup> and Gelecek et al.<sup>[35]</sup> One of the mechanisms associated with homocysteine function in cardiovascular diseases is due to a decrease in HDL levels. Homocysteine decreases HDL concentration in plasma by inhibiting hepatic synthesis of apoprotein A existing in HDL. Decreased HDL concentration and increased homocysteine levels may increase the risk of cardiovascular diseases.<sup>[13,36]</sup> Decreased homocysteine due to participating in regular training probably increase available apoprotein A existing in HDL. Three major factors influencing homocysteine levels except for regular training are mode, intensity and duration of the exercises.<sup>[10,37]</sup> The reason for inconsistency might be different mode, intensity and duration of the training programs in mentioned studies.

The findings revealed that there were significant decreases in lipoprote in Alevels at posttest compared to pretest, and following 12-week of aerobic training significant differences were observed between aerobic and control groups. These results were consistent with Zafari<sup>[19]</sup> but did not match Almeida et al.<sup>[17]</sup> and Firozeh et al.<sup>[16]</sup> Recent data from cross-sectional studies have shown that regular training with moderate-intensity is effective in reducing the concentration of lipoprotein A, but intense training does not induce this effect. Transient increase of lipoprotein A levels immediately after severe or prolonged exercise is because of the role of lipoprotein A in repairing tissues, which have been damaged due to free radicals and severe and prolonged training. One reason for the reduction in lipoprotein A is an anti-oxidant effect of aerobic training, because free radicals oxygen increase expression of inflammatory mediators and attaching molecules.<sup>[16,17]</sup> In addition, studies have shown that antioxidant defense is reinforced by regular training.<sup>[38]</sup> Probably, regular training can decrease lipoprotein A levels by improving the antioxidant system. The reason for this difference is probably related to differences in the subjects of this study as well as the intensity and duration of training sessions. Furthermore, in mentioned studies due to low exercise capacity of subjects, training intensity was lower than this study.

The findings revealed that there were significant decrease in TG levels at posttest compared to pretest, and following 12-week of aerobic training between aerobic and control groups. These results were consistent with Martin *et al.*<sup>[29]</sup> and Akcakoyun<sup>[26]</sup>

but did not match Banitalebi *et al.*<sup>[30]</sup> Aerobic training reduces the risk of cardiovascular diseases, and based on research evidence; sedentary individuals are exposed to these risk factors. One mechanism related to reducing the risks of cardiovascular diseases could be due to reducing TG levels. TG is produced because of diet or by the liver itself.<sup>[39,40]</sup> Lipoprotein lipase is an enzyme catalyzing TG and causing the release of free fatty acids from TG in order to provide energy during aerobic training. Thus, a high correlation exists between lipoprotein lipase enzyme activity and blood TG removal.<sup>[26,41]</sup> Probably, aerobic training increases the activity of lipoprotein lipase enzyme and the enzyme activity lead to reducing the levels of TG at the posttest.

Present research findings have indicated that cholesterol levels decreased significantly posttest compared to pretest in an aerobic group, and also significant differences were observed after 12-week of aerobic training between the control and aerobic groups. These results were consistent with Szymanska et al.<sup>[42]</sup> but did not match Banitalebi et al.<sup>[30]</sup> One of the first and the most obvious changes observed during aerobic training is reduced plasma insulin.<sup>[43]</sup> Therefore, probably one of the factors that may influence plasma cholesterol is plasma insulin levels. And it can be stated that reduction in plasma insulin leads to activation of lipolysis from fat tissue and increasing the concentration of free fatty acids in plasma. And simultaneously, insulin reduction and glucagon increase. Both hormones lead to increased activity of ketogenesis which then changes the cholesterol precursor buildup.

Research findings showed that there were statistically significant decreases in an aerobic group in LDL levels at posttest compared to pretest, and following 12-week of aerobic training significant differences were observed between aerobic and control groups. These results were consistent with Monda et al.<sup>[44]</sup> but did not match Banitalebi et al.<sup>[30]</sup> From physiological and molecular mechanisms involved in the reduction of LDL levels, it can be stated that exercising leads to increased lipoprotein lipase activity. Because of the effect of this enzyme increase on cholesterol-rich lipoprotein catabolism, the amount of LDL reduces due to physical activity. Since the increase in serum lipid is of cardiovascular diseases risk factors,<sup>[39]</sup> It can be acknowledged that increased aerobic training reduces some of risk factors such as LDL levels.

Research findings showed a significant increase in HDL levels in posttest compared to pretest in an aerobic group, and following 12-week of aerobic training significant differences were observed between aerobic and control groups. These results were consistent with Bemelmans *et al.*<sup>[45]</sup> but did not match Gelecek *et al.*<sup>[36]</sup> Lipoprotein lipase plays an important role in converting LDL to high HDL. Aerobic training increases lipoprotein lipase levels. Hence, one of the reasons for an increase in HDL levels can be its increased production by the liver and alterations in several enzymes such as increased activity of lipoprotein lipase, lecithin cholesterol acyl transferees activity, and decreased activity of hepatic lipase.<sup>[46,47]</sup>

# **CONCLUSIONS**

Limitations of this study include lack of control of sleep and psychological state. The results showed that 3 sessions/week of aerobic training induce a positive influence on homocysteine, lipoprotein A and lipid profile levels in sedentary middle-aged men. Therefore, aerobic training is recommended for prevention of cardiovascular disease.

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