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Impact of High-Intensity Interval Training on Bone Metabolism and the Metabolic and Hormonal Profiles of Postmenopausal Women

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ABSTRACT

Introduction: Although many forms of exercise are known to have positive effects on bone metabolism in postmenopausal women, the effect of high-intensity interval training (HIIT) has not been investigated in this setting. This study aimed to evaluate the impact of the 6-week HIIT program on body composition, biochemical parameters, and bone turnover markers in overweight and obese postmenopausal women.

Methods: A total of 32 postmenopausal women were randomly assigned to exercise (n=15) or control (n=17) groups. The blood samples and body composition were analyzed. The exercise group participated in a 6-week stationary bike HIIT exercise [(3 days/week; 30 sec work-90 sec resting intervals with 90-95% of the heart rate reserve-12 to 16 min/day)]. The control group was not involved in any exercise program.

Results: In the exercise group, significant reductions were noted in waist and hip circumference, low-density lipoprotein, total cholesterol, triglycerides, phosphorus, calcium, albumin, bone-specific alkaline phosphatase, type 1 collagen C-terminal telopeptide, and osteocalcin levels, in addition to significant increases in high-density lipoprotein, free thyroxine, thyroid-stimulating hormone, vitamin D (25-hidroksi vitamin D), and cortisol levels, when compared with the control group ($p<0.05$).

Conclusion: Our findings revealed the positive effects of the 6-week HIIT training program in postmenopausal women in terms of reduction in waist and hip circumference, improvement in lipid and hormonal profile, and maintenance of bone metabolism. According to our findings, the 6-week stationary bike HIIT exercise was safe and beneficial for postmenopausal women's health.

Keywords: Bone turnover, CTX, high intensity interval training, menopause, metabolism, osteocalcin

Introduction

During menopause, estrogen levels decrease significantly, leading to various effects on bone tissue, lipid profiles, and glucose metabolism. Estrogen deficiency increases parathyroid hormone (PTH) levels because of decreased bone sensitivity to PTH (1). Additionally, estrogen modifies lipid profiles by boosting high-density lipoprotein (HDL) levels while lowering low-density lipoprotein (LDL) levels, which may contribute to a more atherogenic lipid profile (2). The reduction in estrogen levels during menopause also affects glucose metabolism, decreasing insulin sensitivity, and increasing both insulin secretion and the risk of type 2 diabetes. A major consequence of estrogen deficiency in menopause is rapid bone loss caused by an imbalance between bone resorption and formation. High bone turnover and low bone mineral density (BMD) in osteoporosis can be predicted by biochemical markers such as calcium, PTH, 25-hidroksi vitamin D [25(OH)D], phosphorus, osteocalcin, type 1 collagen C-terminal telopeptide (CTX), and bone-specific alkaline

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phosphatase (Bone-ALP) in which BMD is unavailable (3). Recent studies have suggested that elevated serum PTH, phosphate, and calcium levels during the postmenopausal period may contribute to bone pain and increase the risk of osteoporosis and low BMD (4). Low vitamin D levels further exacerbate this phenomenon by causing secondary hyperparathyroidism and subsequent bone resorption (5). Osteocalcin and Bone-ALP are important markers of bone formation, whereas CTX indicates bone resorption (6,7).

Exercise has been shown to improve physiological and hormonal outcomes in postmenopausal women, positively affecting body composition and bone structure (7,8). Exercise-induced stress stimulates osteoblast activity, promoting new bone formation (7). High-intensity interval training (HIIT) is a popular exercise model that achieves similar benefits to traditional aerobic exercises but in a shorter time (9). HIIT has been associated with better cardiometabolic adaptations and reduced visceral fat in postmenopausal women (10). Despite the known benefits of various exercises on bone metabolism, there are limited data on the effects of HIIT during menopause (11). This study aimed to explore the protective impact of a 6-week HIIT cycling regimen on bone turnover markers, body composition, lipid profiles, and hormonal changes in postmenopausal women.

Methods

Participants

The study included 32 postmenopausal women (age: 53.78±3.93 years, range 48-60 years) diagnosed by a gynecologist. Menopause was defined as the absence of menstruation for at least 12 consecutive months without any other biological cause (12). Sedentarism was defined as self-reported ≤15 minutes of moderate aerobic activity per week (13). Participants were divided into control (n=17) and exercise (n=15) groups. All participants were housewives without a history of tobacco, alcohol, medication, or physical training. The determination of the sample size was based on a power analysis performed using G*Power (3.1.9.2), which yielded an effect size (d) of 1,068 for 95% power at α=0.05, based on Maillard et al. (10).

All participants were evaluated by a family physician and cardiologist. The exercise group was assessed for fitness via treadmill effort testing (NORAV TMX 425, FL, USA) using the modified Bruce protocol (14), with heart rates monitored by GPS (Polar® M400, Finland). Blood pressure was measured according to the American Heart Association Guidelines (15). Following approval from the Marmara University Faculty of Medicine Clinical Research Ethics Committee (approval number: 09.2017.545, date: 01.06.2018), the participants provided written informed consent, and the study complied with the Helsinki Declaration guidelines.

Study Design

A randomized controlled trial with pre- and post-test assessments was conducted over 6 weeks. Pre- and post-tests were administered between 08.00 and 12.00 a.m., with each participant tested on Tuesday and Friday. On day 1, participants completed a personal information form and an exercise stress test. On day 2, blood samples were collected, followed by anthropometric measurements and body composition analysis. The exercise group underwent a 1-week adaptation phase (30 min/day, 3 days/week) of aerobic cycling, followed by an 18-stage HIIT program for 6 weeks (3 days/week, 25-30 min/day). The control group was excluded from participating in an exercise intervention.

Anthropometric and Body Composition Assessment

Height and weight were assessed using participants dressed in minimal attire and without shoes. Body weights and compositions were determined using a Tanita SC 330 (Tanita Corp., Tokyo, Japan). Participants with body mass index values classified as overweight (25-30 kg/m^2) or obese (≥30 kg/m^2) per World Health Organization standards (16) were included. Measurements of waist, abdomen, and hip circumferences were taken with a 0.1 cm precision using a flexible, non-elastic tape (Rosscraft Innovations Inc., Vancouver, Canada), adhering to the Anthropometric Standardization Reference Manual (17). The waist-to-hip ratio was calculated by dividing the waist circumference by the hip circumference.

On the day of the body composition and biochemical tests, participants were instructed to refrain from exercise for at least 48 h and to fast for 12 h before testing. No dietary restrictions were imposed during the program.

Blood Sample Assessments

Blood samples were collected from the antecubital vein, centrifuged at 3000 x g for 10 min, and the serum was stored at -80 °C until analysis. Total protein, HDL, LDL, triglycerides, cortisol, glucose, insulin, thyroid-stimulating hormone (TSH), free thyroxine (free T4), PTH, phosphorus, 25(OH)D, and total Ca^{++} levels were measured using an automated biochemistry analyzer (Abbot Architect I2000SR and c4000). Bone-ALP (Mybiosource Inc, USA), osteocalcin (Elabscience Co., China, cat no: E-EL-H1343), and CTX (Elabscience Co., China) levels were assessed via ELISA.

High-Intensity Interval Training Protocol

Cycle exercise was chosen to improve the safety of overweight and obese participants. After the pre-tests, the exercise group underwent a 1-week adaptation program (3 days/week, 30 minutes/session) of aerobic cycling (40-45 rpm) using a stationary bike (Profitness 8350-R). The HIIT program was conducted on 3 days/week for 6 weeks. Each session included a warm-up at 70% heart rate reserve (HRR). Training intensity increased biweekly: [weeks 1-2: HRR 90-95% (30 sec work/90 sec rest) x 3 sets (total: 12 min); weeks 3-4: HRR 90-95% x 4 sets (total: 14 min); weeks 5-6: HRR 90-95% x 5 sets (total: 16 min)]. HRR was calculated using the Karvonen et al. (18) method, and intensity was monitored using a cardiac rate monitor (Polar M400, Finland). The program followed the HIIT guidelines of the American College of Sports Medicine (19) for sedentary individuals, and each session was supervised by an exercise specialist.

Statistical Analysis

The mean, standard deviation (SD), minimum and maximum values, and percentage changes between pre- and post-tests [(post- and pre-test)/(pre-test x100)] were calculated. Data were analyzed using SPSS 20.0, with a 95% confidence interval and $p<0.05$ set as significant. The Shapiro-Wilk test was used to assess normality. The Wilcoxon signed-rank test was used for within-group comparisons, and the Mann-Whitney U test was used for between-group comparisons before and after exercise.

Results

Anthropometric and Body Composition Measurements

Descriptive statistics for anthropometric, body composition, biochemical parameters, and bone turnover markers are presented (Tables 1-3). No significant differences were observed between the HIIT (mean ± SD age: 53.42±5.40 years) and control (mean ± SD age: 54.64±5.52 years) groups in the pre-test values, confirming group homogeneity ($p>0.05$).

Body Composition

Within the HIIT group, waist and hip circumferences significantly decreased ($p<0.01$; Table 1), with no significant changes in other body composition metrics ($p>0.05$). The control group exhibited a significant increase in hip circumference ($p<0.05$; Table 1). Inter-group analysis revealed a greater reduction in waist and hip circumferences in the HIIT group compared to controls ($p<0.05$; Table 1), with no significant differences in other body composition parameters ($p>0.05$; Table 1).

Biochemical Parameters

The intra-group analysis showed significant reductions in LDL, total cholesterol (TC), triglycerides (TG), and albumin and increases in HDL, cortisol, TSH, and free T4 levels within the HIIT group ($p<0.001$; Table 2). The control group only exhibited a significant increase in HDL ($p<0.001$; Table 2). Inter-group comparisons indicated that changes in LDL, HDL, TC, TG, cortisol, TSH, free T4, and albumin were more favorable in the HIIT group ($p<0.05$; Table 2). No significant differences were found between the groups for insulin, glucose, and Homeostatic Model Assessment of Insulin Resistance levels ($p>0.05$; Table 2).

Bone Turnover Markers

In the HIIT group, significant reductions were observed in total Ca^{++}, P, Bone-ALP, osteocalcin, and CTX levels, along with an increase in 25(OH)D ($p<0.01$; Table 3), while PTH levels remained unchanged ($p>0.05$; Table 3). In the control group, 25(OH)D, P, Bone-ALP, and PTH levels decreased significantly ($p<0.01$; Table 3), with no significant changes in total Ca^{++}, osteocalcin, and CTX levels. Post-exercise, inter-group analysis showed higher 25(OH)D and P levels in the HIIT group compared to controls ($p<0.01$; Table 3).

Discussion

In postmenopausal women, the 6-week HIIT program, conducted three times per week, significantly improved lipid profiles and bone turnover markers. Notably, waist and hip circumferences were reduced, although no substantial changes were noted in body weight, fat percentage, or lean body mass. These findings are consistent with those of previous studies showing that HIIT can reduce abdominal fat, thereby potentially lowering cardiovascular risk (20,21). The discrepancy observed in other studies could be attributed to variations in exercise duration, frequency, and methodologies, such as longer training periods and differing rest intervals (10,22).

Table 1. Anthropometric and body composition characteristics of both groups (HIIT and control) at baseline and after 6 weeks of training

	HIIT, (n=15)			Control, (n=17)			Baseline differences between groups	Pre-post test differences between groups
	Pre	Post	p[a]	Pre	Post	p[a]	p[b]	p[b]
Height, cm	159.7±5.8 (147-168)	159.8±5.2 (147-168)	0.512	156.8±5.4 (149-167)	156.9±5.0 (149-167)	0.333	0.114	0.114
Weight, kg	84.8±14.4 (63.2-119.1)	85.1±14.4 (60.8-118.4)	0.330	82.5±13.7 (58.9-101.6)	83.0±13.3 (58.9-100.7)	0.393	0.970	0.664
BMI, kg/m^2	33.2±4.9 (27.3-42.2)	33.2±5.0 (26.7-42.3)	0.506	33.2±5.2 (25.9-42.3)	33.4±4.9 (26.0-41.0)	0.409	0.910	0.835
Waist circumference, cm	99.1±10.4 (82.0-117.0)	97.2±10.7 (78.0-117.0)	0.007**	100.9±10.8 (79.0-117.0)	101.9±11.0 (80.0-118.0)	0.064	0.597	0.001**
Hip circumference, cm	120.0±9.8 (105.0-141.0)	118.6±9.5 (104.0-141.0)	0.003**	120.8±10.9 (104.0-140.0)	121.7±11.4 (104.0-140.0)	0.048*	0.940	0.001**
Waist/hip ratio	0.8±0.1 (0.7-0.9)	0.8±0.1 (0.7-0.9)	0.203	0.8±0.1 (0.7-0.9)	0.8±0.1 (0.7-0.9)	0.331	0.955	0.178
Percent body fat, %	41.7±4.8 (32.9-48.4)	42.3±4.5 (32.8-49.5)	0.330	41.6±5.7 (33.7-51.7)	42.6±4.9 (35.5-51.8)	0.062	0.777	0.509
Body fat mass, kg	35.9±9.8 (21.5-57.6)	36.7±9.9 (19.9-58.6)	0.109	34.9±9.9 (21.7-51.9)	35.9±9.5 (22.1-52.2)	0.140	0.955	0.835
Fat-free mass, kg	46.4±4.8 (38.7-58.4)	46.1±4.6 (38.8-56.4)	0.513	45.4±5.2 (34.8-54.0)	44.8±4.5 (34.7-51.6)	0.147	0.955	0.584

Data expressed as mean standard deviations and minimum-maximum. HIIT: High-intensity interval training, BMI: Body mass index, [a]Wilcoxon signed ranks test was performed to compare within groups, [b]Mann-Whitney U test was performed to compare baseline differences between the HIIT and control groups, [b]Mann-Whitney U test was performed to compare pre-post-test differences between the HIIT and control groups. *$p<0.05$; **$p<0.01$

Table 2. Biochemical measurements of both groups (HIIT and control) at baseline and after 6 weeks of training

	HIIT (n=15)			Control (n=17)			Baseline differences between groups	Pre-post test differences between groups
	Pre	Post	p[a]	Pre	Post	p[a]	p[b]	p[b]
LDL, mg/dL	187.6±9.2 (174.1-200.8)	175.9±8.1 (164.1-187.6)	0.001**	185.7±9.3 (171.6-200.1)	186.3±9.7 (171.9-200.3)	0.426	0.462	0.001**
HDL, mg/dL	39.7±2.3 (36.3-43.0)	45.2±2.6 (41.2-48.8)	0.001**	39.2±2.3 (35.7-42.8)	39.9±2.3 (36.4-43.2)	0.001**	0.462	0.001**
TC, mg/dL	194.4±9.4 (180.6-207.9)	185.6±8.7 (174.1-198.8)	0.001**	192.4±9.5 178.1-207.2	190.8±11.3 (168.1-205.9)	0.434	0.462	0.001**
TG, mg/dL	143.0±7.1 (132.6-153.2)	136.4±6.6 (127.7-146.3)	0.001**	141.5±7.2 (130.7-152.7)	140.3±8.5 (123.1-151.8)	0.434	0.462	0.001**
Glukoz, mg/dL	93.6±9.2 (80.1-106.8)	91.2±9.1 (76.7-105.9)	0.233	91.6±9.3 (77.6-106.1)	91.3±9.7 (76.8-105.3)	0.400	0.462	0.479
Insulin, µIU/mL	122.2±9.2 (108.8-135.4)	120.8±9.1 (106.4-135.6)	0.609	120.3±9.3 (106.2-134.7)	120.9±9.7 (106.5-134.9)	0.426	0.462	0.479
HOMA-IR	28.4±4.9 (21.5-35.7)	27.4±4.7 (20.1-35.5)	0.427	27.4-4.8 (20.4-35.3)	27.5±5.1 (20.2-35.1)	0.169	0.462	0.485
Cortisol, µg/dL	19.3±2.0 (14.9-22.8)	21.5±2.5 (16.2-25.7)	0.001**	19.6±2.2 (15.5-23.6)	19.7±2.3 (15.8-23.6)	0.980	0.637	0.001**
TSH, mIU/L	2.1±0.8 (2.0-2.2)	2.4±0.2 (2.1-2.6)	0.001**	2.1±0.1 (1.9-2.2)	2.1±0.1 (1.9-2.2)	0.492	0.462	0.001**
T4, µg/dL	9.1±0.3 (8.6-9.5)	9.7±0.7 (8.8-10.9)	0.001**	9.0±0.3 (8.5-9.5)	8.8±0.4 (7.9-9.2)	0.149	0.462	0.001**
Albumin, g/dL	3.4±0.1 (3.2-3.6)	3.3±0.1 (3.1-3.5)	0.001**	3.4±0.1 (3.2-3.6)	3.3±0.3 (2.8-3.7)	0.484	0.462	0.006**

Data expressed as mean standard deviations and minimum-maximum. HIIT: High-intensity interval training, LDL: Low-density lipoprotein, HDL: High-density cholesterol, TC: Total cholesterol, TG: Triglycerides, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance, TSH: Thyroid-stimulating hormone, T4: Thyroxine, Ca^{++}: Calcium, PTH: Parathyroid hormone, [a]Wilcoxon signed-ranks test was performed to compare within groups, [b]Mann-Whitney U test was performed to compare baseline differences between the HIIT and control groups, [b]Mann-Whitney U test was performed to compare pre-post-test differences between the HIIT and control groups, *p<0.05; **p<0.01

Table 3. Bone turn-over markers in both groups (HIIT and control) at baseline and after 6 weeks of training

	HIIT (n=15)			Control (n=17)			Baseline differences between groups	Pre-post test differences between groups
	Pre	Post	p[a]	Pre	Post	p[a]	p[b]	p[b]
25(OH)D, ng/mL	30.1±2.1 (27-33.2)	31.2±2.1 (28.1-34.3)	0.001**	29.6±2.1 (26.4-33.0)	29.1±2.1 (25.9-32.5)	0.001**	0.462	0.001**
Total Ca^{++} level, mg/dL	7.0±0.4 (6.4-7.6)	6.6±0.4 (5.9-7.2)	0.005**	6.9±0.4 (6.3-7.6)	6.5±1.2 (4.9-8.7)	0.177	0.462	0.637
P, mg/dL	3.1±0.1 (2.9-3.3)	2.9±0.2 (2.7-3.2)	0.005**	3.1±0.1 (2.9-3.3)	2.8±0.3 (2.4-3.5)	0.006**	0.462	0.005**
PTH, pg/mL	40.5±2.5 (36.9-44.1)	39.9±2.5 (36.1-43.8)	0.281	40.0±2.5 (36.2-43.9)	39.9±2.6 (36.1-43.8)	0.060	0.462	0.485
ALP, u/L	54.8±4.1 (48.7-60.7)	52.0±3.9 (45.8-58.4)	0.009**	53.9±4.2 47.6-60.4	52.1±4.2 (45.8-58.1)	0.001**	0.462	0.282
Osteocalcin, µg/L	8.6±0.4 (8.0-9.2)	8.2±0.4 (7.5-8.8)	0.005**	8.56±0.4 (7.9-9.2)	8.1±1.2 (6.5-10.3)	0.177	0.462	0.637
CTX, ng/mL	0.47±0.22 (0.44-0.50)	0.45±0.23 (0.41-0.48)	0.005**	0.47±0.22 0.43-0.50	0.44±0.07 (0.36-0.56)	0.177	0.462	0.637

Data expressed as mean standard deviations and minimum-maximum. HIIT: High-intensity interval training, ALP: Alkaline phosphatase, CTX: C-terminal telopeptide, [a]The Wilcoxon signed-rank test was used to compare within groups, [b]Mann-Whitney U test was performed to compare baseline differences between the HIIT and control groups, [b]Mann-Whitney U test was performed to compare pre-post-test differences between the HIIT and control groups, *p<0.05, **p<0.01

The absence of dietary restrictions and the use of less advanced body composition measurement techniques, such as Dual-energy X-ray absorptiometry (DEXA) and magnetic resonance imaging (MRI), might have influenced the results. Although HIIT did not significantly alter body fat mass, previous research has shown improvements in abdominal and visceral fat when using more precise measurement techniques (20). Additionally, postmenopausal estrogen deficiency may affect fat oxidation, which could contribute to the observed lack of change in fat mass (23).

Regarding blood lipid profiles, HIIT's effects varied across studies. Although some studies have indicated beneficial effects on lipid profiles in individuals with obesity (21), other studies have shown mixed results (24). In this study, reductions in LDL, TC, and TG, along with an increase in HDL-C, suggest that HIIT positively influences lipid profiles in postmenopausal women.

The hormonal responses to HIIT included increases in TSH, cortisol, and free T4 although these values remained within normal limits. This is consistent with the limited research on the effects of chronic HIIT on these hormones (25). The observed increase in cortisol, TSH, and T4 levels suggests that HIIT stimulates the hypothalamic-pituitary-adrenal and thyroid axes, even after six weeks of training.

The influence of HIIT on bone turnover markers in postmenopausal women is novel given the sparse research in this area. Lester et al. (26) observed no significant changes in Bone-ALP, PTH, 25(OH)D, or CTX after an 8-week aerobic and resistance exercise regimen, despite improvements in BMD. In contrast, Alghadir et al. (27) reported increases in osteocalcin and Bone-ALP levels after 12 weeks of aerobic exercise, suggesting enhanced bone formation. The present study found an increase in vitamin D and significant decreases in bone adenosine monophosphate, calcium, and phosphorus, with no notable change in PTH levels.

The reduction in Bone-ALP levels across both the HIIT and control groups suggests that this change may not be related to exercise. Calcium and PTH are crucial for bone metabolism (28), with PTH responding quickly to fluctuations in serum calcium. The lack of change in PTH levels might be attributed to the timing of serum sample collection, which did not occur within the first 20 minutes after exercise. Furthermore, the decrease in calcium could be linked to a reduction in serum albumin levels (29).

Osteocalcin, a marker of bone formation, and CTX, a marker of bone resorption, both decreased in the exercise group, indicating potential reductions in bone formation alongside decreased resorption. Yamazaki et al. (30) observed a decrease in CTX starting from the third month in postmenopausal women following a daily walking program. Conversely, Villareal et al. (11) noted increases in CTX and osteocalcin in older adults using a combined exercise model and diet, although the effects of exercise on these markers remain unclear.

Study Limitations

These results should be considered with the study's limitations in mind, including the lack of DEXA or MRI for assessing body composition and bone health and the absence of a controlled nutrition program.

Conclusion

The 6-week HIIT program provides significant benefits for postmenopausal women, including improved lipid profiles and reductions in waist and hip circumferences, suggesting enhanced cardiovascular health and decreased abdominal fat. Although overall body composition metrics such as body weight and fat percentage remained unchanged, HIIT proved to be an effective, time-efficient exercise strategy.

The program also influenced hormonal levels, with increases in TSH, cortisol, and free T4, indicating activation of the thyroid and adrenal axes, although these changes remained within normal limits. Bone turnover markers showed reductions in Bone-ALP, calcium, phosphorus, osteocalcin, and CTX, suggesting alterations in bone metabolism.

Despite not achieving optimal changes in body composition, the HIIT model is a viable alternative for overweight and obese postmenopausal women who have limited exercise time. It effectively addresses waist and hip circumference, improves lipid profiles, and positively affects hormonal levels while maintaining bone health. Future research should focus on long-term effects, advanced body composition assessments, and dietary interventions.

Ethics

Ethics Committee Approval: This study was approved by the Marmara University Faculty of Medicine Ethics Committee (approval number: 09.2017.545, date: 01.06.2018).

Informed Consent: The participants provided written informed consent.

Footnotes

Authorship Contributions: Surgical and Medical Practices - H.K.; Concept - S.Y., M.K.Y.; Design - S.Y., M.K.Y.; Data Collection or Processing - S.Y., M.K.Y.; Analysis or Interpretation - M.K.Y., A.A., Ö.K., A.G., H.D.; Literature Search - S.Y., M.K.Y.; Writing - S.Y., M.K.Y., A.A., Ö.K.

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