

## The effects of an eight-week aerobic exercise training program on serum leptin and cardiovascular risk factors among obese men with type II diabetes

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**Abstract:** Most diabetics suffer from obesity and one of the factors related to obesity is leptin hormone metabolism disorder. Reducing abnormal levels of this substance in the blood can prevent cardiovascular diseases. Thus, the aim of this study was to examine the effects of aerobic exercise training on serum leptin and cardiovascular risk factors among obese men with type 2 diabetes. In this clinical study, 53 patients in the age of 45±6 who had type 2 diabetes mellitus were selected purposely and classified randomly into two groups, i.e., an aerobic exercise group (27 patients) and a control group (26 patients). The former participated in an eight-week training program three times a week that included 45 to 60 minutes with the intensity of 60 to 80% of maximum heart rate. The subjects' blood samples, physical aspects, and oxygen consumption were taken before and after aerobic exercise training in the exercise group and in the control group. Aerobic exercise training caused a significant reduction in fat percentage ( $p = 0.02$ ) and serum leptin of the patients ( $p = 0.000$ ), and it also significantly increased the HDL-c average ( $p = 0.048$ ) and the maximal oxygen consumption ( $p = 0.000$ ). It caused no significant changes in body weight, body mass index, waist-to-hip ratio (WHR), cholesterol, triglycerides, or LDL-C. This study indicated that metabolic disorders, which are considered to be the most important syndromes of type II diabetes, can be decreased by regular aerobic exercise training. Physical activities mixed with aerobic exercise training can decrease metabolic disorders by reducing the percentage of fatty tissue and serum leptin.

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### 1. Introduction

Most patients with type 2 diabetes suffer from obesity, and one of the factors related to obesity is leptin hormone metabolism disorder. Leptin is a hormone derived from fatty tissues, and it exists in the bound and free structures of human serum. The concentration of serum leptin demonstrates the stored energy level in fatty tissue. Leptin production can be increased by raising the mass of fat. The amount of leptin is indicative of the level of stored fat inside the human body, and it can indicate the existence of an imbalance in the energy condition in the human body (1). Leptin and other molecules secreted from fatty tissue can affect the body's sensitivity to insulin. Also, it has been demonstrated experimentally that leptin plays an important role in the formation of diseases related to obesity disorders, such as atherosclerosis and other cardiovascular problems (2). Thus, leptin can be considered as one of the major factors concerning obesity and heart coronary, and each process that helps reduce abnormal levels of

this substance could help prevent cardiovascular diseases (3).

Lehmann et al. (2001), in an article entitled "Abdominal Fat Reduction and Improvement of Cardiovascular Risk Factors in Patients with Non-Insulin-Dependent Diabetes Mellitus" (NIDDM) reported that a three-month regular aerobic exercise training with the intensity of 50 to 70% of  $Vo_{2max}$  resulted in a 20% reduction in plasma triglyceride concentration (TGC) in the fasting state and an increase in the low density lipoprotein (LDL) level. Also, physical exercises with moderate intensity caused an increase in lipolytic enzymes and an increase in HDL in the plasma (4). Maiorana et al. (200) examined the effects of long-term aerobic exercises (eight weeks) using ergometer bikes and treadmills with the intensity of 70 to 85% of  $Vo_{2max}$  for male patients with type II diabetes. They reported that  $Vo_{2max}$  was increased after such exercises for eight weeks, but they found no changes in LDL, HDL, TG, or body mass index (BMI). However, fat percentage and weight height ratio (WHR) decreased

significantly (5). Bruce et al. (2004) reported the effects of aerobic exercise training on triglyceride content and insulin sensitivity among male patients with type II diabetes. They reported that the percentage of energy consumed, triglycerides, and Vo<sub>2</sub>max increased after the eight-week, aerobic exercise training program at the intensity of 70 to 85% of maximum heart rate, while LDL, HDL, and total cholesterol levels were not changed (6). Ozcelik et al. (2005) reported that 12-week aerobic exercise training using ergometer bikes can reduce weight, percentage of fat, and the density of leptin in obese women (7). Sary et al. (2007) reported that a four-week walking program decreased insulin resistance and leptin density among obese women (8).

Unfortunately, insufficient studies have been conducted concerning the effects of sports activities on leptin levels in diabetic and non-diabetic people in Iran. Taghiyan et al. (2005) examined the effects of a 12-week, aerobic exercise training (running on a treadmill with the intensity of 70 to 80% of maximum heart rate three times a week for 20 minutes during each training session) on plasma leptin level among obese, healthy women. The results indicated that aerobic exercise training reduces the measured percentage of fat; insulin level and plasma leptin can play important roles in controlling the weight of these obese women (9). Haghghi and Hamedinia (2008) examined the effect of a 13-week aerobic exercise training program on the serum of obese, healthy men and reported that such exercises can decrease the leptin level in obese men significantly and cause a positive and significant cohesion between leptin, insulin levels, and fat percentage (10).

Therefore, long-term (more than 12 weeks) and short-term (less than 12 weeks) effects of sports activities on leptin serum levels and on

cardiovascular risk factors among obese people and patients with type II diabetes currently are taken into consideration (11, 13). But it seems that the patients with type II diabetes are more adaptable to leptin reactions and sports activities than other people (14). Thus, the goal of this study was to examine the effect of short-term aerobic exercise training (eight weeks) on serum leptin and cardiovascular risk factors among obese men with type II diabetes.

## 2. Material and Methods

### 2.1. Study Design

Study method was a clinical trial in which pre-test and post-test designs were used on both experimental and control group. The statistical population of this study was 700 male patients with type 2 diabetes who were referred to specific diabetic clinics in Mashhad. These patients volunteered to participate in this research. A screening method was developed for use in selecting participants, and the screening process involved interviews, assessment of medical records, and the types of medicines being used. Ultimately, 53 patients were chosen, and those chosen were 40 to 50 years old and had serum glucose levels that ranged from 150 to 250 mg/dl. The participants were classified randomly into two groups, i.e., the control group and the experimental group. The patients in the control group did not have diabetes complications and they had no medical records in the mentioned clinics. The subjects received letter of informed consent that they were to sign, and they also received the necessary information about the method, the manner of implementing the study, and the possible risks were provided. This study was approved by Moral Committee of Medical Sciences University of Mashhad.

**Table 1.** Eight-week Training Program with Sessions Three Times a Week

week	Warm-up (min)	activity	15-30min HRmax 60-70%	Active rest	15-30min HRmax 40-50%	Cool-down (min)
1-3	10	15min (3×5min)		15min (3×5min)		10
4-6	10	21min (3×7min)		21min (3×7min)		10
7 and 8	5	30min (3×10min)		30min (3×10min)		5

### 2.2. Exercise Protocol

The exercise protocol was an eight-week program with an exercise training program three times each week (Table 1), with each training session lasting 45 to 60 minutes. Each session included warm-up exercises (5 to 10 minutes), the main exercises (30 to 60 minutes), and cool-down exercises (5 to 10 minutes). Warm-up exercises included walking, a general warm-up of the joints, and stretching movements. Exercises on the treadmill

were designed based on a regular duration and intensity so that the subjects did the related exercises during three training sets so that their heart rates detected and stored while they were on the treadmill. In addition to controlling their heart rates, we used the Borg Scale to assess the participants' rate of perceived exertion (RPE) for use in controlling the intensity of the aerobic exercise training, as well as active resting. The subjects did their exercises on the fixed bike and the elliptical trainer according to an

active rest with a pre-determined intensity and duration. At the end of each training session, the subjects did some movements to cool down, including walking with a very low intensity and stretching movements. They did such exercises before and after dinner. The both temperature in the gym was 15 °C. During the first stage of the study, the questionnaire activity coefficient (QAC) was used to control the daily activities of the subjects (15).

### 2.3. Diet and Blood Glucose Control

A 24-hour dietary recall questionnaire was used for controlling the participants' diets at different stages of the training sets. Also, Glucocard II Digital Glucometers (Tanila, 2001) were used to measure blood glucose during the aerobic exercise training sessions.

### 2.4. Measurement of Blood samples

The measurements of leptin concentrations were performed by the radio-immunoassay (RIA) method, using a diagnostic Biochem kit made in Hungary. For measuring total fasting cholesterol, HDL, and LDL levels, a Gama counter device was used together with the Immuno Tech Company's IM3210 kit, made in the Czech Republic. The measurement of TG levels was conducted through an auto analyzer biochemistry Selectra device, built by the Mann Company, which used the enzymatic method.

### 2.5. Measurements of Other Factors

BMI and the subjects' percentages of body fat were measured by the representatives from the Nutrition Department of Mashhad Medical Sciences University using a body composition analyzer (Tanita B\_C418 Model). The  $\text{Vo}_2\text{max}$  was measured by Rockport Walking Test by using a polar heart-rate monitoring device (s 625x), and the following equation was given ( $R = 0.88$ ;  $SE \pm 5$  ml/kg/min).

$$\text{Vo}_2\text{max} = 6965.2 = [20/20 \times (\text{body weight, kg})] - [25.7 \times (\text{age in years})] + [595.5 \times (\text{gender})] - [224 \times \text{test time /minute}] - [11.5 \times (\text{heart rate, in beats/minute})] / (\text{body weight, kg})$$

### 2.6. Statistical Analysis

The research data were 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. To compare pre-test and post-test data means in each test

group, the statistically correlated t test was used. All the statistical tests were performed at the 95% confidence level ( $p < 0.05$ ).

### 3. Results

Table 2 shows the Features of all the subjects in groups, e.g., age, medical record, and body weight, before performing the tests. The results showed no significant difference between the two groups. Table 3 indicates that the serum leptin level and body fat percentage decreased significantly in the experimental group ( $p = 0.02$ ), while there were no changes in the control group. The effects of aerobic exercise training on BMI and WHR were not significant in either group. Also, according to the information provided in Table 3, the experimental group had a significant increase in maximal oxygen consumption ( $p = 0.000$ ), while there was no statistically significant difference in the control group. The average of HDL in the two groups showed a significant increase after finishing the training sets ( $p = 0.048$ ). LDL and total cholesterol levels decreased in the experimental group, but the decrease was not statistically significant ( $p = 0.884$  and  $p = 0.549$ , respectively). Similarly, the triglyceride levels showed no significant change ( $p = 0.723$ ).

### 4. Discussions

The level of serum leptin after the eight-week physical exercise program indicated a favorable decrease ( $p = 0.02$ ). Some researchers have reported that short-term aerobic exercise training cannot change leptin concentration (18, 20). Kraemer pointed out through a review that short-term exercises (less than 60 minutes) and exercises that consume less than 800 calories of energy cannot alter the leptin concentration (14). After implementing a 12-week aerobic exercise training program, Ryan and Elahi (1996) found 28% decrease at serum leptin levels among male patients with type II diabetes (21). Hichkey et al. (1997) examined the effects of aerobic exercise training with the intensity of 60% of maximal heart rate on male and female subjects who had type 2 diabetes. They found no changes in the leptin level in the serum of males, while in spite of females (22). Halle et al. (1999) examined obese male patients with type 2 diabetes after one month of exercise on bicycles and reported that body weights and leptin concentrations were decreased significantly, which led to concomitant reductions in total cholesterol and glucose levels (23).

**Table 2.** Characteristics of Patients with Type 2 Diabetes in the Experimental and Control Groups

Index	Experimental group Mean $\pm$ SD	Control group Mean $\pm$ SD	S or NS
n	27	26	----
Drug treatment before training	2 (metphormin+cloropropamid)	2 (metphormin+cloropropamid)	-----
Age(yr)	44.93 $\pm$ 5.35	45.56 $\pm$ 5.41	Ns
Diabetes history(yr)	5.2 $\pm$ 2.4	5.38 $\pm$ 3.4	Ns
High (cm)	172.36 $\pm$ 5.17	173.09 $\pm$ 7.30	Ns
Weight (kg)	84.86 $\pm$ 5.54	86.03 $\pm$ 4.96	Ns
Fat%	29.94 $\pm$ 6.35	31.14 $\pm$ 6.07	Ns

S: Significant at ( $p < 0.05$ ); Ns: Not significant at ( $p < 0.05$ )

**Table 3.** Measurement indices in the experimental and control groups before and after the eight-week aerobic exercise training program

Index	control		experimental		sig
	Pre-test	Post-test	Pre-test	Post-test	
Weight	11.7 $\pm$ 84.8	11.5 $\pm$ 84.9	18.8 $\pm$ 86	17.5 $\pm$ 85.8	0.35
Body mass index	3.9 $\pm$ 28.6	4 $\pm$ 28.7	5 $\pm$ 28.2	4.9 $\pm$ 28	0.089
WHR	0.07 $\pm$ 1	0.07 $\pm$ 0.99	0.05 $\pm$ 0.96	0.07 $\pm$ 0.95	0.998
Fat%	6.1 $\pm$ 31.1	5.4 $\pm$ 31.5	6.4 $\pm$ 29.9	5.1 $\pm$ 27.9	0.014*
VO2 max	4.3 $\pm$ 31.5	3.5 $\pm$ 30.5	6.4 $\pm$ 31.4	5.9 $\pm$ 34.9	0.000*
Cholesterol	47.4 $\pm$ 194.4	51.4 $\pm$ 193.6	39.8 $\pm$ 192.8	41.9 $\pm$ 186.5	0.549
TG	97.4 $\pm$ 177.2	64.4 $\pm$ 171.7	88.4 $\pm$ 196.3	102.9 $\pm$ 202.7	0.723
HDL	7.6 $\pm$ 39.8	10.5 $\pm$ 45.1	6.1 $\pm$ 36.1	9.8 $\pm$ 46.8	0.048*
LDL	40.5 $\pm$ 117.1	32.1 $\pm$ 105.6	29.7 $\pm$ 113.96	26.1 $\pm$ 101	0.884
leptin	1.1 $\pm$ 4.8	1.1 $\pm$ 4.1	1.6 $\pm$ 4.8	1.02 $\pm$ 2.5	0.02*

\*: significant at ( $p < 0.05$ )

Some studies indicated that, if the mentioned exercises result in the reduction of fatty tissue, this process can decrease plasma level (14, 24, and 25). According to Kohrt et al. (1996), the reduction of the leptin concentration is the indirect result of such physical exercises. Thus, the reduction of BMI reduction is related to the reduction of leptin (26), although this finding is incompatible with the results provided by Pasman et al. in 1998. They declared that endurance training can decrease insulin, body fat percentage, and leptin levels (27). The obvious differences between the subjects and the exercise protocols can probably explain the differences related to the exercise and leptin levels in different studies. Studies conducted by Perusse et al. (1997) and Ostlund et al. (1996) emphasized the relationship between leptin and physical exercise through fat changes inside the human body (28, 29). In this study, the eight-week, aerobic exercise training program resulted in a 67% reduction in the body fat of the subjects, while no changes were found in abdominal obesity (which was measured indirectly through WHR) in either group. Thang et al. (2002) examined the effects of aerobic exercise training on men with upper-torso obesity. After a 12-week training program, they found that obesity changes and the reduction of the leptin were in accordance with under-skin fat tissue (30). Hence, we concluded that the subjects' reductions in fat percentage (6.7%) indicated the differences in the under-skin fatty strata

in the control group. Thus, it was considered that under-skin fat is the main source of leptin secretion compared to visceral fat (31) and that under-skin fat tissue secretes more leptin than visceral fats (3); thus, the reduction of under-skin fat inside the body can moderate the reduction of the leptin level as the result of aerobic exercise training. On the other hand, the lack of changes in BMI and WHR, the reduction of the percentage of body fat, the reduction of the leptin concentration, and the increase in the maximal consumption of oxygen indicate that changes in the concentration of leptin may result from other factors, such as:

1. Aerobic exercise training, which produces some changes due to leptin clearance
2. Aerobic exercise training, which produces some changes in the ratio of free or binding leptin to plasma proteins so that it can change the intensity of leptin activity (30)
3. Aerobic exercise training, which may increase the sensitivity of tissue to leptin, with the leptin concentration being adaptable according to this sensitivity
4. Aerobic exercise training, which affects obesity and has an effect on insulin resistance and physical structure. It might be possible that insulin adaptation and leptin depend on each other (4).
5. Leptin level reduction due to weight loss, which can decrease ob gene of under-skin fat cells;

thus, the reduction of the leptin level due to aerobic exercise training may decrease the under-skin fatty tissue of the subjects significantly.

6. Aerobic exercise training, which can increase the lipolysis reaction to the beta adrenergic in under-skin fatty tissue, and, consequently, it can decrease the concentrations of the ob gene and serum leptin (33).
7. Aerobic exercises, during which the capillary density is increased, i.e., more blood and oxygen are transferred to muscular tissue so that the density of mitochondria and the capacities of the oxidative enzymes can be increased in the muscles' mitochondria, increasing oxygen transfer in the chain enzymes and creating effective enzyme activities in fat oxidation, especially for the beta oxidation-cycle enzymes (34). Therefore, the muscles use the metabolism of fat tissues to produce the energy that is required.

The findings of this study indicated that the eight-week, aerobic exercise training program played a vital role in controlling body weight and preventing cardiovascular risk factors by affecting fatty tissue and plasma leptin levels. This process can be useful for preventing and treating type 2 diabetes.

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