scientific reports

Check for updates

OPEN

Effect of exercise on hormonal responses in adolescents with obesity and leptin resistance: a randomized trial

Deokhwa Jeong[1,2], Rudy J. Valentine[2], Kyumin Park[3], Hyeongmo Jeong[5], Jeana Hong[4,6]✉ & Sunghwun Kang[1,5,6]✉

This study examined the effects of regular plyometric exercise on growth hormones, appetite hormones, myokines, and adipokines in adolescents with obesity and leptin resistance. Sixty adolescents (male: 11.9 ± 0.8 years; female: 13.0 ± 1.0 years) with body fat ≥ 30% and leptin ≥ 30 ng/mL participated between July 2023 and October 2024 following IRB approval. Participants were randomized by gender into control or exercise groups ($n = 15$ per gender). The exercise group completed a 12-week program (3 sessions/week, 150 min/week). Twelve participants withdrew (CON, $n = 6$; PE, $n = 6$). Thus, 48 participants completed the study and were included in the final per-protocol analysis. Assessments included body composition, muscle fitness (grip strength, isokinetic torque), and blood biomarkers. Significant improvements were observed in height, muscle mass, fat mass, body fat percentage, BMI, and muscle fitness in the exercise group ($p < 0.05$). GH and IGF-1 increased, with reduced myostatin and elevated follistatin ($p < 0.05$). Leptin sensitivity improved with increased adiponectin ($p < 0.05$). TNF-α showed no significant change. Findings suggest that plyometric exercise is an effective non-pharmacological approach to enhance growth, body composition, muscle fitness, and endocrine regulation in adolescents with obesity and leptin resistance.

Keywords Exercise, Adolescents with obesity and leptin resistance, Growth & appetite hormone, Myokine

According to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), as of 2021, approximately 18% of children and adolescents aged 5–14 years worldwide were classified as having either overweight or obesity, encompassing both categories[1]. Among these individuals, nearly 70% are likely to sustain obesity into adulthood[1], significantly elevating their risk of chronic physiological and psychological disorders[2]. Living with obesity over the long-term is a well-established risk factor for various metabolic diseases, including dyslipidemia, type 2 diabetes mellitus, and cardiovascular diseases[3], and is also associated with irregular menstruation stemming from polycystic ovary syndrome (PCOS) in females[4]. In addition, people with obesity often experience psychological comorbidities, such as depression, anxiety, and low self-esteem, which significantly contribute to an increased risk of premature mortality[5]. These psychological burdens may also discourage physical activity and reinforce sedentary behavior, thereby creating a vicious cycle that perpetuates poor health outcomes[2]. Therefore, early intervention and management for childhood and adolescence living with obesity are crucial to prevent related complications.

Increased sedentary behaviors and poor dietary habits are primary contributors to obesity in children and adolescents[6]. Excess adiposity leads to the overproduction of leptin, an appetite-regulating hormone secreted by adipose tissue, resulting in leptin resistance[7]. Under normal conditions, leptin helps regulate body weight by suppressing appetite and promotes energy expenditure[8]. However, in individuals with obesity, chronically elevated leptin levels are accompanied by impaired leptin receptor signaling and attenuated central leptin activity, a condition referred to as leptin resistance[9]. This dysregulation disrupts appetite regulation and energy homeostasis, contributing to obesity progression and metabolic dysfunction. Leptin resistance therefore

[1]Department of Smart Health Science and Technology Graduate, Kangwon National University, Chuncheon-si 24341, Republic of Korea. [2]Department of Physical Therapy & Kinesiology, University of Massachusetts, Lowell, MA 01854, USA. [3]Center for Sports Science in Gangwon, Chuncheon-si 24239, Republic of Korea. [4]Department of Pediatrics, Kangwon National University College of Medicine, Chuncheon-si 24289, Republic of Korea. [5]Department of Sport Science, Kangwon National University, Chuncheon-si 24341, Republic of Korea. [6]Jeana Hong and Sunghwun Kang contributed equally to this work. ✉email: jnhongmd@kangwon.ac.kr; 94psycho@kangwon.ac.kr

aggravates both psychological and physiological complications in this population[10]. In children and adolescents with obesity, leptin resistance is recognized as a critical pathophysiological mechanism that perpetuates excess adiposity and elevate the risk of chronic diseases in adulthood. Notably, elevated leptin concentrations in this population serve as clinical biomarkers future metabolic disorders[11]. Therefore, promoting physical activity and balanced dietary habits during early life is crucial for enhancing leptin sensitivity and mitigating long-term health risks.

Regular exercise represents a key non-pharmacological strategy for effectively mitigating leptin resistance[12]. Among various exercise modalities, plyometric exercise, which utilizes repetitive stretch shortening cycles to enhance muscle strength, bone loading, and metabolic demand, has shown particular promise for adolescents due to its dual effects on muscle fitness and growth stimulation[13]. Increased physical activity facilitates quantitative and qualitative muscle development and reduces body fat mass[14], enhancing leptin sensitivity through reduced expression of Suppressor Of Cytokine Signaling 3 (SOCS3) and Protein tyrosine phosphatase 1B (PTP1B), major inhibitors of leptin signaling within muscle tissues[15]. Studies involving adolescents with obesity and animal models have consistently demonstrated that regular exercise effectively reduces body fat and circulating leptin levels while increasing muscle mass and leptin sensitivity[16,17]. Furthermore, myokines secreted from skeletal muscles during exercise exhibit anti-inflammatory properties, thereby reducing systemic chronic inflammation and directly contributing to improved leptin sensitivity[18]. Thus, enhancing leptin sensitivity through regular exercise in children and adolescents with obesity is crucial for breaking the vicious cycle and maintaining long-term health.

However, previous studies primarily focused on animal models of obesity[16] or were limited to examining individual physiological parameters such as leptin and adipokine concentration[19], growth hormone, and myokines[20]. Comprehensive studies exploring the integrated physiological impact of regular exercise on growth hormones, appetite-regulating hormones, myokines, and adipokines among children and adolescents with obesity and leptin resistance remain scarce. Therefore, the present study aims to address the limitations of previous research by comprehensively analyzing the integrated effects of regular exercise on growth hormones, appetite-regulating hormones, myokines, and adipokines in adolescents with obesity and leptin resistance. Ultimately, this study seeks to provide fundamental data for establishing more effective and systematic intervention strategies applicable to the management of children and adolescents with obesity.

Methods

Study design and participation

This study complied with the ethical standards of the Declaration of Helsinki and was approved by the Institutional Review Board of Kangwon National University (KWNUIRB-2023-05-007) on May 25, 2023. Adolescents with Obesity and Leptin Resistance were recruited between August 1, 2023, and October 12, 2024. It was retrospectively registered with the Korea Clinical Trials Registry (KCT0010749; July 11, 2025). Written informed consent was obtained from all participants and their legal guardians. Participation was entirely voluntary, and participants were informed that they could withdraw from the study at any time without consequences. However, the study was not registered in a clinical trial registry prior to participant enrollment, which we acknowledge as a limitation. Sixty adolescents with obesity and leptin resistance (body fat percentage $\geq$ 30%; leptin $\geq$ 30 ng/mL), were recruited, comprising 30 males and 30 females. The mean age was 11.9 $\pm$ 0.8 years for males and 13.0 $\pm$ 1.0 years for females. Based on chronological age, participants were estimated to correspond to Tanner stages 2–3, although direct Tanner staging was not performed. Sample size was calculated using G*Power software (version 3.1.9.7; Heinrich Heine University, Düsseldorf, Germany). Assuming an $\alpha = 0.05$, power = 0.80, and a medium effect size ($f = 0.25$), the minimum total sample size required was 48 participants. To account for potential a 20% dropout rate, a total 60 participants were enrolled. Inclusion criteria were: (1) absence of medical or musculoskeletal conditions limiting participation in plyometric exercise and (2) voluntary agreement to participate with guardian consent. Exclusion criteria were: (1) use of weight-loss medication, (2) cardiovascular or cardiopulmonary dysfunction, and (3) musculoskeletal injuries within the previous six months. At baseline, participants underwent body composition and blood assessments after an overnight fast at the Exercise Physiology Laboratory, Department of Sports Science. Participants were then randomized by gender into either a control group (CON, $n = 15$ per gender) or a plyometric exercise group (PE, $n = 15$ per gender) using simple randomization with opaque envelopes. Outcome assessors were blinded to group allocation to minimize measurement bias. The random sequence was generated by an independent researcher not involved in participant recruitment or assessment, and group allocation was implemented by a separate assistant using opaque, sealed envelopes to ensure allocation concealment. The 12-week intervention was followed by identical post-testing. Twelve participants withdrew during the study (male: CON, $n = 3$; PE, $n = 3$; female: CON, $n = 3$; PE, $n = 3$). For ethical transparency, control group participants were given the option to receive the same exercise intervention after the study period. Although offered, no one participated post-intervention. Participants assigned to the control group were instructed to maintain their usual daily routines and were explicitly advised not to engage in any structured or regular physical exercise throughout the 12-week study period. Among those who completed the study, session attendance rates exceeded 95%.

The specific contents of the study design are shown in Fig. 1.

Measurement of body composition

The Body composition variables were assessed using a bioelectrical impedance analyzer (BIA) (Inbody 720 Body Composition Analyzer, Biospace, Seoul, Republic of Korea). Measurements were performed with participants barefoot and wearing light clothing, after removing shoes, socks, and heavy accessories. Weight (kg), fat mass (kg), and skeletal muscle mass (kg) were recorded to the nearest 0.1 kg. Body fat percentage was estimated based

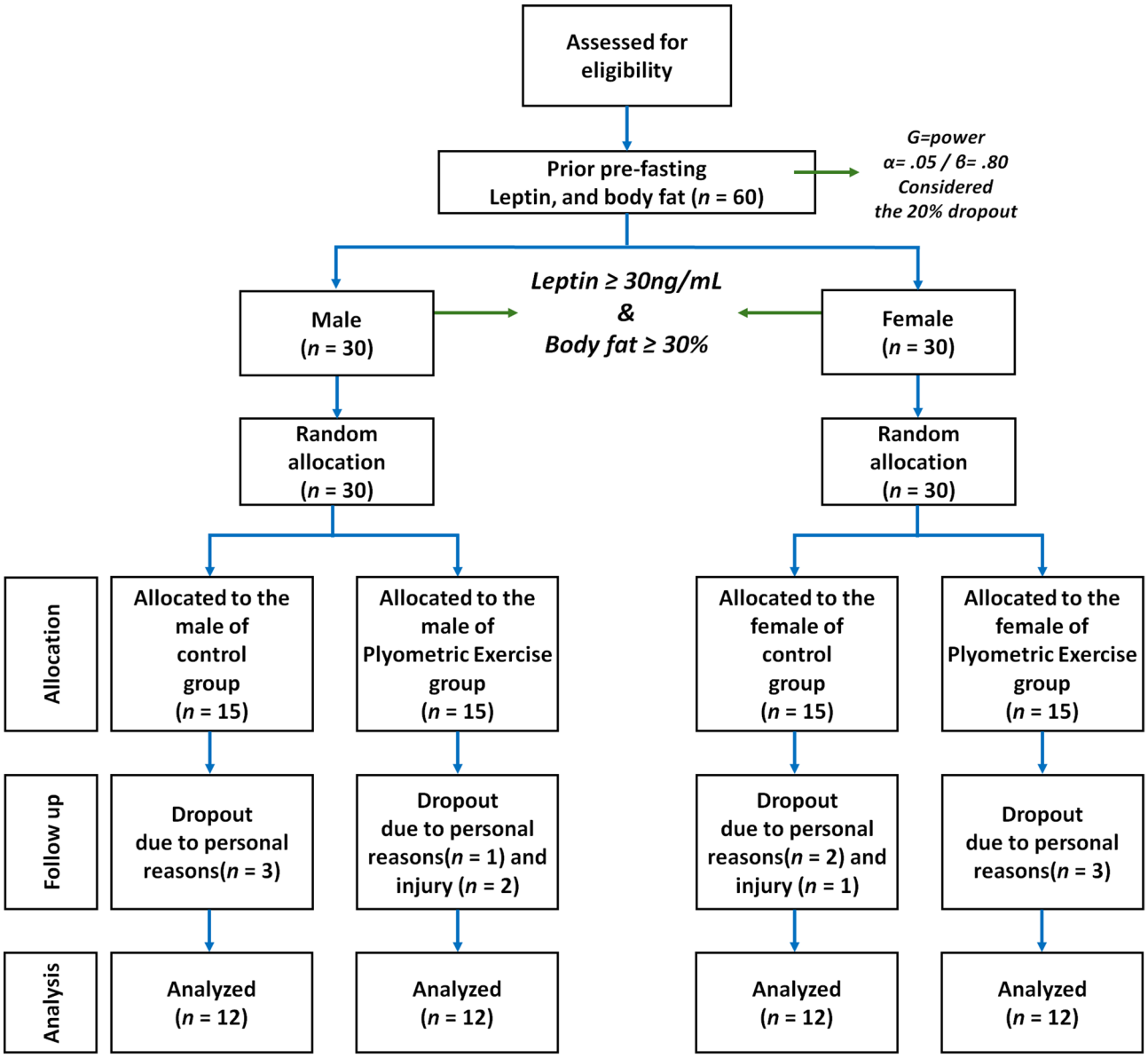

Fig. 1. Study design.

on impedance values obtained from multiple frequencies. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2).

Hematological analysis

Fasting venous blood samples were collected from all participants at baseline and 12 weeks after the intervention. Participants were instructed to refrain from vigorous physical activity for at least 24 h prior to each visit and to maintain normal daily activities without engaging in strenuous exercise. They were also advised to obtain a minimum of 7 h of sleep the night before sample collection. Compliance with these instructions was verbally confirmed on the day of the visit. On each assessment day, participants arrived at the laboratory after a 12-hour overnight fast. Blood samples were collected at 08:00 from the antecubital vein into serum separator tubes (SST). The samples were allowed to clot at room temperature for 30 min before centrifugation. After clotting, the samples were centrifuged at 3,500 g for 10 min at room temperature to obtain serum. The separated serum samples were then aliquoted and stored at − 80 °C until further analysis. Serum levels of growth hormone such as growth hormone(GH), Insulin-like Growth Factor 1 (IGF-1), and Insulin-like Growth Factor-Binding Protein 3 (IGF-BP3)(DY1067, DY291, and DY675: R&D Systems, Minneapolis, MN, USA), appetite hormone such as Insulin(440132, Beckman Coulter, California, CA, USA), leptin, and ghrelin(DY398, and DY8149-05: R&D Systems, Minneapolis, MN, USA), myokine such as irisin, myostatin, and follistatin (DY9420-05, DY788-05, and DY669: R&D Systems, Minneapolis, MN, USA), and adipokine such as adiponectin, and adipose tissue-derived cytokine and tumor necrosis factor-alpha (TNF-α) (DY1065, and DY210: R&D Systems, Minneapolis,

MN, USA) were measured using DuoSet TM enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, Minneapolis, MN, USA) according to the manufacturer's instructions.

Measurement of muscle fitness

A digital handgrip dynamometer (GRIP-D 5101; TAKEI, Co., Tokyo, Japan) was used to measure right and left grip strength. All measurements were entered into an electronic card and transmitted to a computer. Abdominal muscle endurance was assessed by counting the maximum number of sit-ups performed within 30 s. An isokinetic dynamometer (Humac Norm Testing and Rehabilitation, CSMi Medical & Solutions, Stoughton, MA, USA) was utilized to assess unilateral knee maximum strength, muscle power, and endurance. Maximum knee strength(peak torque) was evaluated through isokinetic extension and flexion tests performed at an angular velocity of 60°/s for 3 repetitions. Muscle power was assessed using the same extension and flexion tests conducted at an angular velocity of 180°/s for 15 repetitions. During the assessment, the lateral epicondyle of the femur was precisely aligned with the rotational axis of the dynamometer to ensure proper joint positioning. The participant's body was stabilized using adjustable straps to minimize extraneous movement and isolate knee joint activity. The seat height, footrest, and shoulder pads were adjusted according to each participant's body dimensions to maintain optimal posture and alignment. Additionally, the trunk was stabilized by securing both the upper and lower body, and participants were instructed to firmly grasp the handles of the chest pad with both hands to prevent compensatory movements. Prior to data collection, participants completed a familiarization session to practice the testing procedures and ensure consistent performance. The primary outcome variables included peak torque for knee flexion and extension, normalized to body weight (Nm/kg)[14].

Exercise intervention

We established plyometric training as the primary exercise intervention in this study. The plyometric training protocol consisted of exercises conducted on nonconsecutive days, three times per week (Monday, Wednesday, and Friday) for 12 weeks. Each training session was structured into three segments: a 10-minute warm-up, a 50-minute main exercise session, and a 10-minute cool-down period. This plyometric exercise program was adapted based on methodologies described in previous study[13]. The training volume initially comprised 20–24 jumps per session during the first 4 weeks, progressively increasing to 72–80 jumps per session by the final 4 weeks of intervention. Additional training drills, including sprinting exercises (e.g., A-skips, butt kicks) and throwing movements, were incorporated into the program. Participants were given sufficient recovery intervals between exercises and sets to maintain performance fitness and safety. If participants displayed signs of fatigue or compromised technique, exercises were immediately discontinued. Subjects were instructed to perform each plyometric movement with maximal explosive effort. The exercise intensity and complexity were progressively increased every 4 weeks by adjusting repetitions or introducing more advanced jump variations. Exercise intensity was objectively monitored using Polar heart-rate monitors, targeting an energy expenditure of 300–350 kcal per training session. Target heart rate zones were set at 50–60% HRmax for weeks 1–4, 60–70% HRmax for weeks 5–8, and 70–80% HRmax for weeks 9–12. Real-time heart rate data were displayed on table PCs connected to the Polar system and continuously monitored by exercise physiologist. If participants exceeded their target heart tare zone, exercise intensity was immediately reduced to maintain safety and compliance to the prescribed intensity. All exercise sessions were conducted under the supervision of a certified exercise physiologist.

Specific contents of the exercise program are shown in Table 1.

Statistical analysis

All results are reported as mean ± standard deviation. Statistical analyses were performed using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA). The assumption of normality was verified using the Shapiro-Wilk test, and all variables met the criteria for normal distribution. A two-way repeated measures analysis of variance (ANOVA) was used to evaluate the main effects of group and time, as well as their interaction. When significant interaction effects were observed, post-hoc analyses were conducted using Bonferroni-adjusted pairwise comparisons for between-group differences, and paired-sample t-tests for within-group differences over time. Statistical significance was set at $\alpha = 0.05$. Non-significant trends are reported up to $p = 0.1$ in the text.

Effect sizes were calculated using Cohen's d to quantify the magnitude of intervention effects. First, the mean difference between post- and pre-intervention values was calculated by subtracting the pre-intervention

Composition	Exercise program	Set	Time (min)	Intensity and volume
Warm up	Jogging and dynamic stretching	1	10	
Plyometric exercise	Stationary standing jumps Forward jumps from standing; bounds and hops (tuck, squat and split jump)	12	50	1–4 weeks 20–24 reps 50–60% HR max
	Box jumps Multiple double legs hop from standing (tuck, squat and split jump)	16		5–8 weeks 42–48 reps 60–70% HR max
	Box jumps Ssingle legs jump from standing start Multiple jumps with run-up (tuck, squat split, and box jump)	18		9–12 weeks 72–80 reps 70–80% HR max
Cool down	Walking and static stretching	1	10	

Table 1. Exercise program.

mean from the post-intervention mean. The pooled standard deviation was then computed as the square root of the average of the squared pre- and post-intervention standard deviations. Finally, Cohen's d was obtained by dividing the mean difference by the pooled standard deviation. Effect sizes were interpreted as small (d < 0.2), medium (d ≥ 0.5), and large (d ≥ 0.8) according to conventional criteria[21].

Results

Change in body composition

Changes in body composition parameters are presented in Table 2. Two-way repeated-measures ANOVA indicated significant group-by-time interaction for height ($p = 0.039$). Significant main effects of time were observed for height ($p < 0.001$), muscle mass ($p = 0.001$), fat mass ($p = 0.001$), percent body fat ($p < 0.001$), and BMI ($p = 0.037$). Paired t-tests revealed that MPE ($p < 0.05$) group exhibited significant improvements in height, muscle mass, fat mass, percent body fat, and BMI after 12 weeks compared to baseline. Specifically, height and muscle mass increased by 0.91% and 4.3%, respectively, while fat mass, percent body fat, and BMI decreased by 6.0%, 5.9%, and 1.9% in the MPE group. These changes corresponded to small to moderate effect sizes(Cohen's d = 0.26 for height, 0.27 for muscle mass, -0.32 for fat mass, -0.45 for percent body fat, and −0.21 for BMI). Additionally, FPE group exhibited significant increase in height($p < 0.05$), muscle mass($p < 0.05$), fat mass($p < 0.001$), percent body fat($p < 0.001$), and BMI($p < 0.05$) after 12 weeks compared to baseline. Height and muscle mass increased by 0.56% and 0.3%, respectively, while fat mass, percent body fat, and BMI decreased by 4.1%, 3.2%, and 2.1% in the FPE group. with small effect sizes (d = 0.14 for height, d = 0.02 for muscle mass, d = -0.17 for fat mass, d = -0.27 for percent body fat, and d = -0.19 for BMI), indicating statistically meaningful and potentially clinically relevant effects.

Change in muscle fitness

Changes in muscle fitness parameters are presented in Table 3. Two-way repeated-measures ANOVA revealed no significant group-by-time interaction effects. However, significant main effects of time were observed for right

Variable	Group	Baseline (0 week)	Post (12 weeks)	Cohen'd	*p*-value	Post-hoc
Age	MCON ($n = 12$)[a]	11.89 ± 0.78				
	MPE ($n = 12$)[b]	11.29 ± 2.90				
	FCON($n = 12$)[c]	11.95 ± 2.64				
	FPE($n = 12$)[d]	13.27 ± 0.79				
Height (cm)	MCON ($n = 12$)[a]	156.31 ± 7.37	157.01 ± 6.91	0.10	G: 0.767 T: <0.001 G×T: 0.039	
	MPE ($n = 12$)[b]	157.78 ± 5.56	159.21 ± 5.57*	0.26		
	FCON($n = 12$)[c]	158.26 ± 6.11	158.54 ± 5.86	0.05		
	FPE($n = 12$)[d]	157.02 ± 6.16	157.90 ± 6.07*	0.14		
Weight (kg)	MCON ($n = 12$)[a]	64.51 ± 11.84	64.62 ± 11.12	0.01	G: 0.934 T: 0.938 G×T: 0.394	
	MPE ($n = 12$)[b]	65.80 ± 7.76	65.76 ± 8.56	0		
	FCON($n = 12$)[c]	63.40 ± 9.02	64.12 ± 10.29	0.07		
	FPE($n = 12$)[d]	63.71 ± 9.85	63.01 ± 9.45	− 0.07		
Muscle mass (kg)	MCON ($n = 12$)[a]	21.13 ± 3.02	21.43 ± 3.13	0.10	G: 0.844 T: 0.001 G×T: 0.095	
	MPE ($n = 12$)[b]	21.78 ± 3.14	22.71 ± 3.72*	0.27		
	FCON($n = 12$)[c]	21.43 ± 3.31	21.57 ± 3.22	0.04		
	FPE($n = 12$)[d]	22.11 ± 2.97	22.17 ± 2.65*	0.02		
Fat mass (kg)	MCON ($n = 12$)[a]	24.98 ± 6.14	24.46 ± 5.85	− 0.09	G: 0.798 T: 0.001 G×T: 0.246	
	MPE ($n = 12$)[b]	25.54 ± 4.54	24.02 ± 5.05*	− 0.32		
	FCON($n = 12$)[c]	24.07 ± 5.19	23.83 ± 5.77	− 0.04		
	FPE($n = 12$)[d]	23.30 ± 5.58	22.35 ± 5.62***	− 0.17		
Body fat (%)	MCON ($n = 12$)[a]	38.53 ± 4.27	38.03 ± 3.82	− 0.12	G: 0.478 T: <0.001 G×T: 0.140	
	MPE ($n = 12$)[b]	38.73 ± 4.41	36.43 ± 5.63*	− 0.45		
	FCON($n = 12$)[c]	36.56 ± 5.72	35.88 ± 6.21	− 0.11		
	FPE($n = 12$)[d]	36.05 ± 4.16	34.91 ± 4.38***	− 0.27		
BMI (kg/m^2)	MCON ($n = 12$)[a]	26.38 ± 4.34	26.19 ± 4.03	− 0.02	G: 0.875 T: 0.037 G×T: 0.140	
	MPE ($n = 12$)[b]	26.42 ± 2.49	25.91 ± 2.48*	− 0.21		
	FCON($n = 12$)[c]	25.31 ± 3.15	25.51 ± 3.66	0.06		
	FPE($n = 12$)[d]	25.76 ± 2.91	25.21 ± 2.85*	− 0.19		

Table 2. Change in body composition. Values are expressed as Mean ± SD. MCON, Male Control, MPE, Male Plyometric Exercise, FCON, Female Control, FPE, Female Plyometric Exercise; Analyzed by Two-way repeated ANOVA Interaction effect: $^{\#}p < 0.05$, $^{\#\#\#}p < 0.001$; paired t-test: $^{*}p < 0.05$; $^{***}p < 0.001$; Effect sizes were calculated using Cohen's d and interpreted as small (0.2), medium (0.5), and large (0.8) to evaluate practical significance.

Variable	Group	Baseline (0 week)	Post (12 weeks)	Cohen'd	*p*-value	Post-hoc
Grip strength (right) (kg)	MCON ($n=12$)[a]	19.14 ± 6.03	20.60 ± 5.53	0.25	G: 0.029 T: <0.001 G×T: 0.838	a < b, d
	MPE ($n=12$)[b]	23.90 ± 3.19	26.27 ± 3.12***	0.75		
	FCON($n=12$)[c]	23.54 ± 5.43	24.20 ± 5.30	0.12		
	FPE($n=12$)[d]	25.02 ± 7.17	26.87 ± 6.79*	0.26		
Grip strength (left) (kg)	MCON ($n=12$)[a]	17.74 ± 6.00	20.19 ± 5.00*	0.44	G: 0.045 T: <0.001 G×T: 0.992	a < b, d
	MPE ($n=12$)[b]	23.25 ± 4.86	25.84 ± 4.65*	0.54		
	FCON($n=12$)[c]	22.38 ± 6.92	23.33 ± 8.43*	0.12		
	FPE($n=12$)[d]	22.79 ± 6.83	25.64 ± 6.34*	0.43		
Sit-up (rep)	MCON ($n=12$)[a]	11.36 ± 12.09	14.00 ± 9.31	0.24	G: 0.077 T: 0.066 G×T: 0.195	
	MPE ($n=12$)[b]	13.55 ± 8.14	20.73 ± 7.48	0.92		
	FCON($n=12$)[c]	16.27 ± 9.81	17.64 ± 22.20	0.08		
	FPE($n=12$)[d]	21.00 ± 12.64	21.33 ± 12.50	0.03		
Knee extension peak torque (R) [(Newton-meter/body weight(kg)]	MCON ($n=12$)[a]	147.00 ± 28.18	153.25 ± 29.52	0.22	G: 0.035 T: <0.001 G×T: 0.264	a, b < d,
	MPE ($n=12$)[b]	149.75 ± 18.30	162.67 ± 34.62	0.47		
	FCON($n=12$)[c]	164.42 ± 23.91	169.83 ± 25.29	0.22		
	FPE($n=12$)[d]	176.00 ± 47.24	196.42 ± 43.70***	0.45		
Knee extension peak torque (L) [(Newton-meter/body weight(kg)]	MCON ($n=12$)[a]	140.33 ± 31.13	146.83 ± 29.40	0.21	G: 0.006 T: <0.001 G×T: 0.626	a < d
	MPE ($n=12$)[b]	144.00 ± 30.08	161.67 ± 32.48*	0.56		
	FCON($n=12$)[c]	150.67 ± 17.88	159.58 ± 26.48	0.39		
	FPE($n=12$)[d]	183.58 ± 54.61	198.25 ± 45.89	0.29		
Knee flexion peak torque (R) [(Newton-meter/body weight(kg)]	MCON ($n=12$)[a]	72.42 ± 17.10	75.17 ± 15.82	0.17	G: 0.009 T: <0.001 G×T: 0.095	a < d
	MPE ($n=12$)[b]	69.75 ± 14.45	87.25 ± 20.56*	0.98		
	FCON($n=12$)[c]	78.42 ± 17.67	87.42 ± 18.00*	0.50		
	FPE($n=12$)[d]	93.58 ± 24.47	103.17 ± 22.03*	0.41		
Knee flexion peak torque (L) [(Newton-meter/body weight(kg)]	MCON ($n=12$)[a]	74.00 ± 19.17	79.25 ± 14.04	0.31	G: 0.031 T: <0.001 G×T: 0.641	b < d
	MPE ($n=12$)[b]	68.17 ± 15.94	80.00 ± 18.56*	0.68		
	FCON($n=12$)[c]	78.33 ± 20.54	84.33 ± 16.17	0.32		
	FPE($n=12$)[d]	90.33 ± 28.67	100.75 ± 22.53	0.40		
Knee extension muscle power (R) [(Watt/body weight(kg)]	MCON ($n=12$)[a]	163.00 ± 27.11	177.17 ± 38.03	0.43	G: 0.439 T: 0.163 G×T: 0.866	
	MPE ($n=12$)[b]	172.58 ± 22.34	184.60 ± 39.66	0.37		
	FCON($n=12$)[c]	170.33 ± 32.58	170.00 ± 27.21	− 0.01		
	FPE($n=12$)[d]	192.02 ± 54.91	190.73 ± 57.09	− 0.02		
Knee extension muscle power (L) [(Watt/body weight(kg)]	MCON ($n=12$)[a]	160.08 ± 29.58	166.08 ± 31.00	0.20	G: 0.088 T: 0.221 G×T: 0.797	
	MPE ($n=12$)[b]	169.08 ± 27.28	174.99 ± 31.79	0.20		
	FCON($n=12$)[c]	161.92 ± 39.98	160.25 ± 32.99	− 0.05		
	FPE($n=12$)[d]	188.79 ± 45.66	197.21 ± 42.78	0.19		
Knee flexion muscle power (R) [(Watt/body weight(kg)]	MCON ($n=12$)[a]	83.83 ± 20.24	90.08 ± 18.87	0.32	G: 0.301 T: 0.002 G×T: 0.478	
	MPE ($n=12$)[b]	90.18 ± 11.86	105.12 ± 26.13*	0.74		
	FCON($n=12$)[c]	83.42 ± 30.88	88.25 ± 20.73	0.18		
	FPE($n=12$)[d]	97.81 ± 31.79	104.48 ± 33.20	0.21		
Knee flexion muscle power (L) [(Watt/body weight(kg)]	MCON ($n=12$)[a]	84.92 ± 14.40	89.00 ± 18.52	0.25	G: 0.189 T: <0.001 G×T: 0.062	
	MPE ($n=12$)[b]	85.59 ± 12.71	103.93 ± 18.14*	1.17		
	FCON($n=12$)[c]	83.42 ± 16.24	87.50 ± 14.82	0.26		
	FPE($n=12$)[d]	95.33 ± 28.59	104.83 ± 28.14*	0.33		

Table 3. Change in muscle fitness. Values are expressed as Mean ± SD. MCON, Male Control, MPE, Male Plyometric Exercise, FCON, Female Control, FPE, Female Plyometric Exercise; Analyzed by Two-way repeated ANOVA Interaction effect: $^{\#}p<0.05$, $^{\#\#\#}p<0.001$; paired t-test: $^{*}p<0.05$; $^{***}p<0.001$ Effect sizes were calculated using Cohen's d and interpreted as small (0.2), medium (0.5), and large (0.8) to evaluate practical significance.

and left grip strength (both $p<0.001$), right and left knee extension and flexion peak torques (all $p<0.001$), right knee flexion muscle power ($p=0.002$), and left knee flexion muscle power ($p<0.001$). Paired t-tests indicated that the MPE group showed significant increase in right grip strength($p<0.001$), left grip strength($p<0.05$), left knee extension peak torque, right and left knee flexion peak torque, and right and left knee flexion muscle power after 12 weeks compared to baseline ($p<0.05$). Specifically, right and left grip strength increased by 9.92% and 11.14%, corresponding to moderate to large effect sizes (Cohen's d = 0.75 and 0.54). Left knee extension torque by 12.27% with a moderate effect size (d = 0.56). Right and left knee flexion torque by 25.09% and 17.35% representing

large and moderate effect sizes (d = 0.98 and 0.68), and right and left knee flexion muscle power by 16.57% and 21.43% with moderate to large effect sizes (d = 0.74 and 1.17), respectively, in the MPE group. Additionally, the FPE group showed significant increase in right grip strength($p < 0.05$), left grip strength($p < 0.05$), right knee extension peak torque ($p < 0.001$), right knee flexion peak torque, and left knee flexion muscle power ($p < 0.05$) after 12 weeks compared to baseline. Specifically, right and left grip strength increased by 7.39% and 12.51% corresponding too small to moderate effect sizes (d = 0.26 and 0.43), right knee extension torque by 11.60% with a moderate effect size (d = 0.56), right knee flexion torque by 10.25%, and left knee flexion muscle power by 9.97% in the FPE group with a small effect size (d = 0.33). Finally, the FCON group exhibited significant increase in left grip strength($p < 0.05$), right knee flexion peak torque after 12 weeks compared to baseline ($p < 0.05$). Specifically, left grip strength and right knee flexion torque increased by 4.24% and 11.48% corresponding to small effect sizes (d = 0.12 and 0.50), respectively, in the FCON group.

Change in in growth hormone factors

Changes in growth hormone factors parameters are presented in Fig. 2A. Two-way repeated-measures ANOVA revealed no significant group-by-time interaction effects. Significant main effects of time were observed for GH ($p = 0.007$), and IGF-1 ($p = 0.023$). Paired t-tests revealed that MPE and FPE groups ($p < 0.05$) exhibited significant improvements in GH after 12 weeks compared to baseline. Specifically, GH levels increased by 28.3% in the MPE group corresponding to a large effect size (d = 0.98) and 19.5% in the FPE group also indicating a large effect size (d = 1.04). Additionally, the MPE group ($p < 0.05$), FPE group ($p < 0.001$) exhibited significant improvements in IGF-1 after 12 weeks compared to baseline. IGF-1 levels increased by 21.4% in the MPE group and 18.9% in the FPE group, corresponding to moderate effect sizes (d = 0.51 and 0.54, respectively).

Change in appetite hormone factors

Changes in appetite hormone factors parameters are presented in Fig. 2B. Two-way repeated-measures ANOVA indicated significant group-by-time interaction effects for leptin ($p < 0.001$). Significant main effects of time were observed for insulin ($p < 0.001$), and leptin ($p < 0.001$). Paired t-tests revealed that MPE and FPE groups ($p < 0.05$) exhibited significant improvements in insulin after 12 weeks compared to baseline. Specifically, insulin levels decreased by 36.7% in the MPE group corresponding to a large effect size (d = -0.86), and 42.6% in the FPE group, with a moderate to large effect size (d = -0.73). Additionally, the MPE and FPE groups ($p < 0.001$) exhibited significant improvements in leptin after 12 weeks compared baseline with very large effect sizes (d = -1.86 and − 1.93), but the FCON group exhibited significant deterioration in leptin after 12 weeks. Leptin levels decreased by 24.6% in the MPE group and 25.7% in the FPE group, while it increased by 12.4%in the FCON group with a large effect size (d = 1.66).

Change in myokine factors

Changes in myokine factors parameters are presented in Fig. 2C. Two-way repeated-measures ANOVA indicated significant group-by-time interaction effects for myostatin ($p = 0.036$). Significant main effects of time were observed for myostatin ($p = 0.004$), and follistatin ($p = 0.031$). Paired t-tests revealed that MPE and FPE groups ($p < 0.001$) exhibited significant improvements in myostatin after 12 weeks compared to baseline. Specifically, myostatin levels decreased by 15.9% in the MPE group corresponding to a moderate to large effect size (Cohen's d = -0.73), and 9.7% in the FPE group, indicating a moderate effect size (d = -0.48). Additionally, the MPE group ($p < 0.05$) exhibited significant improvements in follistatin after 12 weeks compared to baseline. Follistatin levels increased by 15.1% in the MPE group with a 15.1% increase, reflecting a large effect size (d = 1.10).

Change in adipokine factors

Changes in adipokine factors parameters are presented in Fig. 2D. Two-way repeated-measures ANOVA indicated significant group-by-time interaction effects for adiponectin ($p = 0.011$). Significant main effects of time were observed for adiponectin ($p = 0.002$). Paired t-tests revealed that MPE ($p < 0.05$), and FPE ($p < 0.001$) groups exhibited significant improvements in adiponectin after 12 weeks compared to baseline. Specifically, adiponectin levels increased by 13.7% in the MPE group (d = 0.68) and 27.6% in the FPE group (d = 0.68), indicating moderate to very large effect sizes, respectively.

Discussion

Childhood and adolescents with obesity disrupt in endocrine signaling pathways such as the GH-IGF-1 axis and insulin signaling, leading to impaired growth, decreased muscle synthesis, excessive fat accumulation, and increased risk of early-onset metabolic disorders[22]. Chronic elevation of leptin further induces leptin resistance, disturbing metabolic and growth-related dysfunctions[6]. Consequently, leptin resistance exacerbates disturbances in endocrine signaling, thereby sustaining excess adiposity and impairing both metabolic function and growth-related health. To prevent obesity induced leptin resistance and associated growth-related impairments in adolescents, plyometric exercise may serve as an effective and practical intervention strategy. Therefore, this study investigated the effects of a 12-week plyometric training program on body composition, growth-related hormones, muscle fitness, and metabolic markers in adolescents with obesity and leptin resistance. The main findings were that plyometric training significantly increased GH and IGF-1 levels, improved height and muscle function, reduced body fat, and favorably modulated hormonal responses by decreasing leptin and insulin while increasing adiponectin.

Regular exercise increases energy expenditure, reduces body fat, and promotes muscle protein synthesis, thereby enhancing muscle mass and fitness[14]. Plyometric exercise, which leverages the stretch reflex mechanism, is recognized as optimal for adolescents, as it effectively combines improvements in muscle strength, bone health, growth stimulation, and fat reduction[13]. In this study, significant improvements in height, body fat percentage,

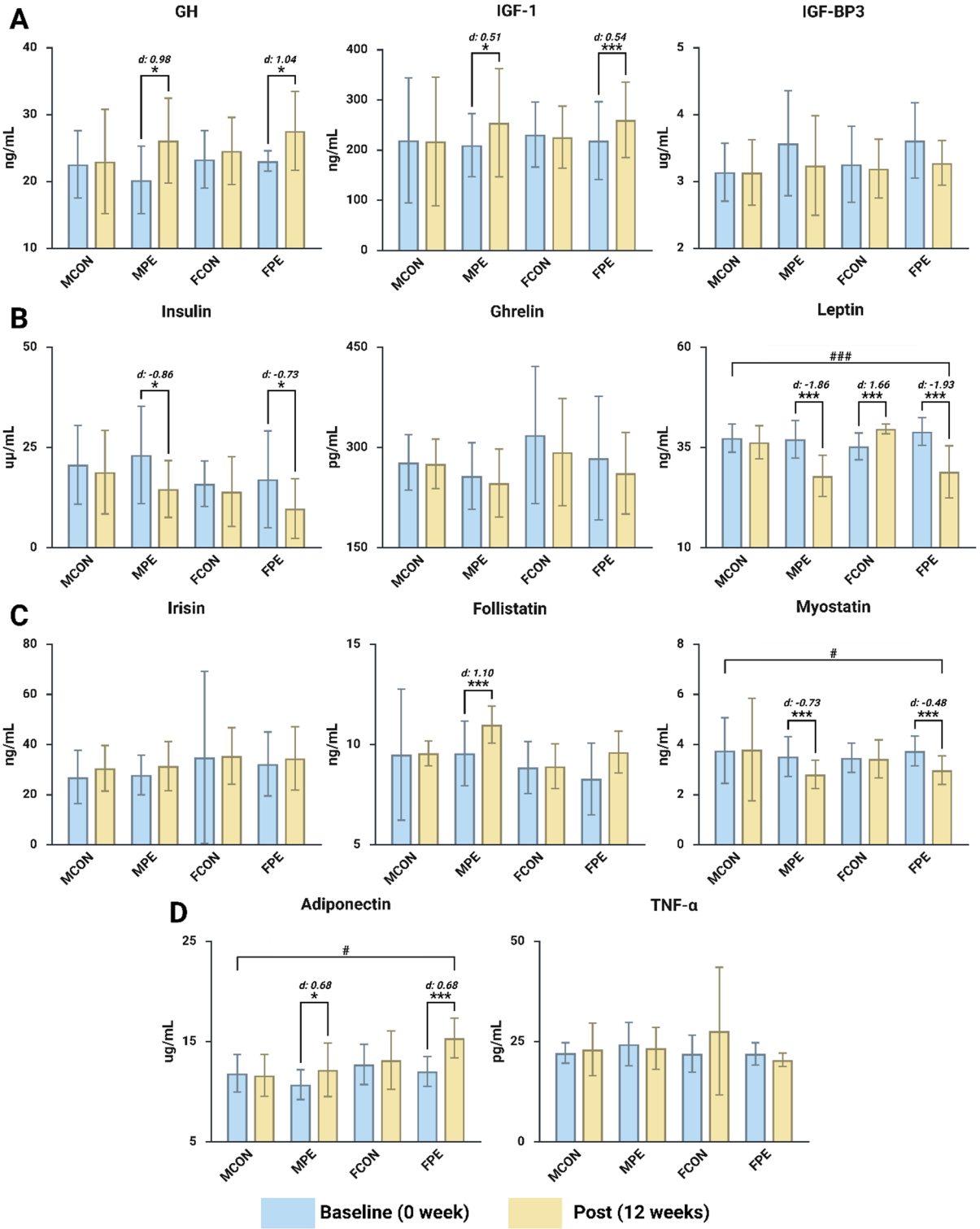

Fig. 2. (**A**) Change in growth hormones. (**B**) Change in appetite hormones. (**C**) Change in myokine factors. (**D**) Change in adipokine factors. Values are expressed as Mean ± SD. MCON, Male Control, MPE, Male Plyometric Exercise, FCON, Female Control, FPE, Female Plyometric Exercise; Analyzed by Two-way repeated ANOVA Interaction effect: $^{\#}p < 0.05$, $^{\#\#\#}p < 0.001$; paired t-test: $^{*}p < 0.05$; $^{***}p < 0.001$; Effect sizes were calculated using Cohen's d and interpreted as small (d < 0.2), medium (d ≥ 0.5), and large (d ≥ 0.8) to evaluate practical significance.

BMI, muscle mass, and muscle fitness were observed post-intervention, irrespective of gender (Tables 2 and 3). These findings effectively address the limitations associated with isolated aerobic or resistance exercise treatments[23,24], demonstrating meaningful physiological and clinical benefits of plyometric-based combined exercise on body composition in adolescents with obesity. Plyometric exercise utilizes repetitive stretch-shortening cycles, effectively increasing energy expenditure and promoting muscle protein synthesis, likely explaining the observed reductions in body fat and increases in muscle mass. These body composition changes were accompanied by small to moderate effect sizes (Cohen's d = 0.26–0.45), indicating physiologically relevant improvements in height fat mass, and BIM, even within a relatively short interventions period. Improvements in body composition also play a crucial role in restoring normal GH-IGF-1-insulin signaling, vital for linear growth in adolescents. Interestingly, this study clearly demonstrates that regular plyometric exercise can activate the GH-IGF-1-insulin axis and positively influence height growth even in adolescents with persistent clinical obesity (≥ 30% body fat). GH (MPE 0.98, PME 1.04), IGF-1 (MPE 0.51, PME 0.54) levels improved with large to moderate effect sizes, suggesting robust activation of the somatotropic axis. Similarly, insulin (MPE − 0.84, PME − 0.73), leptin (MPE − 1.86, PME − 1.93) levels decreased with large to very large effects, indicating strong endocrine adaptations associated with enhanced leptin sensitivity and improved metabolic regulation. These results are consistent with previous findings in obese children treated with growth hormone for three months, in which plasma leptin concentrations showed parallel improvements[25]. The increase in GH appears to be involved not only in linear growth but also in appetite regulations, and our findings suggest a strong association between these mechanisms.

Generally, leptin resistance associated with obesity suppresses GH secretion and GH receptor (GHR) expression, reducing IGF-1 production and impairing longitudinal skeletal growth by limiting growth plate chondrocyte proliferation and differentiation[26]. Thus, the large reduction in leptin (d = -1.86 to -1.93) likely reflects improved receptor sensitivity, which may have facilitated the normalization of GH and IGF-1 secretion and contributed to the restoration of the GH-IGF-1 axis in growing adolescents[27]. Leptin plays a permissive role in linear growth by modulating hepatic GHR sensitivity and directly stimulating IGF-1 synthesis[28]. When leptin sensitivity improved, it may further potentiate GH-IGF-1 axis activation independent of GH concentrations[29]. Collectively, these findings emphasize that plyometric exercise elicits large endocrine adaptations particularly within the GH-IGF-1-insulin axis and leptin signaling that jointly support linear growth and metabolic restoration in adolescent with obesity. These improvements are likely attributable to repeated stretch-shortening stimuli inherent in plyometric exercise, directly enhancing growth plate chondrocyte proliferation and linear growth[30]. GH promotes growth plate chondrocyte proliferation and IGF-1 synthesis, while IGF-1 facilitates chondrocyte differentiation and maturation, thus mediating skeletal growth[27,30]. Enhanced insulin signaling following exercise also likely synergistically improves IGF-1 receptor signaling and optimizes energy metabolism within growth plate chondrocytes, further promoting skeletal growth[31]. Thus, plyometric exercise emerges as an effective clinical strategy to stimulate growth through GH-IGF-1-insulin pathway activation, even when excess adiposity persists in individuals with obesity.

Plyometric exercise has been reported to promote not only linear growth but also muscle growth through molecular regulation of myokines secreted from skeletal muscle[32]. Specifically, exercise-induced decreases in myostatin and increases in follistatin and IGF-1 play critical roles in enhancing muscle mass and fitness by stimulating muscle protein synthesis (MPS) and inhibiting muscle protein breakdown (MPB). Muscle mass is primarily determined by a delicate balance between MPS and MPB, tightly regulated by various myokines[33]. Among exercise-responsive myokines, myostatin is a representative negative regulator of muscle growth, promoting MPB and suppressing MPS by activating Smad2/3 signaling via ActRIIB receptors and inhibiting MyoD expression, thus contributing to muscle atrophy[34]. Conversely, follistatin serves as a positive regulator by neutralizing myostatin activity and activating the Akt1/mTORC1 signaling pathway, thereby enhancing MPS and muscle fitness[35] .. IGF-1 also directly stimulates the Akt1/mTORC1 pathway, playing a central role in muscle growth by further enhancing MPS[36]. Consistent with these molecular mechanisms, this study demonstrated a significant decrease in myostatin levels and significant increases in follistatin and IGF-1 after the plyometric interventions. These adaptations were accompanied by moderate to large effect sizes (Cohen's d = MPE − 0.73, FPE − 0.48 for myostatin, MPE 1.10 for follistatin, and MPE 0.51, FPE 0.54 for IGF-1), indicating robust anabolic signaling activation. The marked follistatin increase and myostatin suppression suggest enhanced muscle protein synthesis efficiency, while elevated IGF-1 further amplified MPS through Akt/mTORC1 signaling, collectively promoting muscle hypertrophy and functional gain. These myokine adaptations corresponded with small to large improvements in muscle fitness indicators, grip strength, knee peak torque, and knee muscle power (MPE 0.54 to 1.17, FPE 0.26 to 0.45). Interestingly, these functional gains were more pronounced in males, which may be attributed to the greater anabolic myokine response observed in this group. Specifically, males showed a moderated increase in muscle mass (d = 0.27) compared with minimal change in females (d = 0.02), a larger reduction in myostatin (d= -0.73 vs. -0.48), and a marked rise in follistatin (d = 1.10, not significant in females). These differences suggest that male participants experienced stronger activation of anabolic signaling pathways and greater suppression of catabolic signaling, resulting in superior improvements in muscle strength and power. In contrast, the relatively attenuated myokine response in females may reflect hormonal modulation, such as estrogen-mediated feedback on muscle protein turnover that partially limits the magnitude of hypertrophic adaptation. The integrated response across the myostatin-follistatin-IGF-1 axis strongly supports a synergistic mechanism in which suppression of catabolic signaling and activation of anabolic pathways jointly enhance muscle function. Our findings provide substantial evidence supporting the myokine-mediated regulatory mechanism centered on suppression of myostatin and activation of follistatin and IGF-1 as the key pathway simultaneously promoting muscle mass and fitness improvements. This aligns with previous studies demonstrating that adolescent plyometric exercise induces favorable myokine shifts, reinforcing the

potential of plyometric training as a clinically meaningful non-pharmacological intervention for improving muscle health and functional performance in adolescents with obesity[37].

Leptin and adiponectin, representative adipokines secreted by adipose tissue, critically regulate energy homeostasis, metabolism, and inflammation. Specifically, leptin primarily regulates appetite suppression and energy expenditure, whereas adiponectin exhibits anti-inflammatory effects, improves insulin sensitivity, and enhances skeletal muscle metabolic function[38]. In this study, leptin levels significantly decreased (MPE − 1.86, PME − 1.93) and adiponectin levels significantly decreased (both 0.68), indicating large to moderate effect sizes and demonstrating complex physiological adaptations closely linked with improved GH-IGF-1 axis and myokine activity. Hyperleptinemia typically inhibits GH secretion and IGF-1 synthesis via SOCS3 and PTP1B-mediated leptin signaling suppression[39]. Thus, the marked reduction in leptin observed reflects improved leptin sensitivity resulting from body fat reduction, enhancing GH-IGF-1 axis activity and restoring normal endocrine feedback. This improvement likely contributed to increased GH receptor responsiveness and facilitated IGF-1 synthesis, consistent with the previously described somatotropic adaptations. Moreover, the increase in adiponectin (both 0.68) may have further promoted skeletal muscle metabolic remodeling through AMPK and PPARα activation, optimizing mitochondrial function and energy utilization. Adiponectin also stimulates IGF-1 synthesis and suppresses myostatin expression, thereby enhancing Akt/mTORC1 signaling and synergistically supporting muscle hypertrophy and metabolic health[40]. The concurrent increase in adiponectin, IGF-1, and follistatin, along with a reduction in myostatin and leptin, provides compelling evidence of integrative endocrine-metabolic cross-talk. These adaptations extend beyond simple changes in body composition, encompassing systemic improvements in growth promotion, muscle function, and metabolic regulation.

However, unlike leptin and adiponectin, TNF-α showed no significant changes post-intervention. This may reflect the fact that participants remained within the clinical classification of obesity (≥ 30% body fat), suggesting that TNF-α expression is more intricately regulated by complex inflammatory pathways (e.g., TLR4–MyD88–NF-κB, JNK, MAPK) rather than moderate fat reduction alone[41]. TNF-α promotes insulin resistance by increasing IRS-1 serine phosphorylation and inhibiting adiponectin synthesis, and thus, significant improvement in TNF-α levels may require more substantial visceral fat loss or longer-term, multifaceted interventions involving suppression of macrophage infiltration and modulation of gut microbiota[42]. Our results are consistent with a previous pediatric study showing no significant changes in TNF-α following 12 weeks of moderate to high intensity exercise in childhood and adolescents with obesity[43]. Therefore, our findings suggest TNF-α modulation may occur at advanced stages of metabolic improvement. These results contrast significantly with previous animal studies and human research. Although animal studies have reported beneficial effects of regular exercise on alleviating leptin resistance and promoting GH-IGF-1 and adiponectin activity[44], these rodent models cannot entirely reflect the physiological characteristics of human adolescents. Additionally, previous human clinical studies often analyzed limited markers such as leptin or adiponectin individually[19], lacking a comprehensive integrative analysis of multiple metabolic pathways including, GH, IGF-1, TNF-α, and myokines[45].

Despite these promising findings, this study has several limitations. First, although participants were stratified by chronological age, pubertal development was not directly assessed using Tanner staging or hormone profiling, which limits the precision of growth-related interpretations. Second, participants were recruited from a specific age and clinical phenotype (obesity with leptin resistance), which may restrict the generalizability of findings to broader pediatric populations. Lastly, outcome measures were assessed only at pre- and post-intervention time points, making it difficult to track the temporal trajectory of changes. Future studies should consider combining plyometric and aerobic training, incorporating pubertal hormone assessments, and conducting longer-term follow-up to evaluate the durability and scalability of these findings across diverse settings.

Conclusion

This study demonstrates that plyometric exercise is an effective intervention for improving both growth and muscle function in adolescents with obesity and leptin resistance. The 12-week program enhanced height and reduced body fat by activating the GH-IGF-1 axis and improving leptin sensitivity. In addition, decreased myostatin and increased follistatin and IGF-1 promoted muscle protein synthesis and improved muscle mass, strength, and power. These integrative adaptations, encompassing myokines, adipokines, and growth and appetite-related hormones, underscore the systemic benefits of plyometric training. Plyometric exercise can therefore serve as a safe, practical, and non-pharmacological approach to enhance growth and metabolic health in adolescents with obesity. However, as this study was limited by its 12-week duration and lack of dietary control, future long-term and multi-factorial studies are warranted to confirm these findings and elucidate the underlying mechanisms more precisely.

Data availability

The data presented in this study are available on request from the corresponding author.

Received: 3 June 2025; Accepted: 9 January 2026
Published online: 14 January 2026

References

1. Kerr, J. A. et al. Global, regional, and national prevalence of child and adolescent overweight and obesity, 1990–2021, with forecasts to 2050: a forecasting study for the global burden of disease study 2021. *Lancet* **405**, 785–812 (2025).
2. Chung, K. H., Chiou, H. Y. & Chen, Y. H. Psychological and physiological correlates of childhood obesity in Taiwan. *Sci. Rep.* **5**, 17439 (2015).
3. Pulgaron, E. R. & Delamater, A. M. Obesity and type 2 diabetes in children: epidemiology and treatment. *Curr. Diab Rep.* **14**, 1–12 (2014).

4. Witchel, S. F., Burghard, A. C., Tao, R. H. & Oberfield, S. E. The diagnosis and treatment of PCOS in adolescents: an update. *Curr. Opin. Pediatr.* **31**, 562–569 (2019).
5. Sáinz, N., Barrenetxe, J., Moreno-Aliaga, M. J. & Martínez, J. A. Leptin resistance and diet-induced obesity: central and peripheral actions of leptin. *Metabolism* **64**, 35–46 (2015).
6. Pan, H., Guo, J. & Su, Z. Advances in understanding the interrelations between leptin resistance and obesity. *Physiol. Behav.* **130**, 157–169 (2014).
7. Enriori, P. J., Sinnayah, P., Simonds, S. E., Rudaz, C. G. & Cowley, M. A. Leptin action in the dorsomedial hypothalamus increases sympathetic tone to brown adipose tissue in spite of systemic leptin resistance. *J. Neurosci.* **31**, 12189–12197 (2011).
8. Gonzalez-Gil, A. M. et al. Myokine–adipokine cross-talk: potential mechanisms for the association between plasma Irisin and adipokines and cardiometabolic risk factors in Mexican children with obesity and the metabolic syndrome. *Diabetol. Metab. Syndr.* **11**, 1–16 (2019).
9. Scarpace, P. J., Matheny, M., Tümer, N., Cheng, K. Y. & Zhang, Y. Leptin resistance exacerbates diet-induced obesity and is associated with diminished maximal leptin signalling capacity in rats. *Diabetologia* **48**, 1075–1083 (2005).
10. Frithioff-Bøjsøe, C. Leptin, adiponectin, and their ratio as markers of insulin resistance and cardiometabolic risk in childhood obesity. *Pediatr. Diabetes*. **21**, 194–202 (2020).
11. Jiménez-Pavón, D. et al. Physical activity, fitness, and serum leptin concentrations in adolescents. *J. Pediatr.* **160**, 598–603 (2012).
12. Peng, J., Yin, L. & Wang, X. Central and peripheral leptin resistance in obesity and improvements of exercise. *Horm. Behav.* **133**, 105006 (2021).
13. Nobre, G. G. et al. Twelve weeks of plyometric training improves motor performance of 7- to 9-year-old boys who were overweight/obese: a randomized controlled intervention. *J. Strength. Cond Res.* **31**, 2091–2099 (2017).
14. Jeong, D. et al. Effects of resistance exercise and essential amino acid intake on muscle quality, myokine, and inflammation factors in young adult males. *Nutrients* **16**, 1688 (2024).
15. Bharath, L. P. et al. Combined resistance and aerobic exercise training reduces insulin resistance and central adiposity in adolescent girls who are obese: randomized clinical trial. *Eur. J. Appl. Physiol.* **118**, 1653–1660 (2018).
16. Kang, S., Kim, K. B. & Shin, K. O. Exercise training improves leptin sensitivity in peripheral tissue of obese rats. *Biochem. Biophys. Res. Commun.* **435**, 454–459 (2013).
17. García-Hermoso, A., Ramírez-Vélez, R., Díez, J., González, A. & Izquierdo, M. Exercise training-induced changes in exerkine concentrations may be relevant to the metabolic control of type 2 diabetes mellitus patients: a systematic review and meta-analysis of randomized controlled trials. *J. Sport Health Sci.* **12**, 147–157 (2023).
18. Carhuatanta, K. A. K. et al. Voluntary exercise improves high-fat diet-induced leptin resistance independent of adiposity. *Endocrinology* **152**, 2655–2664 (2011).
19. Vasconcellos, F. et al. Health markers in obese adolescents improved by a 12-week recreational soccer program: a randomised controlled trial. *J. Sports Sci.* **34**, 564–575 (2016).
20. Kasyanova, Y. V., Vasyukova, O. V., Okorokov, P. L., Zuraeva, Z. T. & Bezlepkina, O. B. Myokines in obese adolescents with aerobic exercise. *Probl. Endokrinol (Mosk).* **68**, 102–110 (2022).
21. Cohen, J. *Statistical Power Analysis for the Behavioral Sciences* 2nd edn (Routledge, 2013).
22. Vijayakumar, A., Novosyadlyy, R., Wu, Y., Yakar, S. & LeRoith, D. Biological effects of growth hormone on carbohydrate and lipid metabolism. *Growth Horm. IGF Res.* **20**, 1–7 (2010).
23. Williams, C. F., Bustamante, E. E., Waller, J. L. & Davis, C. L. Exercise effects on quality of life, mood, and self-worth in overweight children: the SMART randomized controlled trial. *Transl Behav. Med.* **9**, 451–459 (2019).
24. Alberga, A. S. et al. Effects of aerobic and resistance training on abdominal fat, apolipoproteins and high-sensitivity C-reactive protein in adolescents with obesity: the HEARTY randomized clinical trial. *Int. J. Obes.* **39**, 1494–1500 (2015).
25. Zadik, Z. et al. Interrelationship between insulin, leptin and growth hormone in growth hormone-treated children. *Int. J. Obes.* **25**, 538–542 (2001).
26. Löhr, H. et al. Diet-induced growth is regulated via acquired leptin resistance and engages a pomc-somatostatin-growth hormone circuit. *Cell. Rep.* **23**, 1728–1741 (2018).
27. Eliakim, A. et al. Reduced exercise-associated response of the GH-IGF-I axis and catecholamines in obese children and adolescents. *J. Appl. Physiol.* **100**, 1630–1637 (2006).
28. Chan, J. L. et al. Leptin does not mediate short-term fasting-induced changes in growth hormone pulsatility but increases IGF-I in leptin deficiency States. *J. Clin. Endocrinol. Metab.* **93**, 2819–2827 (2008).
29. Brown, R. J. et al. Metreleptin-mediated improvements in insulin sensitivity are independent of food intake in humans with lipodystrophy. *J. Clin. Invest.* **128**, 3504–3516 (2018).
30. Dekker, J. et al. Wnt signaling–related osteokines and transforming growth factors before and after a single bout of plyometric exercise in child and adolescent females. *Pediatr. Exerc. Sci.* **29**, 504–512 (2017).
31. Bang, P. Pediatric implications of normal insulin-GH-IGF axis physiology. *Endotext*. https://www.ncbi.nlm.nih.gov/books/NBK279164/ (2024).
32. Battafarano, G., Rossi, M., Marampon, F., Minisola, S. & Del Fattore, A. Bone control of muscle function. *Int. J. Mol. Sci.* **21**, 1178 (2020).
33. Børsheim, E., Tipton, K. D., Wolf, S. E. & Wolfe, R. R. Essential amino acids and muscle protein recovery from resistance exercise. *Am. J. Physiol. Endocrinol. Metab.* **283**, E648–E657 (2002).
34. Langley, B. et al. Myostatin inhibits myoblast differentiation by down-regulating myod expression. *J. Biol. Chem.* **277**, 49831–49840 (2002).
35. Winbanks, C. E. et al. Follistatin-mediated skeletal muscle hypertrophy is regulated by Smad3 and mTOR independently of myostatin. *J. Cell. Biol.* **197**, 997–1008 (2012).
36. Cornish, S. M., Bugera, E. M., Duhamel, T. A., Peeler, J. D. & Anderson, J. E. A focused review of myokines as a potential contributor to muscle hypertrophy from resistance-based exercise. *Eur. J. Appl. Physiol.* **120**, 941–959 (2020).
37. Vissing, K. et al. Muscle adaptations to plyometric vs. resistance training in untrained young men. *J. Strength. Cond Res.* **22**, 1799–1810 (2008).
38. Skurk, T., Alberti-Huber, C., Herder, C. & Hauner, H. Relationship between adipocyte size and adipokine expression and secretion. *J. Clin. Endocrinol. Metab.* **92**, 1023–1033 (2007).
39. Ozata, M., Dieguez, C. & Casanueva, F. F. The Inhibition of growth hormone secretion presented in obesity is not mediated by the high leptin levels: a study in human leptin deficiency patients. *J. Clin. Endocrinol. Metab.* **88**, 312–316 (2003).
40. Lamming, D. W. Diminished mTOR signaling: a common mode of action for endocrine longevity factors. *Springerplus* **3**, 1–11 (2014).
41. Preedy, M. K., White, M. R. & Tergaonkar, V. Cellular heterogeneity in TNF/TNFR1 signalling: live cell imaging of cell fate decisions in single cells. *Cell. Death Dis.* **15**, 202 (2024).
42. Sethi, J. K. & Hotamisligil, G. S. Metabolic messengers: tumour necrosis factor. *Nat. Metab.* **3**, 1302–1312 (2021).
43. Lopes, W. A. et al. Effects of 12 weeks of combined training without caloric restriction on inflammatory markers in overweight girls. *J. Sports Sci.* **34**, 1902–1912 (2016).
44. Hamrick, M. W. et al. Leptin mediates IGF-1 in aged mice. *Exp. Gerontol.* **70**, 92–98 (2015).
45. Sugiharto, Merawati, D., Pranoto, A. & Susanto, H. Physiological response of endurance exercise as a growth hormone mediator in adolescent women's. *J. Basic. Clin. Physiol. Pharmacol.* **34**, 61–67 (2023).

Acknowledgements
We thank the study participants and their parents, the Exercise Physiology Lab at Kangwon National University, Department of Pediatrics, Kangwon National University College of Medicine, Center of Gangwon Sport Science, and Department of Physical Therapy & Kinesiology at the University of Massachusetts Lowell.

Author contributions
D.J. was responsible for developing the methodology, conducting formal statistical analyses, managing and curating the dataset, drafting the original manuscript, and preparing data visualizations. R.J.V. contributed to the preparation of data visualizations and critically revised the manuscript during the review and editing process. K.P. conducted formal analyses and participated in data collection and investigation activities. H.J. was involved in data investigation and provided key research resources for the study. J.H. and S.K. contributed to the conceptual design of the study, supervised the research process, reviewed and edited the manuscript, managed the project, and secured funding for the study. All authors have read and approved the final version of the manuscript and agree to its submission.

Funding
This study was funded by National Research Foundation of Korea (NRF-2021R1F1A1046801) and by a research grant from the Institute of Medical Sciences at Kangwon National University (2025).

Declarations

Ethics approval
All methods described above were performed in accordance with relevant guidelines and regulations. This study was approved by the Institutional Review Board(IRB) of Kangwon National University for human subjects (KWNUIRB-2023-05-007).

Informed consent
Informed consent was obtained from all participants involved in the study.

Competing interests
The authors declare no competing interests.

Additional information
Correspondence and requests for materials should be addressed to J.H. or S.K.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

© The Author(s) 2026