

The Effect of Short Term Aerobic Training on Serum Insulin and Insulin Resistance in Adult Obese Females

Ashraf Amini^{1*}, Zahra Mirakhori¹, Mojtaba Eizadi²

1. Assistant Professor, Department of Physical Education and Sport Sciences, Amirkabir University of Technology, Tehran, Iran.
2. Assistant Professor, Department of Exercise Physiology, Faculty of Humanities Sciences, Islamic Azad University, Saveh Branch, Saveh, Iran.

***Correspondence:** Ashraf Amini, Assistant Professor, Department of Physical Education and Sport Sciences, Amirkabir University of Technology, Tehran, Iran.
Tel: (98) 912 308 4720
Email: aminia2018@yahoo.com

Received: 11 April 2020

Accepted: 22 June 2020

Published in August 2020

Abstract

Objective: Obesity is associated with inflammatory process and many different diseases. The objective of this study was to assess the impact of short term aerobic training on serum resistin and insulin resistance in adult obese women.

Materials and Methods: In this quasi-experimental study, thirty untrained adult obese females matched for age 35-45 years old with body mass index (BMI) 30-36 kg/m² were divided randomly into exercise (aerobic intervention; 6 weeks, 3 days/weekly, %55-70HRmax) and control (no training) groups. Pre and post-training of fasting blood samples were collected for measure serum resistin. Insulin resistance was calculated by HOMA-IR. Data were analyzed by the independent samples T-test.

Results: Aerobic training resulted in significant decrease in BMI (32.1 (± 2.76) vs 31.6 (± 2.80) kg/m², *P*-value: 0.023), body fat percentage (44.7 (± 4.55) vs 44 (± 4.33), *P*-value: 0.028) and fasting glucose (94 (± 8.9) vs 79 (± 5.8) mg/dl, *P*-value: 0.011) in exercise group. No changes were observed on insulin resistance (1.43 (± 1.11) vs 1.18 (± 0.57) HOMA-IR, *P*-value: 0.124) and serum resistin (2.20 (± 1.07) vs 1.58 (± 0.87) ng/ml *P*-value: 0.062) by training program. All variables remained unchanged in control subjects.

Conclusion: Despite improving fasting glucose, a short-term aerobic training is not associated with anti-inflammatory property for obese females. Improved glucose could be likely attributed to other changes in metabolic markers in response to exercise training and further studies are necessary to clarify possible mechanisms.

Keywords: Aerobic training, Inflammation, Insulin resistance, Obesity

Introduction

The increasing prevalence of obesity and insulin resistance among Iranian women is remarkable (1). In the last decade 48% of Iranian women were obese or overweight (2). Increased levels of obesity and body fat percentage along with age increase in

children navigating through maturity and adulthood, increased insulin resistance, type 2 diabetes, and cardiovascular diseases, have always been recognized over recent years (2,3). Scientific studies addressing adults have indicated that chronic inflammation plays a

significant role in the pathogenesis of diseases such as atherosclerosis (2,3), type 1 and type 2 diabetes (4,5), cancer (6), some neurological diseases (7), and immune system diseases (8). The inflammatory markers are associated with obesity and metabolic syndrome (9). The cytokines such as interleukin 6 (IL-6), tumor necrosis factor- α (TNF- α), and interleukin-1 beta (IL-1B) are often categorized as inflammatory cytokines associated with obesity and metabolic syndrome (9).

It has been indicated that resistin plays a crucial role in obesity and insulin resistance in diabetic patients due to pro-inflammatory pathways (10). The resistin, as an adipocyte-secreted hormone, belongs to either a family of proteins with a cysteine-rich carboxylic terminus called resistin-like molecule or proteins in the inflammatory regions. The increased systemic levels of resistin are associated with impaired insulin function and imbalance of blood glucose levels (11). However, the molecular mechanisms through which the resistin receptors mediate their effects on the hypothalamus in controlling homeostasis and key insulin-sensitive tissues are still unidentified (12).

Although the role of genetics and heredity in the development of obesity and its associated disorders such as hormonal disorders is irrefutable, more recent scientific evidence states that the role of environmental factors such as nutrition and physical activity or inactivity also play a major role in this regard. However, in terms of their responses to exercise training, various controversial findings are present about their response to a variety of exercise trainings. For example, in a recent study, serum resistin level was significantly decreased in response to 12 months of training in obese subjects (13); however, another study indicated no significant change after 14 months of training in this regard (14). Some studies have also suggested that longer training programs with a weight loss of at least 5% in obese individuals lead to a significant reduction in inflammatory cytokines (15), while others did not report any

significant change at cytokine levels despite weight loss following long-term training programs (16). Also, a significant decrease in the level of cytokines such as resistin and IL-6 without any weight loss was reported (17).

Moreover, despite extensive studies addressing the effect of various exercise training on the levels of inflammatory or anti-inflammatory cytokines among healthy or patient populations, the response of serum resistin to aerobic training on obese women is less pronounced. Hence, the present study aim was measurement of six weeks aerobic training effect on serum resistin levels as well as insulin resistance in adult obese women.

Materials and Methods

In this quasi-experimental study, thirty inactive obese women aged 35-45 years old were recruited and divided into exercise (n= 15) and control (n= 15) group. Sample size was decided according two mean comparison equation.

All participants were asked to provide informed consent before carrying out the study. Inclusion criteria for study groups were determined obesity ($30 \leq \text{BMI} \leq 36$). All subjects were non-athletes and no smoker, not pregnant and non-alcoholics. They were included in the study if they had not done any physical activity in the previous 6 months; they did not use medicines or therapies for obesity and had no history of injury or disease that would prevent daily exercise. Individuals with history of chronic or acute respiratory infections, cardiopulmonary disease, and neuromuscular disease were excluded from the study. Individuals having overt diabetes were also excluded from the study.

In the physiology laboratory, anthropometric measurements were obtained (in the morning) from all subjects who had light clothing with no shoes. Two measurements were made every 1 minute and the average of two measurements was used for analysis. Obesity was measured by body mass index (BMI) as division of body weight (kg) by the square of height (in meters) (18). Weight was measured to the nearest 100

g using digital scales (OMRON) (19). After a normal expiration, waist circumference was determined under the midline of the participant's armpit, at the midpoint between the top of the hip and the lower part of the last rib. Hip girth was obtained at the level of the greatest protrusion of the gluteal muscles with underwear. Body fat percentage was measured using bioelectrical impedance method (Omron Body Fat Analyzer, Finland).

Training program

The exercise group took part in an aerobic exercise training intervention for 6 weeks (3 days a week). Each training session was monitored by an exercise physiologist or a physician. The participants fulfilled a 5-10 min warm-up each session, accompanied by aerobic exercise training at 60-75% (heart rate maximum) HRmax and a 5-min cool down (20). The exercise intensity in each session was controlled and recorded based on the percentage of the maximum heart rate by the Polar pacemaker. The main program of each session was in the form of running in defined intensities, so that the participants exercised the first two weeks at %60-65HRmax, weeks 3 and 4 at %65-70 Hrmax, and the last 2 weeks at %70-75 HRmax (20) (table 1). The control group were trained to maintain their routine activities. The subjects were trained to have their habitual diet during the study. In fact, this study was conducted solely to indicate the impact of aerobic training without calorie restriction on dependent variables.

Laboratory Analyses

For measuring biochemical variables, fasting blood samples were collected prior to and 48 h after last exercise session. The participants were asked not to do any heavy physical activity before blood sampling for 48 h. Serums were separated and stored at -80°

immediately after each blood sampling until the assays were performed. ELISA method (Enzyme-linked Immunosorbent Assay for quantitative detection of human resistin) was applied to determine serum resistin, using a Biovendor- Laboratorial kit (Biovendor Company, Czech). The intra-assay coefficients of the method sensitivity and variation were, respectively, 0.033 and 2.8% ng/mL. Oxidase method (Pars Azmoon kit, Tehran) determined glucose. ELISA method (Demeditec, Germany) was used to determine insulin. The inter-assay and intra-assay coefficients of the method variation were, respectively, 2.88 and 2.6%. Insulin resistance was indicated based on the HOMA-IR as the fasting plasma glucose (mM) product, and insulin (μU/ml) was divided by the constant 22.5 (21).

Data analysis

Data were analyzed by computer using the Statistical Package for Social Sciences (SPSS) for Windows, version 15.0. The Kolmogorov-Smirnov normality test was used to analyze normal distribution of data. Variables between two groups were compared at baseline using independent student's T-test. The mean differences between pre and post-training values on all metabolic and anthropometric variables were determined by paired T-test. The significance level was indicated at a P-value ≤ 0.05.

Ethical considerations

The study was approved by the ethics committee of Amirkabir University of Technology (IR.SSU.REC.1397.426).

Results

Baseline (pre-training) and post-training data are presented in Table 1. Data are expressed as mean ± standard deviation (SD). The anthropometrical indexes were not

Table 1. Distribution of exercise intensity while running during the training program

weeks	Exercise intensity (%HRmax)	Time (min)
First and second	%60 ≤ intensity ≤ %65	3 × 5 minute
Third and fourth	%65 ≤ intensity ≤ %70	2 × 10 minute
Fifth and Sixth	%70 ≤ intensity ≤ %75	2 × 15 minute

significantly different between groups at baseline (P -value > 0.05, Table 2).

Aerobic training significantly decreased body weight, BMI, body fat percentage, abdominal obesity and no change in visceral fat. All these variables remained no change in control group (P -value > 0.05, Table 2).

Based on independent T-test, no baseline differences were found between groups for serum resistin, glucose, insulin and insulin resistance (P -value > 0.05, table 3). Exercise group obtained significant decrease in fasting glucose when compared with baseline. But this variable remained no change in control group (table 3). Despite the improvement in glucose but serum resistin, insulin and insulin resistance did not change by aerobic training in exercise group. On the other hand, no significant changes were observed in these variables by training program in exercise

subjects. None of the variables relating to control subjects changed (P -value > 0.05, table 3).

Discussion

Despite the fact that clinical trials have supported higher levels of resistin in the presence of obesity and metabolic syndrome (22,23), its serum levels after six weeks of aerobic training in adult obese women did not change significantly in the present study. Moreover, although the mentioned training program led to a significant decrease in fasting glucose level in this population that previously had inactive lifestyle, it did not result in a significant change in the insulin resistance index.

Recent studies acknowledge the role of exercise such as long-term aerobic and

Table 2. Pre and post-training of anthropometric characteristics of studied groups.

Variables	Exercise group			Control group			Pre-test difference (P -value) †	Post-test difference (P -value) ¥
	Pre-test	post-test	P -value *	Pre-test	post-test	P -value *		
Age (year)	38.4 (7.65)	38.4 (7.65)	----	37.3 (2.39)	37.3 (2.39)	----	0.348	0.348
Height (cm)	162 (4.86)	162 (4.86)	----	161 (4.66)	161 (4.66)	----	0.441	0.441
Weight (kg)	83 (8.45)	82 (8.56)	0.021	83.7 (4.81)	83.6 (4.71)	0.414	0.359	0.014
AC (cm)	109 (7.4)	107 (8)	0.033	109 (6.12)	109 (5.28)	0.236	0.561	0.028
BMI (kg/m ²)	32.1 (2.76)	31.6 (2.80)	0.023	31.1 (1.58)	31.71 (1.57)	0.458	0.611	0.031
BF (%)	44.7 (4.55)	44 (4.33)	0.028	44.1 (2.95)	43.5 (2.62)	0.745	0.745	0.019
Visceral fat	8.2 (1.07)	8 (1.16)	0.098	7.9 (1.07)	7.8 (1.09)	0.658	0.632	0.113

AC, abdominal circumference; BMI, body mass index, BF, body fat percentage

* represent significant level between pre and post test (intra-group change: data by paired T-test)

† represent significant level of pre-test between groups (inter-group change: data by independent T-test)

¥ represent significant level of post-test between groups (inter-group change: data by independent T-test)

Table 3. Mean and standard deviation of clinical markers of studied groups.

Variables	Exercise group			Control group			Pre-test difference (P -value) †	Post-test difference (P -value) ¥
	Pre-test	post-test	P -value *	Pre-test	post-test	P -value *		
Resistin (ng/ml)	2.20 (1.07)	1.85 (0.87)	0.062	2.25 (0.96)	2.21 (0.95)	0.536	0.541	0.092
Glucose (mg/dl)	94 (8.9)	79 (5.8)	0.011	97 (8.7)	96 (8.8)	0.521	0.459	0.023
Insulin (µU/ml)	6.2 (4.8)	6 (2.98)	0.235	6.1 (3.16)	6.1 (2.92)	0.234	0.365	0.235
Insulin resistance (HOMA-IR)	1.43 (1.11)	1.18 (0.57)	0.124	1.46 (0.74)	1.45 (0.71)	0.415	0.732	0.184

* represent significant level between pre and post test (intra-group change: data by paired T-test)

† represent significant level of pre-test between groups (inter-group change: data by independent T-test)

¥ represent significant level of post-test between groups (inter-group change: data by independent T-test)

resistance trainings in reducing the chronic inflammation, especially in individuals who have high levels of inflammatory mediators (24). In this regard, most studies have supported the effects of a variety of short- or long-term training programs on the levels of inflammatory or anti-inflammatory mediators in healthy or sick and obese or normal populations (25-27). Studies that have accentuated the impact of long-term training programs on the levels of these cytokines in obese populations have attributed improvements in the inflammatory profile to weight loss or reduction of body fat percentage. For example, in one study, weight loss was associated with decreased level of leptin and increased level of IL-10 in obese mice as a result of long-term resistance trainings in the form of running on treadmill (28).

Some other studies have also reported a decrease in the serum resistin levels in obese or diabetic patients in response to two and three months of aerobic exercise, respectively (25,26). The lack of changes in serum resistin level in the present study or some other studies may be explained by considering the fact that some studies have specified at least 10% of weight loss as a pre-requisite to improve the metabolic or inflammation profile in obese populations (29). Although reduction of weight and body fat percentage was significant in the present study, their level was far less than 5% as compared to the levels prior to the training program. Some findings have indicated that three months of moderate-intensity aerobic exercise can lead to an improvement in oxidative stress indices such as superoxide dismutase as well as an improvement in insulin resistance and inflammatory profile independent of weight loss (30).

In a relatively recent study, although a 3-month cycling program (twice per week for up to 45 min) was associated with a decrease in serum resistin levels in a group of type 2 diabetic men, it did not result in a significant change in serum levels of adiponectin and

leptin (25). In another study, 12 weeks of resistance training with no changes in body composition resulted in a significant reduction in CRP, leptin, and TNF- α and no significant change in IL-10 in adult obese women (31). The incompatibility of the response of inflammatory cytokines with cardiovascular risk factors to long-term aerobic trainings has also been reported by some other studies (32).

In line with no changes in the serum resistin levels in the present study, the 6-week exercise training did not affect insulin resistance in middle-aged obese women although the fasting glucose levels decreased. Some studies have pointed to the effective role of resistin in insulin resistance and development of type 2 diabetes (33). Researchers believe that increasing the expression of resistin in muscle myocytes by inhibiting GLUT4 mRNA reduces the absorption of insulin-dependent glucose by 28-31% (34). The mentioned findings specify the role of resistin in the pathogenesis of insulin resistance in skeletal muscles. Moreover, it has been revealed that resistin leads to an increased glucose production in hepatic gluconeogenesis by over-expression of genes that encode enzymes of hepatic gluconeogenesis pathways, glucose-6-phosphatase (G6Pase), and AMPK-dependent phosphoenolpyruvate (35). Despite the presented piece of evidence, some studies have reported the incompatibility of resistin response and insulin resistance with aerobic trainings. For example, in the study conducted by Giannopoulou et al., it has been indicated that 14 weeks of aerobic training led to a significant decrease in insulin resistance without any changes in the resistin level (36), while Jones et al reported a significant reduction in serum resistin levels without any changes in insulin resistance following eight weeks of aerobic training (37). On the other hand, some studies have mentioned that resistin had no effect on glucose oxidation and glycogen synthesis (34). Based on the mentioned evidence, reduction of fasting glucose levels in response to the training program in the present study may be attributed

to other environmental factors or other hormonal changes, independent of the serum resistin levels, following the training program. Moreover, lack of diet management during the training programs is one of the main limitation and constraints affecting the ultimate outcome, so that lack of improvements in some cytokines may be attributed to the lack of diet management. Some studies have always emphasized the potential impact of diet regime along with exercise trainings on inflammatory profile. In another study, a 3-month aerobic training without diet management did not lead to changes in serum resistin levels in obese men (38). In this regard, based on the obtained findings, some researchers have suggested that the combination of exercise training with a diet regime, rather than any of them alone, always has more effects on the levels of cytokines and insulin resistance levels (39-41). In addition, one of the limitations of this study is the small number of patients. Also, lack measuring other inflammatory or anti-inflammatory cytokines that affect blood glucose is the weak points or limitation of our study. However, improving blood glucose in the absence of changes in insulin resistance and serum resistin as an inflammatory mediator is one of the strengths of the study.

References

1. Amiri Parsa T, Khademosharie M, Hamedinia MR, Azarnive MS. Evaluation of the Factors Associated with Overweight and Obesity in 30-to 50-year-old Women of Sabzevar. *Iranian Journal of Epidemiology*. 2014;9(4):75-83.(in Persian)
2. Kelishadi R, Alikhani S, Delavari A, Alaedini F, Safaie A, Hojatzadeh E. Obesity and associated lifestyle behaviours in Iran: findings from the first national non-communicable disease risk factor surveillance survey. *Public health nutrition*. 2008;11(3):246-51.
3. Moghimi-Dehkordi B, Safaie A, Vahedi M, Pourhoseingholi MA, Pourhoseingholi A, Zali MR. The prevalence of obesity and its associated demographic factors in Tehran, Iran. *Health and Development Journal*. 2012;1(1):22-30.
4. Cobbold C. Type 2 diabetes mellitus risk and exercise: is resistin involved?. *The Journal of sports medicine and physical fitness*. 2018;59(2):290-7.
5. Hotamisligil GS. Inflammation and metabolic disorders. *Nature*. 2006;444(7121):860-7.
6. De Visser KE, Eichten A, Coussens LM. Paradoxical roles of the immune system during cancer development. *Nature reviews cancer*. 2006;6(1):24-37.
7. Britschgi M, Wyss-Coray T. Immune cells may fend off Alzheimer disease. *Nature medicine*. 2007;13(4):408-9.
8. Vogt B, Führrohr B, Müller R, Sheriff A. CRP and the disposal of dying cells: consequences for systemic lupus erythematosus and rheumatoid arthritis. *Autoimmunity*. 2007;40(4):295-8.

Conclusions

Six weeks of aerobic training cannot affect serum resistin and insulin resistance in adult obese women. This lack of change can be attributed to the short training period, slight reduction in body weight and body fat percentage as well as small number of samples studied. Despite the lack of changes in resistin and insulin resistance, the reason for significant reductions in glucose level was probably the change in other hormonal mediators in response to exercise training.

Acknowledgements

The authors express their sincere gratitude to all participants and laboratory of Atieh Hospital for performing genetic tests and Eliza.

Funding

This work was supported financially by Amirkabir University of Technology, Tehran, Iran.

Conflict of Interest

No conflict of interest was declared.

9. Wärnberg J, Cunningham K, Romeo J, Marcos A. Physical activity, exercise and low-grade systemic inflammation. *Proceedings of the Nutrition Society*. 2010;69(3):400-6.
10. Tripathi D, Kant S, Pandey S, Ehtesham NZ. Resistin in metabolism, inflammation, and disease. *The FEBS Journal*. 2020.
11. Stepan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, et al. The hormone resistin links obesity to diabetes. *Nature*. 2001;409(6818):307-12.
12. Benomar Y, Gertler A, De Lacy P, Crépin D, Hamouda HO, Riffault L, et al. Central resistin overexposure induces insulin resistance through Toll-like receptor 4. *Diabetes*. 2013;62(1):102-14.
13. Park SH, Han TK, Ann ES, Yoon ES, Kim B, Kang HS. Effect of training intensity on subcutaneous adipose leptin, adiponectin, interleukin 6, and tumor necrosis factor mRNA expression in middle-aged women. *The FASEB Journal*. 2008;22:118-118.
14. Giannopoulou I, Fernhall B, Carhart R, Weinstock RS, Baynard T, Figueroa A, et al. Effects of diet and/or exercise on the adipocytokine and inflammatory cytokine levels of postmenopausal women with type 2 diabetes. *Metabolism*. 2005;54(7):866-75.
15. Rava A, Pihlak A, Kums T, Purge P, Pääsuke M, Jürimäe J. Resistin concentration is inversely associated with objectively measured physical activity in healthy older women. *Aging Clinical and Experimental Research*. 2020;32(3):475-81.
16. De Luis DA, Aller R, Izaola O, Sagrado MG, Bellio D, Conde R. Effects of a low-fat versus a low-carbohydrate diet on adipocytokines in obese adults. *Hormone Research in Paediatrics*. 2007;67(6):296-300.
17. Kadoglou NP, Perrea D, Iliadis F, Angelopoulou N, Liapis C, Alevizos M. Exercise reduces resistin and inflammatory cytokines in patients with type 2 diabetes. *Diabetes care*. 2007;30(3):719-21.
18. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. *Human kinetics books*. 1988;4(3):34-42.
19. Michael IP, John D, Smith G, Richard G. Accuracy of the Omron HBF-500 Body Composition Monitor in Male and Female College Students. *International Journal Exercise Science*. 2011; 4(1): 93-101.
20. Behboudi L, Izadi M. The effect of six weeks aerobic training on body composition and serum level of IL-10 in middle-aged obese females. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2017;20(8):51-60.(in Persian)
21. McAuley KA, Williams SM, Mann JI, Walker RJ, Lewis-Barned NJ, Temple LA, et al. Diagnosing insulin resistance in the general population. *Diabetes care*. 2001;24(3):460-4.
22. Fontana L, Eagon JC, Trujillo ME, Scherer PE, Klein S. Visceral fat adipokine secretion is associated with systemic inflammation in obese humans. *Diabetes*. 2007;56(4):1010-3.
23. Haider DG, Schindler K, Prager G, Bohdjalian A, Luger A, Wolzt M, et al. Serum retinol-binding protein 4 is reduced after weight loss in morbidly obese subjects. *The Journal of Clinical Endocrinology & Metabolism*. 2007;92(3):1168-71.
24. You T, Arsenis NC, Disanzo BL, LaMonte MJ. Effects of exercise training on chronic inflammation in obesity. *Sports Medicine*. 2013;43(4):243-56.
25. Wenning P, Kreutz T, Schmidt A, Opitz D, Graf C, Voss S, et al. Endurance exercise alters cellular immune status and resistin concentrations in men suffering from non-insulin-dependent type 2 diabetes. *Experimental and Clinical Endocrinology & Diabetes*.;121(08):475-82.
26. Bai Y, Zhang J, Jiang S, Sun J, Zheng C, Wang K, et al. Effects of the body fat mass and blood sugar and plasma resistin to slim exercise prescription for overweight and obesity students. *Wei sheng yan jiu= Journal of hygiene research*. 2013;42(4):538-42
27. Xu M, Duan Y, Xiao J. Exercise Improves the Function of Endothelial Cells by MicroRNA. *J Cardiovasc Transl Res*. 2019;12(5):391-393.
28. Jenkins NT, Padilla J, Arce-Esquivel AA, Bayless DS, Martin JS, Leidy HJ, et al. Effects of endurance exercise training, metformin, and their combination on adipose tissue leptin and IL-10 secretion in OLETF rats. *Journal of applied physiology*. 2012;113(12):1873-83.
29. Dow CA, Thomson CA, Flatt SW, Sherwood NE, Pakiz B, Rock CL. Predictors of improvement in cardiometabolic risk factors with weight loss in women. *Journal of the American Heart Association*. 2013;2(6):e000152.

30. Samjoo IA, Safdar A, Hamadeh MJ, Raha S, Tarnopolsky MA. The effect of endurance exercise on both skeletal muscle and systemic oxidative stress in previously sedentary obese men. *Nutrition & diabetes*. 2013;3(9):e88-e88.
31. Phillips MD, Patrizi RM, Cheek DJ, Wooten JS, Barbee JJ, Mitchell JB. Resistance training reduces subclinical inflammation in obese, postmenopausal women. *Medicine & Science in Sports & Exercise*. 2012;44(11):2099-110.
32. Januszek R, Mika P, Konik A, Petriczek T, Nowobilski R, Nizankowski R. The effect of treadmill training on endothelial function and walking abilities in patients with peripheral arterial disease. *Journal of Cardiology*. 2014;64(2):145-51.
33. Kang S, Chemaly ER, Hajjar RJ, Lebeche D. Resistin promotes cardiac hypertrophy via the AMP-activated protein kinase/mammalian target of rapamycin (AMPK/mTOR) and c-Jun N-terminal kinase/insulin receptor substrate 1 (JNK/IRS1) pathways. *Journal of Biological Chemistry*. 2011;286(21):18465-73.
34. Li FP, Li ZZ, Zhang M, Yan L, Fu ZZ. Effects of resistin on skeletal glucose metabolism. *Frontiers of medicine in China*. 2010;4(3):329-35.
35. Luo Z, Zhang Y, Li F, He J, Ding H, Yan L, et al. Resistin induces insulin resistance by both AMPK-dependent and AMPK-independent mechanisms in HepG2 cells. *Endocrine*. 2009;36(1):60-9.
36. Giannopoulou I, Fernhall B, Carhart R, Weinstock RS, Baynard T, Figueroa A, et al. Effects of diet and/or exercise on the adipocytokine and inflammatory cytokine levels of postmenopausal women with type 2 diabetes. *Metabolism*. 2005;54(7):866-75.
37. Jones TE, Basilio JL, Brophy PM, McCammon MR, Hickner RC. Long-term exercise training in overweight adolescents improves plasma peptide YY and resistin. *Obesity*. 2009;17(6):1189-95.
38. Shahgholi Abasi R, Izadi M, Soheili SH, Imanzadeh R. Serum resistin and insulin resistance responses to long-term physical exercise in the absence of diet control in middle-aged obese men. *Journal of Mazandaran University of Medical Sciences*. 2012;21(86):126-30.(in Persian)
39. Bouchonville M, Armamento-Villareal R, Shah K, Napoli N, Sinacore DR, Qualls C, et al. Weight loss, exercise or both and cardiometabolic risk factors in obese older adults: results of a randomized controlled trial. *International journal of obesity*. 2014;38(3):423-31.
40. Fayh AP, Lopes AL, Fernandes PR, Reischak-Oliveira A, Friedman R. Impact of weight loss with or without exercise on abdominal fat and insulin resistance in obese individuals: a randomised clinical trial. *British journal of nutrition*. 2013;110(3):486-92.
41. Beavers KM, Ambrosius WT, Nicklas BJ, Rejeski WJ. Independent and combined effects of physical activity and weight loss on inflammatory biomarkers in overweight and obese older adults. *Journal of the American Geriatrics Society*. 2013;61(7):1089-94.