

THE EFFECT OF AEROBIC TRAINING ON SERUM ADIPONECTIN AND LEPTIN LEVELS AND INFLAMMATORY MARKERS OF CORONARY HEART DISEASE IN OBESE MEN

■ Accepted
for publication
09.07.2012

AUTHOR: Akbarpour M.

Department of Physical Education, University of Qom, Qom, Iran

ABSTRACT: The aim of this study was to investigate the effect of 12 weeks of aerobic training on the serum levels of adiponectin and leptin and on inflammatory markers of coronary heart disease in obese men. Sixteen non-athlete obese men were randomly assigned to one of two experimental groups. The experimental group underwent aerobic training consisting of three sessions per week for 12 weeks, while the control group did not participate in the training programme during the study period. Five millilitres of venous blood was taken from each participant at the beginning of the study, during week six and at the end of week 12 to measure the levels of leptin, adiponectin, C-reactive protein, interleukin-6 and tumour necrosis factor- α . The findings showed that aerobic training led to decreases in the levels of CRP ($P=0.002$), IL-6 ($P = 0.001$) and leptin ($P = 0.003$) and an increase in the level of adiponectin ($P = 0.002$) in the experimental group relative to the control group. In addition, the level of TNF- α decreased in the experimental group after the 12-week aerobic training period, although this change was not statistically significant. According to the results of this study, regular aerobic exercise decreases the potential risk of coronary heart disease by improving the plasma levels of IL-6, adiponectin, leptin and CRP. Additionally, aerobic exercise can be used as effective non-pharmacological treatment to prevent diseases.

KEY WORDS: aerobic training, leptin, adiponectin, inflammatory markers, coronary heart disease, obese men

Reprint request to:
Mohsen Akbarpour
Department of Physical Education,
University of Qom, Qom, Iran
Tel: +989131839198
E-mail: akbarpour.mohsen@gmail.com

INTRODUCTION

From a biological point of view, fat tissue is an active tissue and secretes proteins including TNF- α , IL-6, IL-8, leptin and adiponectin [18]. Clinical studies have shown that the level of adiponectin gene expression and the serum concentration of adiponectin are lower among individuals with type 2 diabetes, coronary heart disease and high blood pressure than among healthy people, and the concentration of adiponectin decreases in obese people, obese pigs and obese mice [19,22]. In contrast, the level of leptin increases as the result of obesity. Adiponectin plays an important role in overcoming insulin resistance caused by an individual's diet. Studies in rodents have shown that adiponectin decreases the level of blood glucose and prevents fat accumulation in the skeletal muscle [4,6,31]. In comparison with other molecules secreted from fat cells, this protein has protective metabolic effects and anti-inflammatory properties. In addition, the level of adiponectin in human blood is inversely related to the level of insulin resistance [20]. Regarding leptin, some scholars have considered this hormone to be a warning mechanism for adjusting the body's fat content [4]. This hormone, along with insulin, affects coronary performance and the sympathetic nervous

system [19,30]. Increases in the level of leptin, which has been found to be an independent factor associated with coronary heart disease in many studies, are associated with poor performance of the vessel wall [11,29,30]. In addition to the relationship of obesity with leptin and adiponectin, inflammatory markers also cause changes in the body composition and endocrine glands [18,40], and some studies have reported a relationship between both obesity and increases in the levels of TNF- α , IL-6 and CRP inflammatory markers and the increased risk of coronary heart disease [3,4,23,26,32,35]. Therefore, any activity that can change the abnormal level of these substances in the blood may help prevent coronary heart disease. Physical activity can be considered an effective factor in improving obesity. However, there is contradictory information on the effect of physical activity on the levels of leptin, adiponectin and inflammatory markers (CRP, IL-6 and TNF- α). A number of researchers have

Abbreviations:

TNF- α	Tumor Necrosis Factor- α
IL-6	Interleukin-6
IL - 8	Interleukin-8
CRP	C- reactive protein

shown that the plasma concentrations of leptin and adiponectin are not substantially influenced by physical activity in healthy people [4,5,28,29,36-38]. Kobayashi et al. observed that 50 days of walking led to an improvement in the adiponectin level in healthy men with a normal weight [25], whereas Elloumi et al. observed that two months of participating in an aerobic training programme with moderate intensity increased the adiponectin level and decreased the leptin level in obese adolescent boys [14].

Additionally, it has been determined that regular physical activity and training decrease the levels of inflammatory markers and decrease the risk of coronary heart disease [3]. The results of the studies conducted in this field have shown that regular exercise significantly decreases the levels of TNF- α , IL-6, IL-1 β and CRP [8,10,23,26,35,43] and that there is a relationship between higher levels of physical activity/physical fitness and lower levels of these inflammatory markers [34]. In addition, some scholars, including Fahey [16] and Arsenault [2], have reported a lack of change in the levels of inflammatory markers during long-term aerobic training.

The present study was undertaken for several reasons. First, the results regarding the effect of aerobic activity on the serum levels of adiponectin, leptin and inflammatory markers are contradictory. Second, there are differences in the baseline level of physical fitness, sex, age and training programme of the participants in past studies. Third, there is a lack of studies investigating the effects of long-term aerobic training on the serum levels of adiponectin, leptin levels and inflammatory markers in obese men. Finally, there is a lack of convincing evidence regarding the effect of long-term exercise on the levels of adiponectin, leptin and inflammatory markers. Therefore, in the present study, we attempted to examine the effect of 12 weeks of aerobic training on the serum levels of adiponectin, leptin and inflammatory markers (CRP, IL-6 and TNF- α) in obese men.

MATERIALS AND METHODS

Participants. This semi-experimental two-group study was approved by the Ethical and Research Committee of the University of Qom and performed in accordance with the principles outlined in the Declaration of Helsinki. The obese, male, non-athletic students who volunteered to participate in this study received an informed consent form and each participant gave informed consent before enrolment. Then they filled out a questionnaire that included questions regarding personal characteristics, health, smoking and physical training history. Then, their heights and weights were measured, and their body mass index (BMI) values were calculated (weight in kilograms divided by the squared height in metres). Among the 167 volunteers who qualified for this study, 60 people were chosen using random sampling with replacement. The participants were not athletic, and their age ranged from 20 to 25 years old. Their BMIs were between 30 and 33 kg·m⁻². Additionally, they had no history of smoking or allergy and had taken no medicine for at least 2 weeks before the

TABLE I. GENERAL CHARACTERISTICS OF THE SUBJECTS

Variable	Group	Experimental training group (N=30)	Control group (N=30)	F	P
Age (year)		23.2 ± 2.5	22.7 ± 2.7	6.325	0.684
Weight (kg)		86.94 ± 5.8	88.76 ± 7.51	7.623	0.892
Height (cm)		170.13 ± 4.45	172.03 ± 6.47	6.146	0.712
$\dot{V}O_2$ max (ml·kg ⁻¹ ·min ⁻¹)		36.14 ± 2.43	35.96 ± 1.78	1.697	0.541
BMI		30.05 ± 2.26	30.60 ± 2.45	2.06	0.522
Body fat %		23.89 ± 2.73	24.58 ± 2.61	3.52	0.683

start of the research period. The participants were not allowed to take any medications during the research period, and they followed their own normal diet. Then, all subjects were allocated to either the experimental or control group, with 30 people in each group, using simple random sampling. The participants' general characteristics are given in Table 1.

Physiological measurements

To measure weight and height, a digital scale and a tape were used, respectively. The BMI was also calculated (squared height in metres / weight in kilograms), and the body fat percentage was determined by measuring the amount of subcutaneous fat in the chest, abdomen and thigh and then using these values as input for the Jackson and Pollock equation [44].

To estimate the aerobic power of the subjects, we conducted a 2400-m walking and running test. The aerobic power of each subject was calculated using the following equation [44]:

$$\dot{V}O_2\text{max (mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}) = 88.02 - 0.1656 \times (\text{weight(kg)}) + 2.76 \times (\text{time(min)}) + 3.716 \times 1$$

The training programme

First, the maximum heart rate was determined for each person using the following formula: 208-(0.7 × age) [42].

In this study, the experimental group participated in a 12-week aerobic training programme (3 sessions per week). The aerobic training programme included a 10-min warm-up consisting of fast walking, slow running and stretching. Then, continuous running was performed with intensity between 75 and 85% of the maximum heart rate of the participant. The running period was 15 min for the first session, and every two sessions 1.5 min was added to the running period in a stepwise manner until the running period reached 30 min. The running period was then kept at 30 min until the last session of the training programme (the end of the 12th week). The exercise intensity was controlled using a belt heart rate sensor (polar beat), and at the end of each session, there was a cool-down period consisting of slow running and stretching for 10 min.

Blood sampling

To investigate biochemical variables, in the first stage, the participants of each group were barred from participating in any sport activity until two days before the test and were told to maintain their normal diet. Then, 5 ml of blood was collected from each participant after 12 h of fasting. The blood was taken from the left-hand antecubital vein while sitting and resting. The blood sampling was conducted at 8 a.m. for both the experimental and control groups. After this stage, the experimental group participated in an aerobic training programme for 12 weeks (3 sessions per week). After 6 and 12 weeks of aerobic training, the second and third stages of blood collection from the participants in the control and experimental groups were performed in a manner similar to that for the first stage. Blood was collected 48 h after the last training session and after a 12 h fast.

The subjects in the control group did not participate in any training programme and proceeded with their normal daily routine. All protocols were approved by the Graduate Council of the Faculty of Physical Education and Sports Science, University of Qom.

Biochemical measurements

To measure the levels of inflammatory markers (serum TNF- α , CRP and IL-6), the ELISA (enzyme-linked immunosorbent assay) method was applied using kits from the French Diaclone Company. These kits had sensitivities of less than 7, 2 and 8 $\mu\text{g} \cdot \text{mL}^{-1}$, respectively.

The measurement of plasma adiponectin concentration was performed using the ELISA method with the Adipogen Adiponectin kit (Adipogen Co, South Korea), which has a sensitivity of 0.1 $\mu\text{g} \cdot \text{mL}^{-1}$. The inter test coefficient of variation was less than 3.9% for this kit, and of the intra test coefficient of variation was less than 8.6%. The plasma concentration of leptin was measured by the ELISA method using a leptin kit (Mediagnost, Reutlingen, Germany) with a sensitivity of 0.1 $\text{ng} \cdot \text{mL}^{-1}$. The intra test coefficient of variation was less than 5%.

Additionally, the participants' diets during the research were monitored using the 24-h food recall questionnaire standardised by the Nutrition Group, Tehran University of Medical Sciences (in week 0, week 6 and week 12).

Statistical method

Statistical analysis of the data was performed for each group using the means and standard deviations. Then, the Kolmogorov-Smirnov test was used to ensure that the data were normally distributed. Student's t test was used to perform the between-group analysis of variance with repeated measures. ANOVA3 was used for within-group evaluation along with the Greenhouse-Giser (GG) correction. The t-test with the Bonferroni correction was used to identify significant differences by determining the difference location to reduce the error for paired samples. The significance level was $P \leq 0.05$ for all the calculations, and all statistical tests were conducted using SPSS software (version 13, Michigan, USA).

RESULTS

The results obtained from the current study showed that 6 and 12 weeks of aerobic training increased $\dot{V}O_2\text{max}$ ($P=0.0001$), decreased the percent body fat ($P=0.001$) and decreased the body mass index ($P=0.001$) relative to the control group. In addition, after 6 weeks of training, the serum levels of leptin (0.19), CRP ($p=0.27$) and IL-6 ($P=0.36$) decreased in the control group, and the plasma level of adiponectin ($P=0.31$) increased, but this change was not statistically significant. After 12 weeks of training, the serum levels of leptin ($P=0.012$), CRP ($P=0.002$) and IL-6 ($P=0.001$) significantly decreased in the control group. In addition, the plasma level of adiponectin ($p=0.002$) significantly increased relative to the level at the pre-test stage (before doing the exercise), whereas the serum levels of serum leptin, adiponectin, CRP and IL-6 in the ex-

TABLE 2. CHANGES IN LEVELS OF INFLAMMATORY MARKERS, LEPTIN AND ADIPONECTIN IN EXPERIMENTAL AND CONTROL GROUP

Variable	Group	Pre-test (week 0)	Mid-test (week 6)	Post-test (week 12)
$\dot{V}O_2\text{max}$ ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$)	Experimental group	35.83 \pm 2.3	37.93 \pm 1.15 † ‡	39.9 \pm 1.8 † ‡
	Control	36.84 \pm 1.7	35.84 \pm 2.1	36.03 \pm 1.8
Body fat (%)	Experimental group	23.74 \pm 2.85	21.18 \pm 1.49 † ‡	19.78 \pm 1.5 † ‡
	Control group	24.36 \pm 2.04	23.83 \pm 1.8	23.99 \pm 2.2
CRP ($\text{pg} \cdot \text{mL}^{-1}$)	Experimental group	1.70 \pm 0.43	1.43 \pm 0.4	1.06 \pm 0.46 † ‡
	Control	1.68 \pm 0.51	1.72 \pm 0.45	1.65 \pm 0.42
TNF- α ($\text{pg} \cdot \text{mL}^{-1}$)	Experimental group	13.32 \pm 3.28	12.94 \pm 3.11	10.16 \pm 3.25
	Control group	13.07 \pm 2.82	13.57 \pm 2.67	12.80 \pm 2.95
IL-6 ($\text{pg} \cdot \text{mL}^{-1}$)	Experimental group	7.42 \pm 3.21	5.26 \pm 3.45	1.93 \pm 0.69 † ‡
	Control group	8.01 \pm 3.86	8.62 \pm 4.07	8.23 \pm 3.34
Adiponectin ($\mu\text{g} \cdot \text{mL}^{-1}$)	Experimental group	16.75 \pm 1.48	17.44 \pm 1.78	18.43 \pm 1.65 † ‡
	Control group	16.52 \pm 1.33	16.47 \pm 1.49	16.53 \pm 1.51
Leptin ($\text{ng} \cdot \text{mL}^{-1}$)	Experimental group	2.34 \pm 0.27	2.30 \pm 0.25	2.25 \pm 0.22 † ‡
	Control group	2.32 \pm 0.20	2.34 \pm 0.24	2.31 \pm 0.21

† denotes a significant difference relative to the pre-test level ($p < 0.05$)

‡ denotes a significant difference between the experimental and control groups ($p < 0.05$)

perimental group were not significantly different between the mid-test (week 6) and post-test (week 12) periods [CRP ($P = 0.091$), IL-6 ($P = 0.065$), leptin ($P = 0.062$) and adiponectin ($P = 0.071$)] (Table 2). No within-group differences were observed between the stages for the control group ($P > 0.05$).

DISCUSSION

The results of the independent t test revealed a significant difference in the serum levels of leptin, adiponectin, CRP and IL-6 in the experimental group relative to the levels in the control group after 12 weeks of aerobic training. In the experimental group, the serum levels of leptin, CRP and IL-6 were 36.76%, 76.55% and 2.6% lower than the corresponding levels in the control group, and the level of adiponectin was 11.49% higher than that in the control group [CRP ($P = 0.002$), IL-6 ($P = 0.001$), leptin ($P = 0.003$) and adiponectin ($P = 0.001$)]. In the pre-test stage (week 0) and the mid-test stage (week 6), no significant differences were observed in the levels of the research variables between the control and experimental groups ($P > 0.05$).

As far as TNF- α is concerned, the results of the analysis of variance with repeated measures did not show any significant differences within the control and experimental groups. Although the level of TNF- α decreased in the experimental group after 6 and 12 weeks of training, this change was not significant. Furthermore, the results of the independent t test did not show a significant between-group difference between the control and experimental groups at the three test stages ($P > 0.05$).

In this research, the focus was to determine the effects of exercise on the levels of adiponectin, leptin and coronary heart inflammatory markers (serum TNF- α , CRP and IL-6 and). Appropriate levels of these factors in the blood can prevent diseases such as metabolic syndrome, type 2 diabetes and coronary heart disease. To this end, the levels of leptin, adiponectin and coronary heart inflammatory markers (serum TNF- α , CRP and IL-6) were measured before and after the training period.

The results of the present research showed that 6 and 12 weeks of aerobic training with moderate intensity can increase $\dot{V}O_{2\max}$ and decrease the body fat percentage and the body mass index in obese men. Additionally, the results showed a decrease in the levels of CRP and IL-6, both inflammatory markers, and a decrease in the plasma level of leptin in obese men after 12 weeks of aerobic training with moderate intensity. After 12 weeks of aerobic training, the plasma levels of leptin, CRP and IL-6 in the experimental group were significantly lower than the levels in the control group. Additionally, significant differences in these factors were observed in the experimental group between the pre-test and post-test stages. After the first 6 weeks of aerobic training in the experimental group, the changes in the plasma levels of leptin, CRP and IL-6 were negligible, most likely because the training period, training intensity and duration were not sufficient to have significant effects on these factors. As the length of the training period increased, there was a significant

decrease in the plasma levels of leptin, CRP and IL-6 in the experimental group after 12 weeks. These results were in line with the reports of Miyatake [33], Fatouros [17], Kohut [26], Kadoglou [23], Eriksson [15], Walther [43], Nicklas [35], Campbell [8], Elloumi [14] and Christiansen [10], which reported a decrease in the plasma levels of leptin, CRP and IL-6 as a result of aerobic training. However, the findings of this research were different from those of Fairey [16], Ara [1] and Arsenault [2]. This discrepancy can be attributed to the differences among the studied groups in terms of race, training period, intensity, duration and type of training [34].

The present research demonstrated a significant increase in the plasma level of adiponectin due to 12 weeks of aerobic training in the experimental group compared with the control group. Moreover, a significant difference was observed in the plasma level of adiponectin in the experimental group between the pre-test and post-test stages. This increase was not significant after the first 6 weeks of the training programme. The increase in the plasma level of adiponectin as a result of 12 weeks of aerobic training was most likely a preventive factor for diseases related to adiponectin [4,5]. In this research, the increase in the level of adiponectin after adjusting to the aerobic activity was similar to the results of a number of previous studies [4,5,14,17]. In a previous study, eight young obese women exhibited a significant decrease in the levels of leptin and fat after participating in an aerobic training programme for seven weeks; moreover, their level of adiponectin increased [27]. In another study, after obese and insulin-resistant individuals performed 19 weeks of aerobic training along with diet modification, their visceral fat levels decreased and the levels of adiponectin increased [41]. Other studies found that training had no effect on the level of adiponectin. This discrepancy may be due to differences in age, sex, the type of training programme and the intensity and duration of the training [21,39].

Regarding TNF- α , the results obtained from this study showed no significant within-group differences in the level of serum TNF- α . In contrast, in the experimental group, the TNF- α level decreased by 2.86% and 23.76% after 6 and 12 weeks of aerobic training, respectively. These results were in line with the findings of Fairey [16] and Arsenault [2].

The results obtained from this study showed a significant decrease in the levels of CRP ($p = 0.002$), IL-6 ($P = 0.001$) and leptin ($P = 0.012$) and an increase in the level of adiponectin ($P = 0.002$) after 12 weeks of aerobic training. The change in the level of TNF- α was not significant.

Various studies have shown that the hormones adiponectin and leptin and inflammatory mechanisms have key roles in the pathological processes involved in several chronic diseases, such as coronary heart disease, cancer, type 2 diabetes and chronic obstructive pulmonary disease. It seems that chronic low-grade inflammation is reflected by high levels of CRP, IL-6, TNF- α and leptin [3,4,34], and with regard to the relationship between physical activity and lower levels of inflammation, heart-protective mechanisms can be sug-

gested. A common concept regarding the pathophysiological mechanisms of inflammation associated with atherosclerosis is the production of cytokines along with inflammation in response to oxidised low-density lipoprotein (LDL) stimulation and macrophages along with atherosclerotic plaques [34]. The cytokines associated with inflammation that are produced during this process include IL-1B, IL-6 and TNF- α . It was determined in laboratory experiments that different combinations of cytokines stimulate the production of CRP and leukocytes [9]. Research has shown that participation in regular sport activity decreases the level of oxidised LDL and the serum levels of IL-6 and CRP [2,34]. Therefore, the effect of regular exercise on the levels of IL-6 may be responsible for the decrease in CRP in the experimental groups. In contrast, the relationship between physical activity and lower levels of inflammation can be created through the relationship between endurance training and lower degrees of general and abdominal obesity. It has been found that obese people produce higher levels of leptin and mediators of inflammation including , IL-8 and IL-6, compared with thin people in the control group, whereas obese people have lower levels of adiponectin compared with thin people [2,19,22]. Endurance training can decrease the production of mediators of inflammation from fat tissues by directly affecting fat tissue and increasing dipoles (by increasing the activity of hormone-sensitive lipase) and can increase the production of anti-inflammatory mediators such as IL-10 by fat tissue [6]. The result of these changes is that aerobic training can decrease the circulating levels of inflammatory markers (CRP) by decreasing the sources of inflammation. Moreover, fat tissues are considered an endocrine organ because they secrete various substances, such as , IL-6, leptin and adiponectin [18]. It is likely that stimulates the production of IL-6, which, as a powerful stimulator, leads to the production of liver CRP [6,35]. Therefore, the high level of fat tissues in obese people leads to the increase in the serum level of CRP (in a cascade manner). In addition, TNF- α is one of the primary and most basic mediators of inflammatory processes that is related to the high level in fat tissues (especially visceral fat) and its levels in the circulation indicates the production of this factor in fat tissues [3]. There are different findings on the effect of exercise on the level of TNF- α ; some studies have reported a decrease [6], and others have shown no change [2] in response to physical training. In the present research, it was determined that the serum level of TNF- α did not change in response to 12 weeks of aerobic training because the half-life of TNF- α was low in the blood [7]. Therefore, based on these findings, TNF- α cannot be considered a stable marker for inflammation. Thus, CRP can be used for determining the status of systemic inflammation [12]. CRP is an inflammatory indicator that is made by liver cells in response to inflammatory factors

and is secreted from the liver [6,35]. Therefore, the present study is in line with the investigations that show a negative correlation between physical fitness and chronic inflammation and that demonstrate that physical training leads to reduced inflammation as indicated by the levels of CRP and IL-6 [16]. Therefore, there is a relationship between increases in the levels of inflammatory markers as a result of obesity and atherosclerosis [6].

Furthermore, lower levels of inflammation caused by compatibility with physical activity can be attributed to the anti-oxidation effects of physical activity. Although the level of anti-oxidants was not measured in the present study, research evidence has shown that aerobic training noticeably decreases oxidation stress by increasing the anti-oxidant capacity of the body [45]. Regular physical training inhibits the release of the inflammatory mediators IL-1 β , IL-6 and TNF- α from fat tissues by decreasing the stimulation of the sympathetic system and increasing the production of anti-inflammatory cytokines; as a result, the concentration of cell adhesive molecules decreases [13,45].

Additionally, many scholars believe that increases in the adiponectin concentration and decreases in the plasma level of leptin after long-term physical activity are a result of the decrease in weight and body fat and of the improvement of body composition due to a change in the balance between the received and consumed energy [24,25]. Many studies have investigated the relationship between body composition and plasma levels of leptin and adiponectin, and most of the findings have demonstrated a negative relationship between weight, body mass index, waist size, fat distribution (waist-to-hip ratio) and fat mass on the one hand and adiponectin on the other, and a positive relationship between these factors and leptin [4,19].

Finally, it seems that the amount of training can be a factor affecting the responses of plasma inflammatory markers, leptin and adiponectin (CRP, IL-6 and TNF- α); in other words, long-term physical activity affects the concentration of the plasma inflammatory markers, leptin and adiponectin (CRP, IL-6 and TNF- α) [28].

Therefore, this study showed that regular and long-term aerobic physical training leads to a significant decrease in the levels of CRP, IL-6 and leptin and an increase in the level of adiponectin.

CONCLUSIONS

In summary, it can be concluded that regular aerobic training decreases the risk of coronary heart disease by improving the plasma levels of IL-6, adiponectin, leptin and CRP, and therefore aerobic activity can be used as an effective non pharmacological treatment for preventing these diseases.

REFERENCES

- Ara I., Perez-Gomez J., Vicente-Rodriguez G., Chavarren J., Dorado C., Calbet J.A.L. Serum free testosterone, leptin and soluble leptin receptor changes in a 6-week strength-training programme. *Br. J. Nutr.* 2006;96:1053-1059.
- Arsenault B.J., Cote M., Cartier A., Lemieux I., Despres JP, Ross R., Earnest C.P., Blair S.N., Church T.S. Effect of exercise training on cardiometabolic risk markers among sedentary, but metabolically healthy overweight or obese post-menopausal women with elevated blood pressure. *Atherosclerosis* 2009;207:530-533.
- Beavers K.M., Hsu F.C., Isom S., Kritchevsky S.B., Church T., Goodpaster B., Pahor M., Nicklas B.J. Long-term physical activity and inflammatory biomarkers in older adults. *Med. Sci. Sports Exerc.* 2010;42:2189-2196.
- Bouassida A., Chamari K., Zaouali M., Feki Y., Zbidi A., Tabka Z. Review on leptin and adiponectin responses and adaptations to acute and chronic exercise. *Br. J. Sports Med.* 2010;44:620-630.
- Bouassida A., Lakhdar N., Benaissa N., Mejri S., Zaouali M., Zbidi A., Tabka Z. Adiponectin responses to acute moderate and heavy exercises in overweight middle aged subjects. *J. Sport Med. Phys. Fitness* 2010;50:330-335.
- Bruun J.M., Helge J.W., Richelsen B., Stallknecht B. Diet and exercise reduce low-grade inflammation and macrophage infiltration in adipose tissue but not in skeletal muscle in severely obese subjects. *Am. J. Physiol.* 2006;290:E961-967.
- Bruunsgaard H. Physical activity and modulation of systemic low-level inflammation. *J. Leukocyte Biol.* 2005;78:819-835.
- Campbell P.T., Campbell K.L., Wener M.H., Wood B.L., Potter J.D., McTiernan A., Ulrich C.M. A yearlong exercise intervention decreases crp among obese postmenopausal women. *Med. Sci. Sports Exerc.* 2009;41:1533-1539.
- Chaikate S., Harnroongroj T., Chantaranipapong Y., Puduang S., Mahaisiriyodom A., Viroonudomphol D., Singhasivanon P., Schelp F.P., Tornee S., Tribunyatkul S., Changbumrung S. C-reactive protein, interleukin-6, and tumor necrosis factor-alpha levels in overweight and healthy adults. *Southeast. Asian J. Trop. Med. Public Health* 2006;37:374-381.
- Christiansen T., Paulsen S.K., Bruun J.M., Pedersen S.B., Richelsen B. Exercise training versus diet-induced weight-loss on metabolic risk factors and inflammatory markers in obese subjects: A 12-week randomized intervention study. *Am. J. Physiol.* 2010;298:824-831.
- Cooke J.P., Oka R.K. Does leptin cause vascular disease? *Circulation* 2002;106:1904-1905.
- Dietrich M., Jialal I. The effect of weight loss on a stable biomarker of inflammation, c-reactive protein. *Nutr. Rev.* 2005;63:22-28.
- Ding Y., Li J., Luan X., Ding Y.H., Lai Q., Rafols J.A., Phillis J.W., Clark J.C., Diaz F.G. Exercise pre-conditioning reduces brain damage in ischemic rats that may be associated with regional angiogenesis and cellular overexpression of neurotrophin. *Neuroscience* 2004;124:583-591.
- Elloumi M., Ben Ounis O., Makni E., Van Praagh E., Tabka Z., Lac G. Effect of individualized weight-loss programmes on adiponectin, leptin and resistin levels in obese adolescent boys. *Acta Paediatr.* 2009;98:1487-1493.
- Eriksson M., Johnson O., Boman K., Hallmans G., Hellsten G., Nilsson T.K., Soderberg S. Improved fibrinolytic activity during exercise may be an effect of the adipocyte-derived hormones leptin and adiponectin. *Thromb. Res.* 2008;122:701-708.
- Fairey A.S., Courneya K.S., Field C.J., Bell G.J., Jones L.W., Martin B.S., Mackey J.R. Effect of exercise training on c-reactive protein in postmenopausal breast cancer survivors: A randomized controlled trial. *Brain Behav Immunol.* 2005;19:381-388.
- Fatouras I.G., Tournis S., Leontini D., Jamurtas A.Z., Sxina M., Thomakos P., Manousaki M., Douroudos I., Taxildaris K., Mitrakou A. Leptin and adiponectin responses in overweight inactive elderly following resistance training and detraining are intensity related. *J. Clin. Endocrinol. Metab.* 2005;90:5970-5977.
- Forsythe L.K., Wallace J.M., Livingstone M.B. Obesity and inflammation: The effects of weight loss. *Nutr. Res. Rev.* 2008;21:117-133.
- Fu Y., Luo N., Klein R.L., Garvey W.T. Adiponectin promotes adipocyte differentiation, insulin sensitivity, and lipid accumulation. *J. Lipid Res.* 2005;46:1369-1379.
- Fuentes T., Ara I., Guadalupe-Grau A., Larsen S., Stallknecht B., Olmedillas H., Santana A., Helge J.W., Calbet J.A., Guerra B. Leptin receptor 170 kda (ob-r170) protein expression is reduced in obese human skeletal muscle: A potential mechanism of leptin resistance. *Exp. Physiol.* 2010;95:160-171.
- Hara T., Fujiwara H., Nakao H., Mimura T., Yoshikawa T., Fujimoto S. Body composition is related to increase in plasma adiponectin levels rather than training in young obese men. *Eur. J. Appl. Physiol.* 2005;94:520-526.
- Jacobi S.K., Ajuwon K.M., Weber T.E., Kuske J.L., Dyer C.J., Spurlock M.E. Cloning and expression of porcine adiponectin, and its relationship to adiposity, lipogenesis and the acute phase response. *J. Endocrinol.* 2004;182:133-144.
- Kadoglou N.P., Iliadis F., Angelopoulou N., Perrea D., Ampatzidis G., Liapis C.D., Alevizos M. The anti-inflammatory effects of exercise training in patients with type 2 diabetes mellitus. *Eur. J. Cardiovasc. Prev. Rehabil.* 2007;14:837-843.
- Kelly A.S., Steinberger J., Olson T.P., Dengel D.R. In the absence of weight loss, exercise training does not improve adipokines or oxidative stress in overweight children. *Metabolism* 2007;56:1005-1009.
- Kobayashi J., Murase Y., Asano A., Nohara A., Kawashiri M.A., Inazu A., Yamagishi M., Mabuchi H. Effect of walking with a pedometer on serum lipid and adiponectin levels in japanese middle-aged men. *J. Atheroscler. Thromb.* 2006;13:197-201.
- Kohut M.L., McCann D.A., Russell D.W., Konopka D.N., Cunnick J.E., Franke W.D., Castillo M.C., Reighard A.E., Vanderah E. Aerobic exercise, but not flexibility/resistance exercise, reduces serum il-18, crp, and il-6 independent of beta-blockers, bmi, and psychosocial factors in older adults. *Brain Behav. Immunol.* 2006;20:201-209.
- Kondo T., Kobayashi I., Murakami M. Effect of exercise on circulating adipokine levels in obese young women. *Endocrine J.* 2006;53:189-195.
- Kraemer R.R., Castracane V.D. Exercise and humoral mediators of peripheral energy balance: Ghrelin and adiponectin. *Exp. Biol. Med.* 2007;232:184-194.
- Kraemer R.R., Chu H., Castracane V.D. Leptin and exercise. *Exp. Biol. Med.* 2002;227:701-708.
- Lawlor D.A., Smith G.D., Kelly A., Sattar N., Ebrahim S. Leptin and coronary heart disease risk: Prospective case control study of British women. *Obesity* 2007;15:1694-1701.
- Liu T.C., Liu Y.Y., Lee S.D., Huang C.Y., Chien K.Y., Cheng I.S., Lin C.Y., Kuo C.H. Effects of short-term detraining on measures of obesity and glucose tolerance in elite athletes. *J. Sport Sci.* 2008;26:919-925.
- Maghsoud P., Azarbayjani M.A., Agaalinejad H. Effect of exercise at different times of day on the inflammatory markers of cardiovascular disease risk in obese men. *Ann. Biol. Res.* 2011;2:213-220.
- Miyatake N., Takahashi K., Wada J., Nishikawa H., Morishita A., Suzuki H.,

- Kunitomi M., Makino H., Kira S., Fujii M. Changes in serum leptin concentrations in overweight Japanese men after exercise. *Diabetes Obes. Metab.* 2004;6:332-337.
34. Nicklas B.J., Beavers K.M. Exercise, weight loss, and effects on inflammation. *Curr. Cardiol. Risk Rep.* 2010;4:284-292.
35. Nicklas B.J., Hsu F.C., Brinkley T.J., Church T., Goodpaster B.H., Kritchevsky S.B., Pahor M. Exercise training and plasma c-reactive protein and interleukin-6 in elderly people. *J. Am. Geriatr. Soc.* 2008;56:2045-2052.
36. Numao S., Katayama Y., Hayashi Y., Matsuo T., Tanaka K. Influence of acute aerobic exercise on adiponectin oligomer concentrations in middle-aged abdominally obese men. *Metabolism* 2011;60:186-194.
37. Numao S., Suzuki M., Matsuo T., Nomata Y., Nakata Y., Tanaka K. Effects of acute aerobic exercise on high-molecular-weight adiponectin. *Med. Sci. Sports Exerc.* 2008;40:1271-1276.
38. Olive J.L., Miller G.D. Differential effects of maximal- and moderate-intensity runs on plasma leptin in healthy trained subjects. *Nutrition* 2001;17:365-369.
39. Polak J., Moro C., Klimcakova E., Hejnova J., Majercik M., Viguier N., Langin D., Lafontan M., Stich V., Berlan M. Dynamic strength training improves insulin sensitivity and functional balance between adrenergic alpha 2a and beta pathways in subcutaneous adipose tissue of obese subjects. *Diabetologia* 2005;48:2631-2640.
40. Prestes J., Shiguemoto G., Botero J.P., Frollini A., Dias R., Leite R., Pereira G., Magosso R., Baldissera V., Cavagliari C. Effects of resistance training on resistin, leptin, cytokines, and muscle force in elderly post-menopausal women. *J. Sport Sci.* 2009;27:1607-1615.
41. Shadid S., Stehouwer C.D., Jensen M.D. Diet/exercise versus pioglitazone: Effects of insulin sensitization with decreasing or increasing fat mass on adipokines and inflammatory markers. *J. Clin. Endocrinol. Metab.* 2006;91:3418-3425.
42. Tanaka H., Monahan K.D., Seals D.R. Age-predicted maximal heart rate revisited. *J. Am. Coll. Cardiol.* 2001;37:153-156.
43. Walther C., Mobius-Winkler S., Linke A., Bruegel M., Thiery J., Schuler G., Halbrecht R. Regular exercise training compared with percutaneous intervention leads to a reduction of inflammatory markers and cardiovascular events in patients with coronary artery disease. *Eur. J. Cardiovasc. Prev. Rehabil.* 2008;15:107-112.
44. Williams M.H. *Nutrition for Health, Fitness and Sport.* 6th Ed. WCB/McGraw-Hill, New York 2002;pp.156-200.
45. Ziccardi P., Nappo F., Giugliano G., Esposito K., Marfella R., Cioffi M., D'Andrea F., Molinari A.M., Giugliano D. Reduction of inflammatory cytokine concentrations and improvement of endothelial functions in obese women after weight loss over one year. *Circulation* 2002;105:804-809.