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Effect of combined exercise on adiponectin expression and selected metabolic indices: Investigating changes related to cardiovascular health and blood glucose control in elderly obese men

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ABSTRACT

Introduction: Aging and obesity are associated with metabolic and cardiovascular dysfunctions, partly due to impaired adipokine regulation and insulin sensitivity. This study aimed to investigate the effect of combined exercise on adiponectin expression and selected metabolic indices related to cardiovascular health and blood glucose control in elderly obese men.

Material & Methods: This quasi-experimental study with a pre-test–post-test design included 40 obese elderly men (mean age: 61.90 ± 2.84 years; BMI: 31.01 ± 1.53 kg/m²), who were randomly assigned to experimental (n = 20) and control (n = 20) groups. The experimental group participated in a combined exercise program (aerobic and resistance) for 16 weeks, three sessions per week, each lasting 90 minutes. Blood samples were collected 48 hours before and after the intervention to assess levels of adiponectin, insulin, HbA1c, cholesterol, and HDL. Data were analyzed using SPSS version 26 through paired t-tests and ANCOVA.

Results: The results demonstrated that combined exercise significantly increased adiponectin levels (P= 0.0001). The experimental group showed notable improvements in the adiponectin-to-insulin ratio (P= 0.0001) and the total cholesterol-to-HDL cholesterol ratio (P= 0.04), along with a reduction in HbA1c levels (P= 0.01). No significant changes were observed in the control group.

Conclusion: The findings suggest that combined exercise significantly increased adiponectin levels and improved metabolic markers, including the adiponectin-to-insulin and total-to-HDL cholesterol ratios. HbA1c levels also decreased, indicating better glycemic control.

Keywords: Combined exercise, Adiponectin, Aging, Metabolic health.

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1. Introduction

Obesity in the elderly is recognized as a global health issue, associated with an increased risk of cardiovascular diseases, type 2 diabetes, and metabolic disorders (1). This condition can lead to impaired insulin sensitivity, poor blood glucose control, and heightened chronic inflammation, which, in turn, threatens overall health (2). In this context, metabolic and inflammatory markers play a crucial role in assessing the health status of obese elderly individuals. Studies have shown that changes in these markers can have significant effects on insulin sensitivity and glucose control, directly correlating with the risk of cardiovascular diseases (1, 2). Among the inflammatory mediators secreted by adipose tissue, adiponectin is unique due to its anti-inflammatory properties. It enhances insulin sensitivity and exerts protective effects on the vascular endothelium and smooth muscle cells. However, in obese individuals, adiponectin levels are markedly reduced, primarily due to inflammation, which suppresses its production (3). In obese individuals, reduced adiponectin levels contribute to conditions such as chronic inflammation, reduced insulin sensitivity, and increased risk of cardiovascular disease(4). This complex relationship highlights the role of adiponectin in metabolism and cardiovascular health and suggests that targeted therapies to increase adiponectin may be useful as a strategy to combat obesity and its complications (5). Hypoadiponectinemia has been shown to correlate with a significantly increased risk of coronary artery disease, underscoring its clinical relevance (6). Insulin resistance (IR), a hallmark of obesity and metabolic syndrome, is strongly linked with the modern sedentary lifestyle characterized by high caloric intake and minimal physical activity. This pathological state is fueled by elevated levels of proinflammatory cytokines such as TNF-α, IL-6, and MCP-1, and is reflected in increased circulating levels of C-reactive protein (CRP). The combination of chronic inflammation and IR results in altered insulin signaling, and endothelial dysfunction, and promotes atherogenesis(7). Adipocyte hypertrophy in obese individuals further exacerbates IR and systemic inflammation. Enlarged adipocytes, especially in visceral adipose tissue, become resistant to insulin and exhibit increased lipolysis, leading to elevated free fatty acid (FFA) levels. This excess of FFAs contributes to lipotoxicity, a condition characterized by the accumulation of toxic lipid metabolites such as ceramides and diacylglycerol, which interfere with insulin signaling pathways and sustain the cycle of insulin resistance. Moreover, mitochondrial dysfunction in obese adipose tissue also contributes to the generation of these lipotoxic metabolites, further impairing metabolic health (8). Emerging evidence indicates that aerobic and resistance training exert their effects through distinct physiological mechanisms, underscoring the need for further investigation (9). Contraction of muscle fibers during exercise initiates a range of metabolic and mitochondrial adaptations, enhances insulin-mediated glucose uptake in skeletal muscles, and contributes to the reduction of hyperinsulinemia. Furthermore, exercise facilitates inter-organ communication through the release of myokines, which function as endocrine regulators. These myokines have been shown to stimulate GLP-1 secretion, promote lipolysis, and increase glucose uptake by adipocytes, collectively contributing to improved insulin sensitivity (10). Resistance training in adults with diabetes was more effective than aerobic training in increasing maximal oxygen consumption over 12 weeks or longer without apparent differences in HbA1c, BMI, and lipid profiles (11). In the study of Pahlavani et al. (2022), aerobic exercise led to an increase in adiponectin, while in the study of Lin et al. (2021), this exercise did not cause an increase in obese individuals(12, 13). In the study of Zhou et al. (2022), combined exercise was more effective than aerobic or resistance exercise alone in improving plasma glucose and lipid metabolism in elderly people (14). A study found that aerobic exercise programs of 12 weeks or longer improved blood sugar control and BMI in adults with type 2 diabetes, but longer or more intense interventions provided no additional benefit for HbA1c(15). Although both aerobic and resistance training appear to improve glycemic control independently, a network meta-analysis found that combining both is more effective at reducing HbA1c than either alone in older adults (16). In the study by Wrench et al. (2022), 12 weeks of exercise training did not affect lipid profiles (15). Zhang et al. (2024) showed that 10 weeks of exercise training had no significant effect on lipid profile, or insulin sensitivity (17). Despite scattered evidence on the beneficial effects of various types of exercise training on inflammatory, metabolic, and adiponectin levels, there is still no clear consensus on the most effective type of exercise in the obese elderly population. Also, the conflicting results of some studies on the effect of exercise on adiponectin levels, insulin sensitivity, and lipid indices indicate the need for a more comprehensive review. Therefore, it is unclear to what extent combined exercise can produce synergistic effects in improving these indices. Therefore, the present study aims to investigate the effect of combined exercise on adiponectin expression and selected metabolic indices: Investigating changes related to cardiovascular health and blood glucose control in healthy men.

2. Methodology

2.1. Materials and methods

This quasi-experimental study used a pre-test and post-test design. Its target population consisted of elderly obese men in the city of Lahijan.

2.2. Participants

Participants voluntarily enrolled in the study, and 40 elderly obese men (mean age: 61.90 ± 2.84 years; BMI: 31.01 ± 1.53 kg/m²) with no history of cardiovascular, liver, or kidney diseases, diabetes, vision problems, and no regular physical activity for 6 months were selected. Exclusion criteria included any injury or missing more than 3 sessions. Participants were divided into two groups: the experimental group (EG), which followed a 16-week combined aerobic and resistance exercise program, and the control group (CG), which received no exercise intervention. The research was registered with the Islamic Azad University Ethics Committee, Rasht Branch, under the number IR.IAU.RASHT.REC.1402.025.

2.3. Measurements

Anthropometry: A Beurer digital scale, made in Germany with an accuracy of 1 gram, was used to measure the participants' weight. Height was also measured using a SOEHNLE wall-mounted height gauge, made in Germany, with an accuracy of 0.5 centimeters. Additionally, the Body Mass Index (BMI) was calculated by dividing the body weight (in kilograms) by the square of the height (in meters)(18).

Blood Sampling and Assessment of Inflammatory Indices: For biochemical marker measurement, 5 milliliters of blood were collected from participants after 10 hours of fasting and placed in EDTA-containing tubes. Blood samples were taken 48 hours after the last training session to avoid acute effects of exercise and to allow a more accurate assessment of chronic adaptations. After centrifugation at 4°C, the serum was separated, and the tests were performed. Plasma was stored at -20°C for further analysis. Adiponectin gene expression was measured using PCR and the Pars Tous kit (made in Iran, cat no A101161). Primer sequences were as follows: adiponectin forward, 5'-TTAAAACCTCCCCCAAGCAGA-3', and reverse, 5'-GCACTTAGAGATGGAGTTGGC-3'. GAPDH primers were used as an internal control: forward 5'-[sequence]-3' and reverse 5'-[sequence]-3'.

This study utilized capillary electrophoresis (CE) with the CAPILLARYS 2 ELECTROPHORESIS device from SEBIA, France, to measure glycosylated hemoglobin (HbA1c) levels. Blood samples were placed in capillary tubes and separated under the influence of an electric field. The concentration of HbA1c was determined by analyzing the molecules' migration time.

The ratio of total cholesterol to high-density lipoprotein (HDL) is calculated as an index for assessing metabolic status and risk of cardiovascular diseases. Total cholesterol and HDL levels were measured using enzymatic colorimetric and enzymatic photometric methods, respectively, by Pars Azmoun Iran Company..

2.4. Intervention

2.4.1 Exercise program

The exercise group followed a 90-minute combined workout program three times a week for 16 weeks. This program included 10 minutes of warm-up, 20 to 35 minutes of resistance training, 30 to 45 minutes of aerobic exercise, and 10 minutes of cool-down and recovery(19-21). The aerobic and resistance exercises were performed between 6:00 and 7:30 AM (20). The warm-up consisted of 10 minutes of walking, light jogging, stretching, and flexibility exercises. This was followed by 20 to 35 minutes of bodyweight resistance exercises targeting the upper, lower, and core muscles, including squats, lunges, sit-ups, planks, side planks (for both sides), tricep dips on the floor, modified push-ups, and cobra stretches. In the first weeks, participants started with 2 sets of 10 repetitions, gradually increasing to 3 sets of 15 repetitions by week 16, based on the principle of progressive overload (21). The aerobic session lasted 45 minutes at 50 to 70 percent of the target heart rate and increased to 60 minutes by the end of the program (19). The intensity and duration of exercises were gradually increased according to the participants' abilities, reaching 70 percent of the maximum heart rate by the 8th to 10th session. Heart rate was measured both at rest and after aerobic exercises using a Polar heart rate monitor. With each increase in intensity, the target heart rate was raised by 10 percent each week. The target heart rate was calculated using the Karvonen formula:

(Target heart rate) = (Resting heart rate) + (Exercise intensity percentage) × (Maximum heart rate - Resting heart rate)

At the end of each session, a 10-minute cool-down period was included, which involved light jogging, walking, and stretching. This exercise program continued for 16 weeks, and during this period, the control group did not participate in any exercise intervention.

2.5. Statistical Methods

Data analysis was performed using SPSS version 26. First, the normality of the data was assessed using the Shapiro-Wilk test, and the homogeneity of variances was evaluated using Levene's test. To compare pre- and post-intervention data, paired t-tests were used, and for group differences, ANCOVA was applied. Bonferroni post hoc tests were conducted in case of significance, with a significance level set at 0.05.

3. Results

The characteristics of the study participants are summarized in Table 1.

Table 1. *Descriptive statistics from the pre-test are provided*

Measurement index	Standard deviation ± mean
Age (years)	61.90 ± 2.84
Height (cm)	1.68 ± 0.05
Weight (kg)	88.78 ± 8.98
Body Mass Index (BMI) (kg.m2)	31.01 ± 1.53

The Shapiro-Wilk test showed that the data were normally distributed. According to Levene's test, equality of variances was observed, and the results of the ANCOVA test are reported in Table 2. In Figure 1, a significant increase in adiponectin levels was observed in the experimental group from the pre-test to the post-test, while the control group exhibited no significant changes. Notably, the difference between groups was statistically significant. Figure 2 shows the adiponectin-to-insulin ratio, where a remarkable rise was recorded in the experimental group post-intervention, compared to negligible change in the control group. In Figure 3, representing the Chol/HDL ratio, a significant reduction was observed in the experimental group post-intervention. The control group, however, showed no meaningful change. Figure 4 demonstrates changes in HbA1c, a marker of blood glucose regulation. The experimental group experienced a significant decrease, indicating improved glycemic control, while the control group experienced a slight increase, leading to a significant difference between the two groups in the post-test.

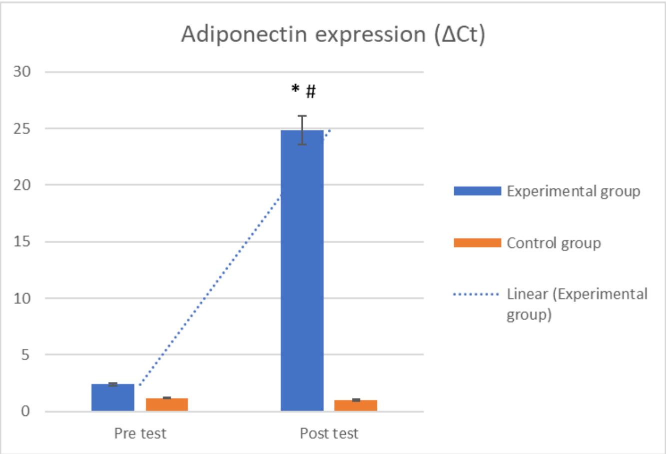

Figure 1. *Comparison of the mean adiponectin in two groups*

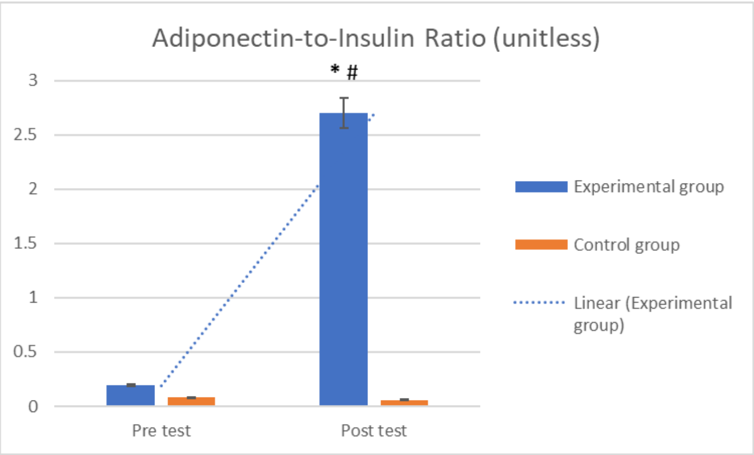

Figure 2. *Comparison of the mean adiponectin to insulin ratio in two groups*

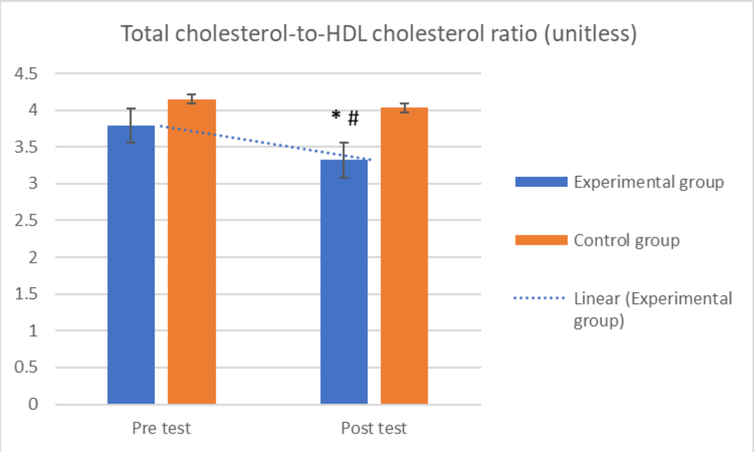

Figure 3. *Comparison of the mean Chol/HDL ratio in two groups*

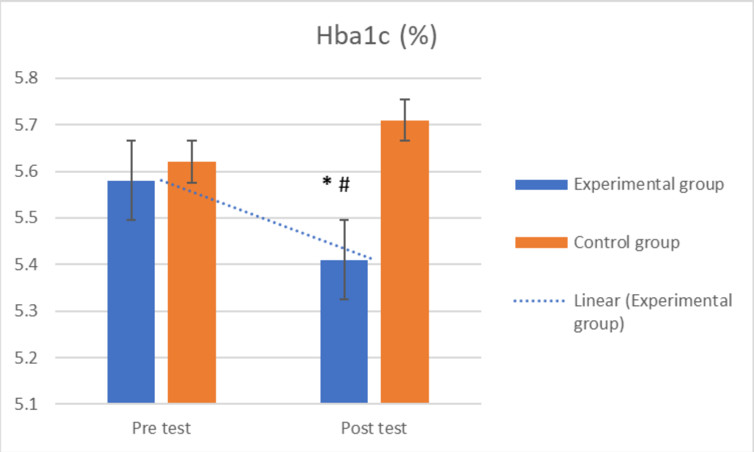

Figure 4. *Comparison of the mean HbA1c in two groups*

Table 2. *Summary of Research Variable Results Comparing PreTest and Post-Test in the Experimental and Control Groups*

Group	Adiponectin	adiponectin to insulin	Chol/HDL	HbA1c
EG	*↑	*↑	*↓	*↓
CG	×	×	×	×

4. Discussion

The present findings reinforce the growing body of evidence supporting the effectiveness of combined aerobic and resistance training in improving key metabolic parameters in older adults. In particular, the intervention significantly enhanced adiponectin levels and improved glycemic control, as reflected by reduced HbA1c and a more favorable adiponectin-to-insulin ratio. Additionally, a decrease in the total-to-HDL cholesterol ratio was observed, suggesting improvements in lipid metabolism. Given the rising prevalence of metabolic disorders among aging populations, the development of structured, physiologically informed exercise interventions particularly for individuals with obesity or insulin resistance has become a critical public health priority(22). Exercise, particularly in the form of combined training, facilitates multi-organ metabolic regulation through the muscle–adipose–pancreas axis. In this context, myokines such as IL-6, irisin, and FGF21 act as endocrine mediators that influence glucose uptake, fatty acid oxidation, and β-cell function (23). These myokines also promote adiponectin secretion and improve insulin sensitivity via activation of pathways like AMPK and PI3K-Akt, thereby contributing to enhanced metabolic homeostasis (10). Previous studies, including Zhou et al. (2022), have reported that combined training yields greater improvements in glucose and lipid metabolism than aerobic or resistance training alone in elderly individuals (14). Furthermore, a network meta-analysis has shown that combined interventions are more effective at reducing HbA1c compared to either modality in isolation (16). This superior efficacy is likely attributed to the concurrent activation of multiple molecular pathways, including PI3K/Akt (insulin signaling), AMPK (glucose transport and lipid metabolism), and PGC-1α (mitochondrial biogenesis and oxidative capacity). The effects of exercise on adiponectin levels, however, have not been consistently reported. While Pahlavani et al. (2022) observed increased adiponectin following aerobic training, Lin et al. (2021) found no significant changes in obese individuals (12, 13). These discrepancies may arise from interindividual variability in adiposity, low-grade chronic inflammation, or dysfunctional adipocyte signaling, particularly prevalent in older adults with insulin resistance. Impairments in adiponectin receptor signaling (AdipoR1/R2–AMPK–p38 MAPK) could contribute to a blunted response to physical activity in this population (24). The evidence regarding lipid metabolism remains mixed. Some studies, such as those by Wrench et al. (2022) and Zhang et al. (2024), have found no significant changes in total cholesterol or HDL following short to moderate-duration training programs (15, 17). These results may reflect the delayed nature of lipid profile adaptation, which typically requires more prolonged or higher-intensity interventions (25). Additionally, age-related declines in lipoprotein lipase (LPL) activity and reduced HDL turnover could further attenuate the lipid response in older individuals (26). In summary, combined training activates a range of interrelated physiological pathways, making it a particularly effective intervention for improving adiponectin levels, enhancing insulin sensitivity, reducing HbA1c, and favorably modulating lipid profiles in older adults. Nonetheless, individual variability in response shaped by baseline metabolic status, visceral adiposity, and systemic inflammation highlights the importance of personalized exercise prescriptions to optimize outcomes and promote sustainable improvements in cardiometabolic health. Despite the outcomes observed, the present study has limitations, including a relatively small sample size and a short intervention period, which may limit the generalizability of the findings. Future studies should consider more diverse and larger populations, incorporate extended follow-up durations, and include more precise biomarkers particularly those reflecting inflammatory and antioxidant activity. Investigating the molecular pathways linking exercise-induced adipokine modulation with improved metabolic function may further advance our understanding of the mechanistic underpinnings of combined training in aging populations.

5. Conclusion

The results of this study demonstrated that combined exercise (aerobic and resistance training) significantly increased adiponectin levels and improved key metabolic markers, such as the adiponectin-to-insulin ratio and the total cholesterol-to-HDL ratio, in elderly obese men. Moreover, the significant reduction in HbA1c levels indicated enhanced blood glucose control following the intervention. These findings highlight the beneficial effects of combined exercise on metabolic profile, insulin sensitivity, and cardiometabolic health in this population. Accordingly, implementing combined exercise as a non-pharmacological and effective strategy may be valuable in preventive and therapeutic programs for elderly individuals with obesity, contributing to improved quality of life and reduced risk of chronic diseases.

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Conflict of interests: The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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