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Metabolic responses of diet–exercise combinations in women with obesity: a comparative lifestyle intervention study with different diet types

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Full Title: Metabolic Responses of Diet–Exercise Combinations in Women with Obesity: A Comparative Lifestyle Intervention Study with Different Diet Types

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Abstract

Background/Aim: Obesity represents a major global public health challenge, particularly among women, and is associated with adverse metabolic and endocrine outcomes. his study evaluated the effects of ketogenic, intermittent fasting (IF), and semi-vegetarian diets, alone or combined with home-based exercise, on anthropometric, metabolic, and hormonal parameters in women with obesity. **Methods**: The study employed a pretest–posttest controlled experimental design with 108 women aged 19–45 years, comprising 96 participants with obesity and 12 with normal body weight. Participants were assigned to nine groups: control (C), obese (O), obese with exercise (OE), obese with exercise plus semi-vegetarian diet (OEVD), obese with semi-vegetarian diet (OVD), obese with exercise plus intermittent fasting (OEIF), obese with intermittent fasting (OIF), obese with exercise plus ketogenic diet (OEKD), and obese with ketogenic diet (OKD). Participants completed ketogenic, intermittent fasting (IF), or semi-vegetarian dietary interventions, either alone or combined with home-based exercise, for 6 weeks. Anthropometric parameters were assessed using bioelectrical impedance analysis, while biochemical markers (adiponectin, insulin-like growth factor 1 (IGF-1), irisin, myostatin, glucose, and insulin) were analyzed via ELISA. Statistical analyses were performed using mixed-design ANOVA, Pearson's correlation, and principal component analysis. **Results:** The C and O groups exhibited no significant changes, whereas intervention groups showed reductions in body mass, body mass index (BMI), and body fat ($p < 0.001$). Single interventions were associated with changes in anthropometric measures (OIF:10.42% body mass,7.61% BMI, 9.86% body fat; OE: 9.49%, 6.65%, 13.49%; OVD: 9.07%, 8.17%, 6.21%; OKD: 8.12%, 6.91%, 9.78%). Diet-plus-exercise intervention groups generally exhibited larger change

s, with OEVD achieving the greatest reductions (12.69%, 13.46%, 13.95%), followed by OEKD (10.68%, 9.16%, 11.17%) and OEIF (8.76%, 9.64%, 12.04%). Moreover, adiponectin, irisin, IGF-1, and myostatin levels changed significantly in exercise-only and diet-plus-exercise groups compared with those of the C and O groups. Additionally, intervention groups exhibited significant alterations in glucose and insulin concentrations, whereas no significant changes were observed in

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the C and O groups. **Conclusion:** Lifestyle modifications integrating dietary strategies with home-based exercise are associated with changes in metabolic and hormonal parameters in women with obesity.

Keywords: Adipokines, exercise therapy, fasting, IGF-1, ketogenic diet, myokines, obesity, semi-vegetarian diet

Introduction

Obesity remains a major public health challenge of the 21st century. According to a global analysis by the NCD Risk Factor Collaboration (NCD-RisC, 2024), over one billion individuals were classified as obese in 2022, with projections indicating continued growth in the coming decade. Beyond aesthetic concerns, obesity is a major risk factor for chronic diseases, including type 2 diabetes, hypertension, cardiovascular disorders, and several cancers (Hruby & Hu, 2015; Bray et al., 2017). Its higher prevalence among women is linked to hormonal fluctuations, reproductive phases, reduced physical activity, and sociocultural factors. Homemakers, who spend most of their time in domestic environments, represent a particularly vulnerable group due to sedentary lifestyles and poor dietary habits (Carballo-Fazanes et al. 2020; Lee et al. 2023).

Adipose and muscle tissues function as active endocrine organs that play crucial roles in the pathophysiology of obesity (Pedersen & Febbraio, 2008). Molecules secreted by these tissues (adipokines and myokines) serve as essential biomarkers for elucidating the systemic effects of obesity and assessing therapeutic efficacy. Adipokines regulate energy metabolism, insulin sensitivity, inflammation, and vascular function; notably, adiponectin exhibits strong insulin-sensitizing and anti-inflammatory effects, with lower levels linked to insulin resistance (Achari & Jain, 2017). Similarly, skeletal muscle acts as an endocrine organ by releasing proteins called myokines during contraction (Whitham & Febbraio, 2016; Delezie & Handschin, 2018). These myokines, including insulin-like growth factor 1 (IGF-1), irisin, and myostatin, modulate energy metabolism, glucose homeostasis, muscle–adipose interaction, and inflammation (Kwon et al., 2020).

Dietary habits and physical activity directly affect adipokine and myokine levels, making them vital to obesity management. The ketogenic diet restricts carbohydrate intake and induces ketosis, a metabolic state characterized by enhanced lipid oxidation, reduced insulin levels, and appetite suppression. It is also associated with short-term improvements in body composition and glycemic control (Jensen et al., 2022). Intermittent fasting (IF) improves insulin sensitivity and metabolic flexibility, decreases oxidative stress, and activates autophagy (Longo & Panda, 2016; Patterson & Sears, 2022). Vegetarian diets, rich in fiber and phytochemicals, improve gut microbiota diversity, suppress inflammation, and beneficially modulate adipokine profiles, particularly by increasing adiponectin levels (Kahleova et al., 2018). Combining these dietary strategies with structured exercise programs increases energy expenditure and enhances myokine secretion, thereby optimizing muscle–adipose interaction and metabolic adaptation (Gonzalez-Gil and Elizondo-Montemayor, 2020; Wang et al., 2020). However, most existing studies focus on diet or exercise interventions, limiting insights to sex-specific physiological responses (Karstoft & Pedersen, 2016; Beauchamp et al., 2018). Research assessing combined diet–exercise interventions, particularly in domestic or real-life settings, also remains limited (Viana et al., 2019). Therefore, this study aimed to investigate the effects of combining ketogenic, intermittent

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fasting, and semi-vegetarian dietary approaches with home-based exercise protocols on anthropometric parameters, as well as on adiponectin, IGF-1, irisin, myostatin, glucose, and insulin levels in housewives with obesity.

Methods

Experimental Design

The study employed a controlled pre-test/post-test comparative design, applying defined nutrition and exercise applications to comparison groups, with biochemical and anthropometric measurements obtained before and after the 6-week study period. Participants were classified according to body mass index (BMI, kg/m²) and divided into nine groups based on World Health Organization (WHO, 2025) criteria. The first group served as the normal-weight comparison group (C), the second as the obesity comparison group (O), and the remaining seven represented distinct lifestyle-based nutrition and/or exercise application models for participants with obesity. The design incorporated a 6-week exercise program, semi-vegetarian diet, IF, and ketogenic diet, each implemented alone or in combination (Figure 1). The exercise program was conducted online under expert supervision three times per week, with each 30-min session consisting of warm-up, main exercise, and cool-down phases. Nutritional intake was monitored using the Food Consumption Record Form. Following baseline assessments, participants participated in their assigned lifestyle applications, and post-test measurements were obtained at the end of the 6-week study period. The exercise program was conducted online under expert supervision three times per week, with each 30-min session comprising warm-up, main exercise, and cool-down phases. Dietary applications included a semi-vegetarian diet, 16:8 IF regimen, and standard ketogenic diet characterized based on specific macronutrient distribution. Dietary intake for each participant was monitored using the Food Consumption Record Form. Reporting guidelines were considered where appropriate, and participants with obesity were assigned to study groups, whereas the normal-weight comparison group was formed separately. Anthropometric parameters (height, weight, body composition, and BMI) were measured using an Omron Karadascan bioelectrical impedance analysis (BIA) device. Biochemical parameters were analyzed using enzyme-linked immunosorbent assay (ELISA), including adiponectin, IGF-1, irisin, myostatin, glucose, and insulin levels. Biological samples were stored at −80°C and analyzed according to international laboratory standards.

Participants

Sample size was calculated using G*Power 3.1.9.2 software based on data from Abbenhardt et al. (2013), with $\alpha = 0.05$ and $1–\beta = 0.95$. The analysis revealed that 108 participants, consisting of nine groups with 12 individuals each, would ensure adequate statistical power. Accordingly, 108 homemakers aged 19–45 years were recruited, including 96 with obesity and 12 with normal weight, none of whom had engaged in dietary interventions during the preceding 3 months. Participation was voluntary, and all participants obtained medical clearance from a healthcare institution confirming no contraindications to exercise (mean age: 37.4 years; height: 162.3 cm; body weight: normal-weight group, 56.72 ± 4.38 kg, group with obesity, 102.5 ± 3.75 kg). Inclusion criteria comprised medical and psychological fitness for exercise, no participation in

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dietary programs within the previous 3 months, or lack of orthopedic limitations. Exclusion criteria included pregnancy or lactation, chronic conditions such as cancer or renal/hepatic failure, psychiatric disorders, history of adverse reactions to venipuncture, or inability to adhere to the intervention protocol (Figure 1).

Home-Based Exercise Protocol

The 6-week exercise protocol was conducted 3 days per week, with each session conducted at 10:00 a.m. under online supervision by a qualified specialist. Each session comprised warm-up, main exercise, and cool-down phases; warm-up activities were designed to minimize injury risk, and cool-down exercises facilitated recovery. Each set was followed by a 1-min rest interval. The program incorporated movements aimed at enhancing cardiorespiratory endurance, muscular strength, and overall fitness. The exercise program included high knees, heel-to-glute kicks, leg raises, squats, push-ups, walking lunges, planks, jumping jacks, and sit-ups, performed in predetermined sets and repetitions, with total session durations of 25–35 min (Table SM-1). Weekly progressions were systematically planned to ensure balanced muscle engagement and adherence to the progressive overload principle, while exercise order and combinations were modified each week to promote adaptation and sustain training intensity throughout the intervention (Table SM-2).

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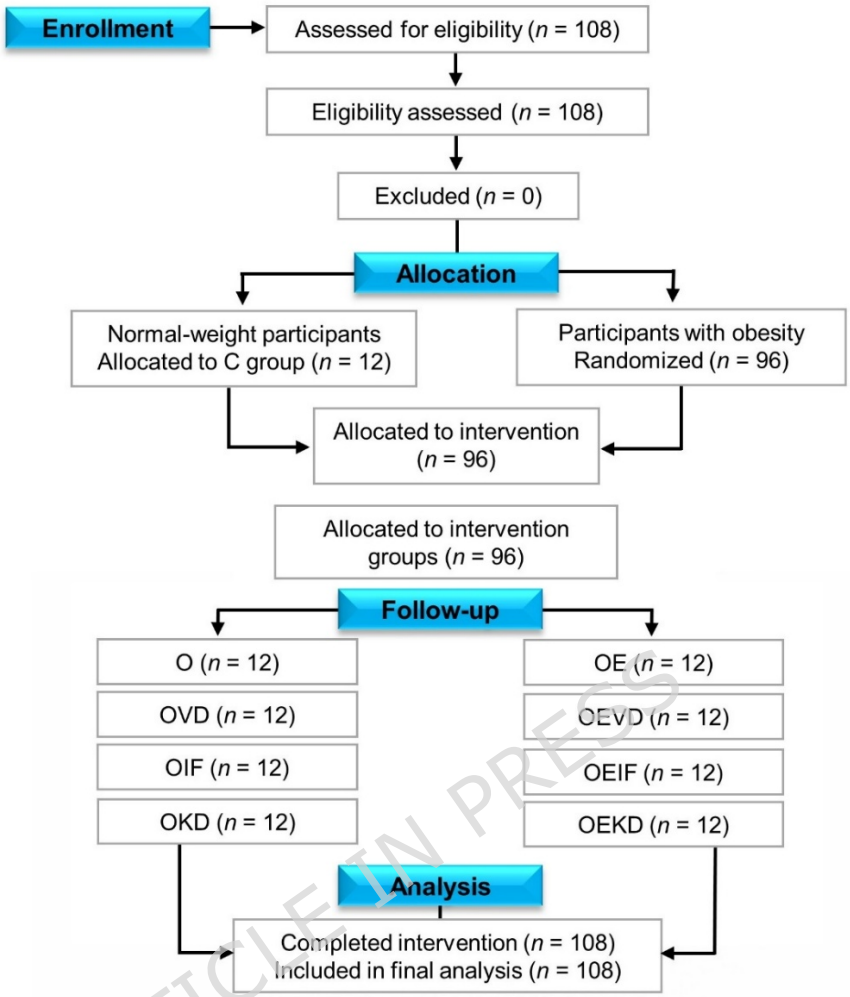


Figure 1. Participant flow diagram illustrating enrollment, group assignment, follow-up, and data analysis. C: control, O: control with obesity, OE: exercise with obesity, OVD: semi-vegetarian diet with obesity, OEVD: exercise semi-vegetarian diet with obesity, OIF: intermittent fasting with obesity, OEIF: exercise intermittent fasting with obesity, OKD: ketogenic diet with obesity, OEKD: exercise ketogenic diet with obesity.

Diet Protocols

Dietary plans were developed on an individual basis by a registered dietitian, taking into account basal metabolic rate (BMR) and total daily energy expenditure (TDEE), with the objective of inducing a moderate caloric deficit. Accordingly, daily energy intake was tailored to individual metabolic requirements and generally ranged between 1400 and 1700 kcal/day across intervention groups.

Three dietary models were applied to the intervention groups according to the experimental design. The vegetarian diet followed a semi-vegetarian model emphasizing grains, legumes, soy products, vegetables, fruits, and oilseeds as primary food sources. Red meat was completely excluded, while poultry and fish intake were limited; eggs, milk, and dairy products were permitted without restriction. This dietary pattern was designed to provide approximately 15–20% of total energy from protein, 50–55% from carbohydrates, and 25–30% from fat. The IF regimen (16:8) consisted

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of a daily 8-hour feeding window comprising two main meals (breakfast and dinner), followed by a 16-hour fasting period that included overnight sleep. During fasting periods, participants refrained from consuming solid foods and were allowed only non-caloric beverages, including water, plain mineral water, unsweetened tea, and black coffee. Despite the time-restricted structure of the IF regimen, total daily energy intake was aligned with individualized caloric targets, with a macronutrient distribution corresponding to approximately 20–25% protein, 40–45% carbohydrates, and 30–35% fat. The ketogenic diet followed the standard ketogenic model, with an approximate macronutrient distribution of 75% fat, 20% protein, and 5% carbohydrates. Grains, starchy vegetables, and most fruits were restricted, while red meat, poultry, fish, eggs, and cheese were allowed in controlled amounts. Low-carbohydrate vegetables, including leafy greens, broccoli, cauliflower, and zucchini, were unrestricted, and consumption of natural fats such as olive oil, butter, ghee, avocado, and oilseeds was encouraged (Table SM-3). Dietary adherence was monitored throughout the intervention period using daily food records, reviewed by a registered dietitian either daily or at intervals of 2–3 days, depending on participant availability. Adherence support was provided through weekly or biweekly dietitian consultations, supplemented by communication via telephone or WhatsApp when necessary. Compliance was operationally defined as adherence to ≥80% of the prescribed dietary protocol, and substantial deviations were promptly identified and addressed through individualized dietary counseling. The C group did not receive a structured dietary intervention and was provided only with general healthy eating advice at baseline, without individualized meal planning or dietary monitoring.

Anthropometric Measurements

Height was measured through a stadiometer (Holtain Ltd., UK). Body weight, composition, fat percentage, muscle ratio, visceral fat, and BMI were assessed with a BIA device (Omron Karadascan HBF-511, Japan).

ELISA

Blood samples were collected from each participant twice, at baseline and post-intervention. Before sampling, participants were informed about the procedure and provided consent. All measurements were taken at 9:00 a.m. following a 12-h overnight fast. Fasting glucose levels were measured using a glucometer (Biojet BG-102, China), after which 8 mL of venous blood was drawn from the left antecubital vein. Samples were placed in EDTA- and aprotinin-containing biochemistry tubes and centrifuged at 4000 rpm for 10 min using a Smart 15 Micro centrifuge. The obtained sera were stored at -80°C until analysis. Plasma levels of adiponectin, IGF-1, irisin, myostatin, glucose, and insulin were measured using ELISA kits following the instructions of the manufacturer (Reed Biotech, SunRed, China). Analyses were conducted using a Bio-Tek ELX50 automatic microplate washer (BioTek Instruments, USA) and ChroMate Microplate Reader P4300 (Awareness Technology Instruments, USA). Kit sensitivity, measurement range, and reproducibility were reported in the catalogs of the manufacturer (Table SM-4).

Statistical Analysis

Statistical analysis was performed using SPSS software (v21.0; IBM Corp., Armonk, NY, USA), and graphs were generated with GraphPad Prism (v8.2, trial; USA). Data were expressed as mean

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± standard deviation (SD). Pre- and post-test values were compared through a mixed two-way ANOVA, with time and group as within-subject and between-subject factors, respectively. When significant effects were identified, Bonferroni-adjusted post hoc tests were conducted. Statistical significance was set at $p < 0.05$, and partial eta squared (ηp^2) values were reported for main and interaction effects. Correlations between variables were examined using Pearson correlation analysis. Multivariate data were assessed through Principal Component Analysis (PCA) in XLSTAT software (New York, USA). This analysis reduced dimensionality and identified intergroup variations based on metabolic and myokine-related biomarkers, including adiponectin, IGF-1, irisin, myostatin, glucose, and insulin from fasting plasma samples. Two principal components were retained: the first (F1) separated metabolic indicators (glucose and insulin) from myokine/adipokine markers (adiponectin, IGF-1, irisin, and myostatin), whereas the second (F2) reflected intergroup variation, particularly distinguishing participants in post-intervention measurements (Yasul et al. 2025; Bolat et. al. 2025; Yılmaz et al. 2025).

Results

Table 2 presents significant main effects of time ($p < 0.001$), group ($p < 0.001$), as well as a significant time × group interaction ($p < 0.001$) for body mass. Simple main effect analyses showed that body mass values at pre-test were significantly higher in the O, OE, OEVD, OVD, OEIF, OIF, OEKD, and OKD groups compared with the C group. Comparisons conducted at post-test revealed significantly lower body mass values in the OE, OEVD, OVD, OEIF, OIF, OEKD, and OKD groups relative to the O group. Statistically significant reductions in body mass from pre-test to post-test were observed in the OE, OEVD, OVD, OEIF, OIF, OEKD, and OKD groups.

Table 2. Changes in body mass before and after the intervention across experimental groups

Factor	Groups	*Pretest*	*Posttest*	*p-value*[1]	Changes	Time	Time × Group	*p-value*[2]
		Mean ± S*d*	Mean ± S*d*		(%)			
Body Mass (kg)	C	56.72 ± 4.38^{b}	56.36 ± 4.75^{d}	0.609	-0.63			
	O	102.5 ± 3.75^{a}	102.2 ± 5.8^{a}	0.759	-0.29			
	OE	101.83 ± 3.09^{a}	92.16 ± 3.0^{bc}	0.002**	-9.49			
	OEVD	102.41 ± 2.31^{a}	89.41 ± 3.6^{c}	0.002**	-12.69	F = 47.245	F = 16.681	F = 24.512
	OVD	103.75 ± 3.93^{a}	94.33 ± 2.28^{b}	0.002**	-9.07	$p < 0.001$***	$p < 0.001$***	$p < 0.001$***
	OEIF	103.50 ± 2.74^{a}	94.43 ± 2.8^{b}	0.002**	-8.76	$np^2 = 0.82$	$np^2 = 0.57$	$np^2 = 0.95$
	OIF	102.33 ± 2.99^{a}	91.66 ± 3.2^{b}	0.001**	-10.42			
	OEKD	103.75 ± 2.98^{a}	92.66 ± 2.9^{bc}	0.002**	-10.68			
	OKD	102.58 ± 2.93^{a}	94.25 ± 3.5^{b}	0.001**	-8.12			

Experimental groups were defined as follows: C: control, O: control with obesity, OE: exercise with obesity, OEVD: exercise semi-vegetarian diet with obesity, OVD: semi-vegetarian diet with obesity, OEIF: exercise intermittent fasting with obesity, OIF: intermittent fasting with obesity, OEKD: exercise ketogenic diet with obesity, OKD: ketogenic diet with obesity. np^2: partial eta squared, *p-value*[1]: within-group comparisons, *p-value*[2], between-group comparisons, **: $p < 0.01$, ***: $p < 0.001$. Superscript letters (a, b, c, d) denote significant group differences based on post hoc comparisons.

Table 3 shows significant main effects of time ($p < 0.001$), group ($p < 0.001$), and a significant time × group interaction ($p < 0.001$) for BMI. Simple main effect analyses showed that BMI values at pre-test were significantly higher in the O, OE, OEVD, OVD, OEIF, OIF, OEKD, and OKD groups compared with the C group. Comparisons conducted at post-test revealed significantly lower BMI values in the OE, OEVD, OVD, OEIF, OIF, OEKD, and OKD groups relative to the O group, with the lowest BMI among participants with obesity observed in the OEVD group. Pre-

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test to post-test comparisons further demonstrated statistically significant reductions in BMI in the OE, OEVD, OVD, OEIF, OIF, OEKD, and OKD groups. Table 4 shows significant main effects of time ($p < 0.001$), group ($p < 0.001$), and a significant time × group interaction ($p = 0.032$) for body fat percentage. Pre-test values indicated that body fat (%) was significantly higher in all groups with obesity than in the C group, with no significant differences among the obesity groups. Post-test comparisons revealed lower body fat values in the C, OE, and OEVD groups than in the O group, with the lowest values among participants with obesity observed in the OE and OEVD groups.

Table 3. Changes in BMI before and after the intervention across experimental groups

Factor	Groups	*Pretest*	*Posttest*	*p-value*[1]	Changes	Time	Time × Group	*p-value*[2]
		Mean ± S*d*	Mean ± S*d*		(%)			
BMI (kg/m²)	C	21.06 ± 1.07[b]	21.03 ± 1.20[d]	0.498	-0.14			
	O	36.51 ± 1.98[a]	36.26 ± 2.00[a]	0.499	-0.68			
	OE	35.63 ± 2.35[a]	33.26 ± 2.63[b]	0.002**	-6.65			
	OEVD	35.49 ± 2.58[a]	30.71 ± 3.06[c]	0.004**	-13.46	F = 35.02	F = 11.68	F = 58.53
	OVD	35.60 ± 1.95[a]	32.69 ± 2.17[b]	0.002**	-8.17	$p < 0.001$***	$p < 0.001$***	$p < 0.001$***
	OEIF	35.86 ± 1.54[a]	32.40 ± 2.13[b]	0.005**	-9.64	$np^2 = 0.78$	$np^2 = 0.48$	$np^2 = 0.82$
	OIF	35.08 ± 1.55[a]	32.41 ± 1.41[b]	0.002**	-7.61			
	OEKD	35.04 ± 0.93[a]	31.83 ± 1.69[bc]	0.003**	-9.16			
	OKD	35.55 ± 2.89[a]	33.09 ± 2.41[b]	0.002**	-6.91			

Experimental groups were defined as follows: C: control, O: control with obesity, OE: exercise with obesity, OEVD: exercise semi-vegetarian diet with obesity, OVD: semi-vegetarian diet with obesity, OEIF: exercise intermittent fasting with obesity, OIF: intermittent fasting with obesity, OEKD: exercise ketogenic diet with obesity, OKD: ketogenic diet with obesity, np^2: partial eta squared, *p-value*[1]: within-group comparisons, *p-value*[2]: between-group comparisons, **: p < 0.01, ***: p < 0.001. Superscript letters (a, b, c, d) denote significant group differences based on post hoc comparisons.

Table 4. Changes in body fat before and after the intervention across experimental groups

Factor	Groups	*Pretest*	*Posttest*	*p-value*[1]	Changes	Time	Time × Group	*p-value*[2]
		Mean ± S*d*	Mean ± S*d*		(%)			
Body Fat (%)	C	24.00 ± 1.75[b]	24.03 ± 1.59[d]	0.999	0.12			
	O	37.37 ± 2.68[a]	37.28 ± 2.73[a]	0.317	-0.24			
	OE	36.67 ± 2.00[a]	31.72 ± 3.54[c]	0.010*	-13.49			
	OEVD	37.90 ± 2.17[a]	32.61 ± 2.90[bc]	0.003**	-13.95	F = 104.521	F = 4.339	F = 36.033
	OVD	38.78 ± 3.93[a]	36.37 ± 2.88[a]	0.015*	-6.21	$p < 0.001$***	$p < 0.001$***	$p = 0.032$*
	OEIF	38.61 ± 3.72[a]	33.96 ± 1.98[ab]	0.005**	-12.04	$np^2 = 0.51$	$np^2 = 0.26$	$np^2 = 0.74$
	OIF	38.61 ± 4.01[a]	34.80 ± 2.72[ab]	0.017*	-9.86			
	OEKD	38.20 ± 3.02[a]	33.93 ± 3.18[ab]	0.006**	-11.17			
	OKD	38.63 ± 2.62[a]	34.85 ± 2.28[ab]	0.003**	-9.78			

Experimental groups were defined as follows: C: control, O: control with obesity, OE: exercise with obesity, OEVD: exercise semi-vegetarian diet with obesity, OVD: semi-vegetarian diet with obesity, OEIF: exercise intermittent fasting with obesity, OIF: intermittent fasting with obesity, OEKD: exercise ketogenic diet with obesity, OKD: ketogenic diet with obesity. np^2: partial eta squared, *p-value*[1]: within-group comparisons, *p-value*[2]: between-group comparisons, *: p < 0.05, **: p < 0.01, ***: p < 0.001. Superscript letters (a, b, c, d) denote significant group differences based on post hoc comparisons.

Figure 2A shows significant main effects of time ($p < 0.001$), group ($p < 0.001$) and a significant time × group interaction ($p < 0.001$) for adiponectin levels. Pre–post analyses indicated that adiponectin levels remained unchanged in the C and O groups, whereas increases were detected in the OE, OEVD, OEIF, and OEKD groups. Post-test comparisons further showed that adiponectin levels in the OE, OEVD, OEIF, and OEKD groups were higher than those observed in the C and

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O groups ($p < 0.001$). Figure 2B demonstrates significant main effects of time ($p < 0.001$), group ($p < 0.001$), and a significant time × group interaction ($p < 0.001$) for irisin levels. There was no significant pre–post change in the C and O groups, whereas the intervention groups showed significant pre–post differences. Figure 2C shows significant main effects of time ($p < 0.001$), group ($p < 0.001$), and a significant time × group interaction ($p < 0.001$) for myostatin levels. Pre–post change was not significant in the C, O, OVD, OIF, and OKD groups, whereas significant pre–post differences were observed in the OE, OEVD, OEIF, and OEKD groups. Post-test comparisons showed that myostatin levels were higher in the intervention groups than in the C and O groups. Figure 2D shows that IGF-1 levels varied significantly over time ($p < 0.001$), between groups ($p < 0.001$) and for the time × group interaction ($p < 0.001$). Pre–post analyses indicated that IGF-1 levels remained unchanged in the in the C and O groups, whereas increases were observed in the OE, OEVD, OEIF, and OEKD groups. The IGF-1 levels were higher in the intervention groups than in the C and O groups, with the highest values observed in the OEVD, OEIF, and OEKD groups.

Figure 3A shows that body mass was positively correlated with body fat percentage and weakly negatively correlated with glucose levels. BMI was strongly positively correlated with body fat percentage and weakly positively correlated with insulin, while a weak negative correlation with glucose was observed. Insulin and glucose levels exhibited a moderate negative correlation, whereas insulin was weakly positively correlated with myostatin and irisin. Glucose levels were moderately negatively correlated with irisin, myostatin, IGF-1, and adiponectin. In addition, adiponectin showed moderate positive correlations with irisin, myostatin, and IGF-1. IGF-1 was moderately positively correlated with irisin and myostatin, and a comparable moderate positive association was observed between myostatin and irisin. Figure 3B shows significant main effects of time ($p < 0.001$), group ($p = 0.032$), and a significant time × group interaction ($p < 0.001$) for glucose levels. Pre–post change was not significant in the C and O groups, whereas significant pre–post differences were observed in the intervention groups. Post-test comparisons showed that glucose levels were lower in the intervention groups than in the C and O groups. Figure 3C indicates significant main effects of time ($p < 0.001$), group ($p = 0.041$), and a significant time × group interaction ($p < 0.001$) for insulin levels. Pre–post change was not significant in the C and O groups, whereas significant pre–post differences were observed in the intervention groups.

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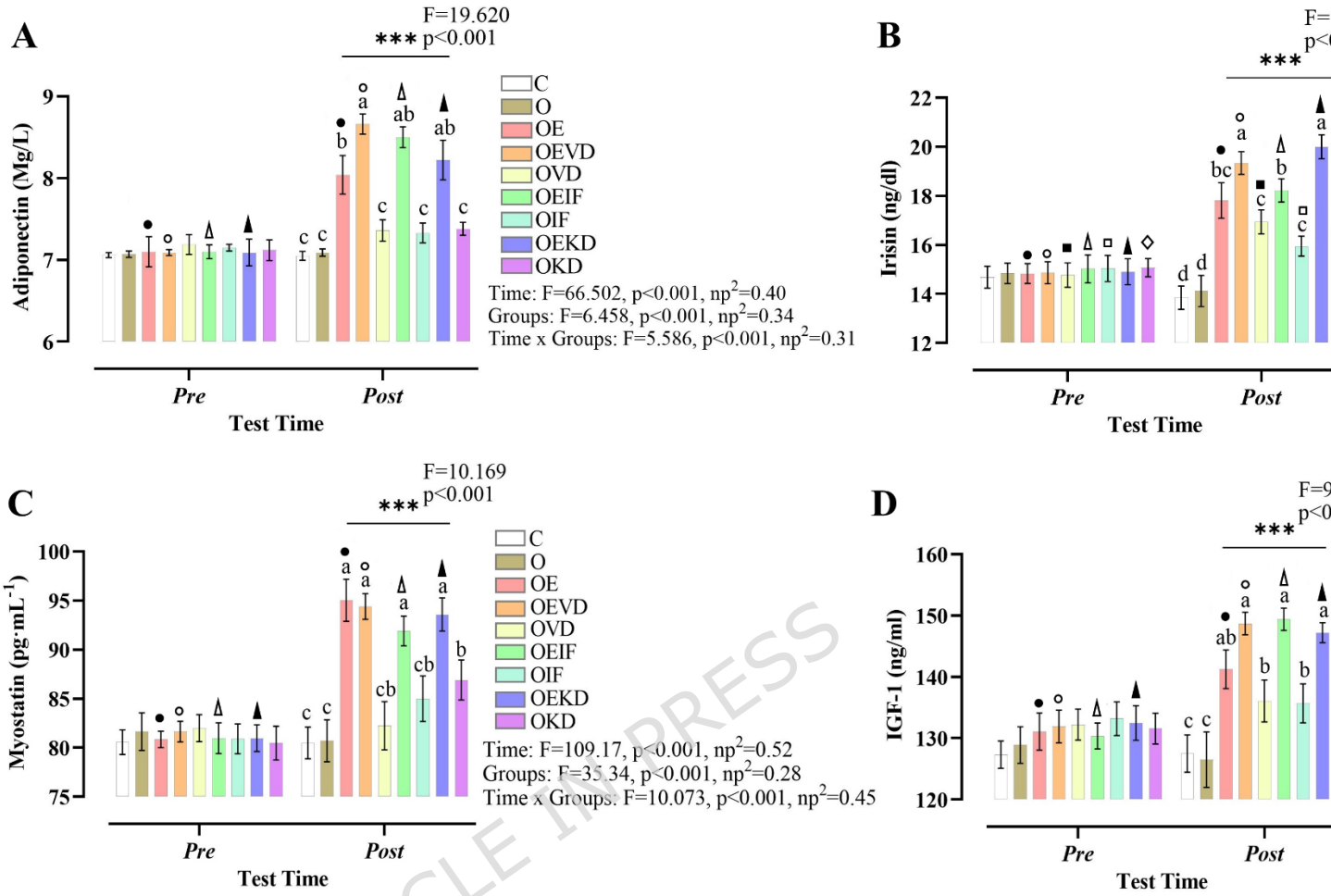


Figure 2. Serum levels of adiponectin (A), irisin (B), myostatin (C), and IGF-1 (D) measured by ELISA at pre- and post-test time points. Experimental groups were defined as follows: C: control, O: control with obesity, OE: exercise with obesity, OEVD: exercise semi-vegetarian diet with obesity, OVD: semi-vegetarian diet with obesity, OEIF: exercise intermittent fasting with obesity, OIF: intermittent fasting with obesity, OEKD: exercise ketogenic diet with obesity, OKD: ketogenic diet with obesity. ***: $p < 0.001$: ns: non-significant, *np²:* partial eta squared. Superscript letters (a, b, c) indicate significant between-group differences based on post hoc comparisons. Matching symbols above the bars indicate significant within-group (pre–post) differences. ELISA: enzyme-linked immunosorbent assay, IGF-1: insulin-like growth factor 1.

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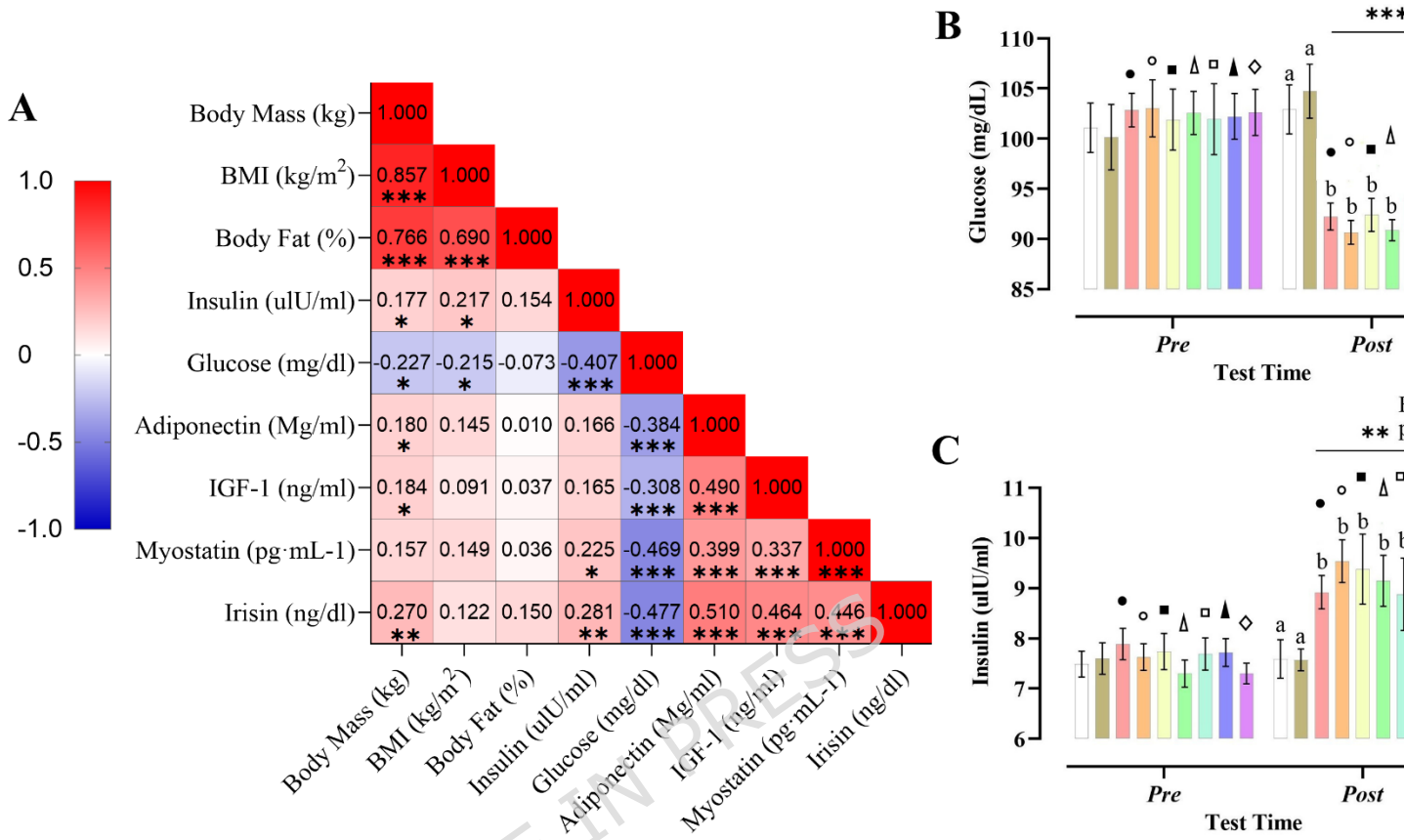


Figure 3. Pearson correlation matrix illustrated as a heat map, where (A) red tones indicate positive and blue tones negative correlations. Correlation strength is classified as small (0.1–0.3), medium (0.3–0.5), and large (0.5–1.0). Serum glucose (B) and insulin (C) levels measured using ELISA at pre- and post-test time points. Experimental groups were defined as follows: C: control, O: control with obesity, OE: exercise with obesity, OEVD: exercise semi-vegetarian diet with obesity, OVD: semi-vegetarian diet with obesity, OEIF: exercise intermittent fasting with obesity, OIF: intermittent fasting with obesity, OEKD: exercise ketogenic diet with obesity, OKD: ketogenic diet with obesity. *: $p < 0.05$: **: $p < 0.01$: ***: $p < 0.001$, ns: no-nsignificant np^2: partial eta squared. Superscript letters (a, b, c) indicate significant between-group differences based on post hoc comparisons. Matching symbols above the bars indicate significant within-group (pre–post) differences. BMI: body mass index, IGF-1: insulin-like growth factor 1, ELISA: enzyme-linked immunosorbent assay.

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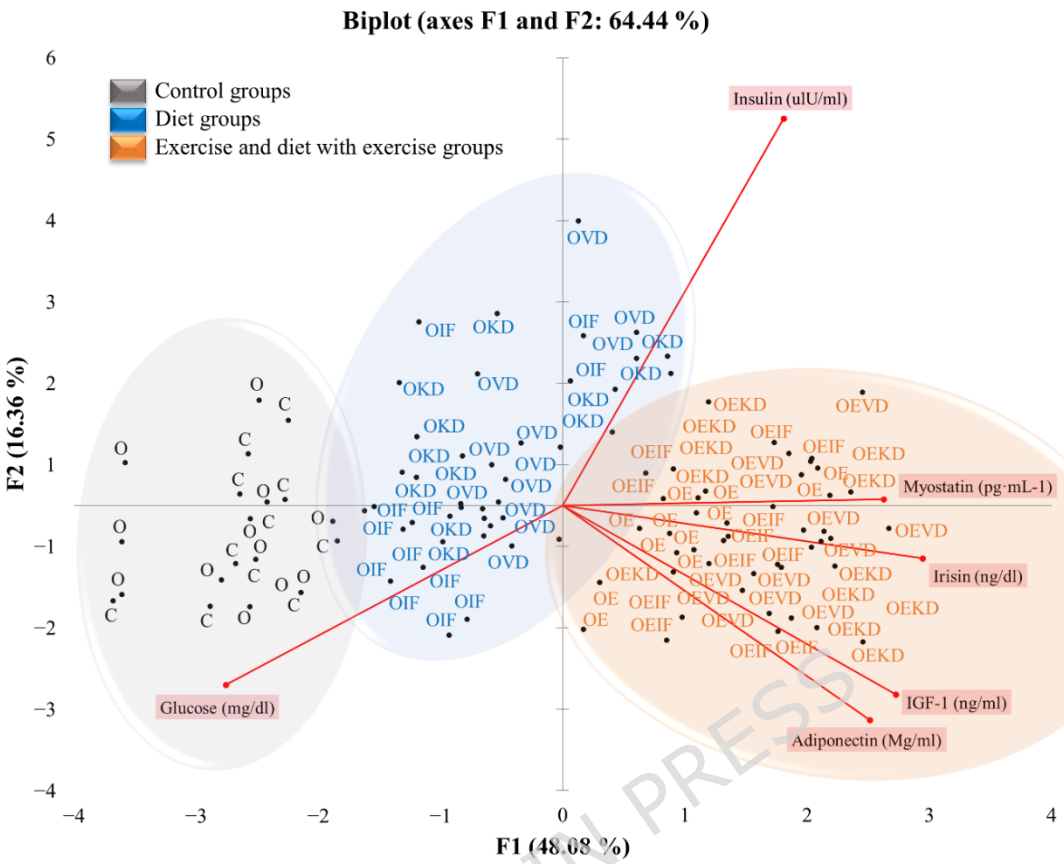


Figure 4. PCA biplot illustrating intergroup variance distribution and separation patterns of plasma samples. Experimental groups were defined as follows: C: control, O: control with obesity, OE: exercise with obesity, OEVD: exercise semi-vegetarian diet with obesity, OVD: semi-vegetarian diet with obesity, OEIF: exercise intermittent fasting with obesity, OIF: intermittent fasting with obesity, OEKD: exercise ketogenic diet with obesity, OKD: ketogenic diet with obesity, PCA: principal component analysis, IGF-1: insulin-like growth factor 1.

The first two components of the PCA explained 64.44% of the total variance (F1: 48.08%: F2: 16.36%; Figure 3). The F1 axis was highly influenced by irisin (21.59%), glucose (18.90%), adiponectin (18.50%), myostatin (17.17%), and IGF-1 (15.71%), while insulin contributed minimally (8.13%). Conversely, the F2 axis was largely composed of insulin (56.22%), with smaller contributions from IGF-1 (17.25%), adiponectin (13.41%), and glucose (12.06%). This distribution pattern suggested that the groups formed three distinct clusters. The C and O groups (black) were located on the negative side of F1, whereas glucose contributed more strongly to this region of the ordination space. The diet-only groups (blue) clustered in the central region, with OVD and OKD partially aligned with insulin, whereas OIF was shifted toward glucose. The diet with exercise combination groups (orange) were positioned on the positive side of F1 and exhibited strong associations with adiponectin, IGF-1, irisin, and myostatin. The OEVD and OEKD groups also appeared more closely aligned with these myokines, while the OE and OEIF groups were positioned closer to the center and, while partially aligned, showed less distinct separation from other combinations. Given that all participants except those in the C group were obese, these

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findings suggest that combining dietary applications with exercise may be associated with changes in metabolic–myokine profiles in individuals with obesity.

Discussion

The responses in C, O, OE, OVD, OIF, and OKD groups suggest that isolated dietary or exercise interventions may be associated with relatively smaller metabolic changes in obesity. In contrast, OEVD, OEIF, and OEKD groups showed more integrated responses, suggesting exercise combined with dietary modification contributes substantially to systemic metabolic regulation. The changes in adiponectin, irisin, myostatin, and IGF-1 observed may reflect endocrine interaction between skeletal muscle and adipose tissue, a key mechanism for regulating energy balance and glucose homeostasis. The dietary models in OVD, OIF, and OKD produced diet-specific effects not fully comparable across anthropometric and metabolic outcomes. Combining diet with exercise in OEVD, OEIF, and OEKD was associated with broader changes, potentially reflecting concurrent modulation of substrate availability, muscle activity, and endocrine signaling. Exercise-based intervention in OE was associated with changes in body composition that may be consistent with increased energy expenditure and enhanced lipid oxidation capacity, mechanisms linked to improved fat-mass regulation in women with obesity (Yiğiter et al., 2025; Swift et al., 2014). Dietary interventions in OVD, OIF, and OKD may involve complementary mechanisms. The semi-vegetarian pattern in OVD lowers dietary energy density while increasing fiber, influencing satiety signaling, gastrointestinal transit, and postprandial insulin dynamics (Küçük & Yıbar, 2021). Intermittent fasting in OIF restructures energy intake timing, supporting insulin sensitivity, hepatic glucose handling, and metabolic flexibility without continuous restriction (Jamshed et al., 2019). The ketogenic model in OKD shifts substrate utilization toward fat-derived fuels via carbohydrate restriction, glycogen depletion, and ketone-mediated appetite regulation (Paoli, 2014). Exercise with dietary change enhances lipid mobilization and oxidation, supporting reductions in adipose tissue (Barry et al., 2014), while improved dietary quality modulates lipid metabolism and adipose function (Bellicha et al., 2021; Mouskeftara et al., 2024). Meta-analytic evidence indicates combined approaches improve maintenance of body-composition adaptations over time (Johns et al., 2014; Kerksick et al., 2018). The OEVD pairs exercise with a semi-vegetarian diet, OEIF with intermittent fasting, and OEKD with ketogenic. Adaptations in OEVD, OEIF, and OEKD may reflect multi-level metabolic regulation rather than additivity across isolated interventions.

Adiponectin functions as a key adipokine linking adipose tissue with skeletal muscle metabolism and insulin sensitivity, making its regulation a potential marker metabolic adaptation. The absence of adiponectin modulation in C and O groups may reflects limited endocrine plasticity of obesity without structured lifestyle intervention. In contrast, OE, OEVD, OEIF, and OEKD groups displayed adiponectin responsiveness, indicating that exercise-driven metabolic signaling may plays a central role in regulating adipokine secretion. Exercise activates skeletal muscle AMPK and PGC-1α pathways, enhancing fatty acid oxidation and insulin sensitivity and promoting adiponectin release (Balasubramanian et al., 2022). Diet interventions in OVD, OIF, and OKD groups resulted in modest adiponectin changes, suggesting dietary modulation influences adipose tissue function without fully engaging muscle-mediated pathways. Semi-vegetarian dietary patterns have been associated with changes in adiponectin through reduced dietary energy density

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and anti-inflammatory effects (Kahleova et al., 2018), while intermittent fasting has been associated with improvements adipokine dynamics via enhanced adipose tissue insulin sensitivity (Kazeminasab et al., 2024). Ketogenic diets shift metabolism toward fat utilization, which may contribute to adiponectin regulation primarily when combined with exercise signaling (Paoli, 2014). Adiponectin increased in OE, OEVD, and OEIF groups, suggesting an exercise-related endocrine response. The OEVD group showed the most favorable BMI outcomes, suggesting adiponectin-related adaptations may have been accompanied by greater anthropometric improvement when exercise was combined with a semi-vegetarian diet.

Irisin is a muscle derived myokine that mediates metabolic processes by linking skeletal muscle signaling to adipose tissue remodeling and energy expenditure. The absence of irisin modulation in C and O groups may reflect its dependence on active muscle engagement rather than passive metabolic change. The OE, OEVD, OEIF, and OEKD groups displayed pronounced irisin responsiveness, suggesting that exercise may represent an important regulatory stimulus. Diet interventions in OVD, OIF, and OKD groups showed modest irisin modulation, suggesting dietary manipulation alone insufficiently activates myokine signaling. Exercise induces PGC-1α expression in skeletal muscle, promoting irisin release and white adipose tissue browning, thereby increasing energy expenditure (Novelle et al., 2013; Elsen et al., 2014). Evidence from exercise interventions has been show that sustained aerobic activity elevates circulating irisin and is associated with improvements in metabolic parameters (Trezzi et al., 2025; Akbulut et al., 2025). Irisin responses were highest in OEVD and OEKD groups, which showed the largest BMI reductions, suggesting that exercise-induced myokine signaling coincided with favorable changes under specific dietary contexts. Variability in irisin regulation across obesity studies indicates that irisin reflects adaptive changes in muscle activity and metabolism rather than adiposity (Pardo et al., 2014; Kurdiova et al., 2014; Crujeiras et al., 2014; Huerta et al., 2015).

Myostatin functions as a negative regulator of skeletal muscle growth and metabolic regulation, and its circulating levels reflect interactions between muscle activity, inflammation, and metabolic state. The stability of myostatin in C and O groups may reflect limited endocrine plasticity without structured intervention. In contrast, elevations in OE, OEVD, OEIF, and OEKD groups suggest that exercise-driven muscle signaling may influences circulating myostatin dynamics. Dietary interventions in OVD, OIF, and OKD groups showed smaller increases, implying diet alone provides weaker regulatory stimulus compared to exercise-inclusive strategies. Although resistance and aerobic exercise suppress myostatin signaling within skeletal muscle tissue, circulating myostatin does not necessarily mirror intramuscular expression, as local and systemic myostatin pools have distinct regulatory mechanisms (McIntosh et al., 2023; Shabkhiz et al., 2021; Eilers et al., 2020; Dichtel et al., 2023). Short term interventions may elicit transient increases reflecting compensatory responses. In obesity, chronic inflammation has been associated with alterations in myostatin release and stability, linking elevated circulating myostatin to insulin resistance rather than impaired muscle adaptation (Szukiewicz, 2023). Measurement timing and plasma dynamics may also contribute to these patterns (Khalafi et al., 2023; Huang et al., 2025).

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Glycemic regulation depends on the coordinated interaction of skeletal muscle glucose uptake, hepatic glucose handling, pancreatic insulin secretion, and anabolic signaling pathways that integrate metabolic and mechanical stimuli. The lack of improvement in the C and O groups may reflects the persistence of insulin resistance and impaired glucose control in obesity without targeted intervention. Dietary strategies applied in the OVD, OIF, and OKD groups may influence glycemic regulation primarily through modulation of substrate availability, delayed intestinal glucose absorption, and improved insulin responsiveness. Exercise-inclusive interventions implemented in the OE, OEVD, OEIF, and OEKD groups engage additional regulatory mechanisms, most notably enhanced skeletal muscle glucose uptake via GLUT-4 translocation, which has been associated with greater peripheral insulin sensitivity (Vitale and Getzin, 2019; Zinn and Rush, 2020). Plant-based dietary patterns further support glycemic stability through low glycemic load, high fiber content, and antioxidant mediated preservation of β-cell function (Yokoyama et al., 2014; Barnard et al., 2015; Glick-Bauer and Yeh, 2014). Ketogenic dietary strategies reduce circulating glucose through carbohydrate restriction and altered fuel utilization (Paoli, 2014), while intermittent fasting enhances insulin sensitivity by improving metabolic flexibility (Jamshed et al., 2019). The concurrent modulation of glucose regulation alongside adiponectin, irisin, myostatin, and IGF-1 suggests that glycemic control in obesity may involve integrated muscle–adipose–pancreatic endocrine adaptations rather than isolated dietary or exercise components.

Limitations

This study provides insight into metabolic adaptations resulting from dietary and exercise interventions in obesity. The exclusive focus on female participants and the 6-week intervention period provides insight into short-term rather than long-term outcomes. Menstrual cycle phase was outside the scope of the study design. Although the sample size was determined through power analysis, individual variability may still have influenced the findings. BIA and ELISA methods provided reliable but indirect measures, suggesting the value of complementary molecular analyses. Despite these limitations, the physiological patterns observed across the intervention models may contribute to the interpretation of lifestyle-based approaches in obesity research.

Conclusion

The C and O groups showed no significant changes in anthropometric measures, glucose–insulin regulation, or endocrine markers, indicating no improvement without structured intervention. Single-modality applications produced comparatively limited effects: the OE group showed exercise-related changes, while the OVD, OIF, and OKD groups reflected diet-specific responses. Changes were observed in glucose, insulin, adiponectin, irisin, myostatin, and IGF-1; however, these patterns appeared less consistent than those observed in the combined application groups. The OEVD, OEIF, and OEKD groups showed concurrent improvements in body composition, glycemic regulation, and endocrine markers, including reductions in body mass, BMI, and body fat percentage, along with changes in adiponectin, irisin, myostatin, and IGF-1. Taken together, the findings suggest that combined diet–exercise applications, particularly OEVD, OEIF, and

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OEKD, were associated with more consistent changes in body composition and metabolic parameters in women with obesity. Lifestyle modifications integrating dietary strategies with home-based exercise were associated with changes in metabolic and hormonal parameters in women with obesity.

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Author's contributions FÇ, FMU, VÇ and D-Y. L., study concept and design. FÇ, PY, ETA and EBS, performed exercise training and diet protocols. FÇ, PY, ETA and EBS, Data collection. TA, PY, EBS, VÇ, S.A and D-Y L., biochemical analyses. YY and SÖ, analyzed the data and visualization. FÇ, EBS, YY, ETA and D-Y L., prepared the original draft. FMU, TA, VÇ, SA and D-Y L., provided supervision. FMU and D-Y L., project administration. The authors reviewed, edited, and approved the manuscript prior to submission.

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Ethics Statement

The methods were performed in accordance with the relevant guidelines and regulations. The experimental protocols were approved by the Non-Interventional Research Ethics Committee of Fırat University, Faculty of Medicine (Decision No: 2023/01-20; 12 January 2023). The study adhered to the principles of the Declaration of Helsinki. Informed consent was obtained from all participants prior to enrollment in the study.

Trial registration This study was retrospectively registered at ClinicalTrials.gov (Identifier: NCT07695480). The registration record is publicly available through ClinicalTrials.gov.

Conflicts of Interest The authors declare no competing interests.

Data availability The datasets generated and analyzed during this study are available from the corresponding author upon request.

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