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Concurrent effects of high-intensity interval training and vitamin D supplementation on bone metabolism among women diagnosed with osteoporosis: a randomized controlled trial

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Abstract

Background Osteoporosis is often responsible for bone fragility and increased fracture risk due to the micro-architectural deterioration of bone tissue. In addition to nutritional supplements, exercise is considered an adjunct factor in safeguarding bone health. This study aimed to investigate the effects of 16-week high-intensity interval training (HIIT) and vitamin D supplementation on bone mineral density (BMD) in women with osteoporosis.

Trial design This study used a four-arm pretest-posttest experimental randomized controlled design.

Methods One hundred twenty sedentary women aged (30–50 years), diagnosed with osteoporosis were recruited in this study. Patients were randomly classified into four groups with 30 patients in each group: control group (normal daily activities), exercise group (HIIT-exercise for 16 weeks), Vitamin D group (vitamin D 800IU/ day for 16 weeks), and concurrent group (HIIT exercise plus vitamin D for 16 weeks). Anthropometric measurements, BMD, and serum levels of vitamin 25-(OH) D, Osteocalcin, s-BAP, and calcium were estimated in all participants before and after exercise training.

Results Serum samples revealed that bone resorption markers, osteocalcin, total calcium, s-BAP, and vitamin 25(OH) D significantly improved in all groups; there was greater improvement in the HIIT training-vitamin D group than in the HIIT training, vitamin D, and control groups. Furthermore, the HIIT training-vitamin D group showed improvements in hip (right and left) and lumbar spine BMD than the HIIT training, Vitamin D, and Control groups. BMD improvements correlated positively with serum osteocalcin levels and total calcium and negatively with BMI and s-BAP.

Conclusions Sixteen weeks of HIIT and vitamin D consumption showed greater benefits for BMD levels in women with osteoporosis than either vitamin D consumption or HIIT training alone. Therefore, HIIT plus vitamin D consumption may be a strategic option to prevent BMD reduction with aging or to slow demineralization.

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Trial registration The study protocol was retrospectively registered at 'ClinicalTrials.gov PRS' under the trial identifier NCT06624657, dated 1/10/2024.

Keywords High-intensity interval training, Bone mineral density, Osteoporosis, Bone metabolism, 25-hydroxyvitamin D (25OH-D)

Introduction

Osteoporosis is a significant global public health issue, alongside heart disease, cancer, and diabetes, due to its association with increased mortality and morbidity among worldwide [1–3]. Pathologically, osteoporosis is defined as slow bone mass loss and micro-architectural deterioration, leading to bone fragility and increased fracture risk [4, 5].

Globally, 30–40% of women are reported to be at a significantly higher risk of osteoporosis during their lifetime [6]. This condition is also leading fractures [7], particularly in patients with rheumatoid arthritis (RA) [8, 9], with a higher prevalence observed in women with RA [10, 11].

In the older population, calcium and vitamin D are physiologically essential and linked to osteoporosis, and should be administered in diets in adequate amounts or prescribed as medicine [12, 13]. Positive effects on femoral bone mineral density (BMD) have been documented in patients with osteoporosis receiving vitamin D alone or with calcium [12–16]. Approximately 60–80% of bone strength correlates with BMD, though overall bone strength depends on many constructing parameters in the skeleton, such as size, shape, and three-dimensional architecture, along with considerable amounts of mineral contents [17–19]. To date, diagnosis of bone strength and prediction of fracture risk have been based on densitometric measurements. Recently, bone turnover biomarkers have been used to evaluate the rate of bone formation and follow-up treatment responses in patients with osteoporosis.

Osteocalcin, a biomarker secreted by osteoblasts during bone remodeling, is elevated in osteoporosis due to reduced hydroxyapatite crystal formation [20, 21].

In osteoporosis, calcium and phosphorus levels required for the formation of the bone matrix (hydroxyapatite), which is responsible for bone mineralization, are reduced. Osteocalcin, which binds strongly to hydroxyapatite, shows increased serum levels in response to osteoporotic conditions [22, 23].

Non-drug modulated strategies based on exercise and physical activity have received great attention for the treatment of bone-related diseases such as rheumatoid arthritis and osteoporosis [24, 25]. Previous studies have reported that bone mass gain was frequent in load-bearing bone sites of participants following physical exercise [26, 27], thus exercise may be considered an important non-drug strategy for preventing osteoporosis in childhood growth [28, 29], by increasing the peak bone mass or in the older adults by decreasing the rate of bone loss [30]. Previously, it was reported that high intensity exercise that fell within a physiological range showed an increment in physical function compared to low–intensity exercise [31, 32].

Many studies based on clinical and experimental ideas have shown that exercise based on dynamic loading is considered more effective than that based on static loading [22], and greater osteogenic effects have also been reported following high impact-related mechanical strain compared to muscle action alone [33, 34]. Exercise intensity significantly influences bone metabolism. Higher gain in bone mass density (BMD) was reported in rats following high-intensity treadmills compared to low-intensity running programs [35, 36]. Similarly, in young men, a reduction in bone resorption activity was reported following an 8-week program of aerobic training, and accelerated bone turnover resulted from anaerobic training [37].

Many exercise programs including strength training appear to have a significant effect on preventing osteoporosis by stimulating osteogenesis, increasing bone mass and bone mineral density, and subsequently improve bone strength [38, 39]. Moreover, exercise training programs with high impact loads, such as high-intensity interval running, have been shown to considerably effective on bone mineral density [36, 40] via a significant osteogenic stimulus. In addition, both the duration and intensity of exercise may induce changes in bone turnover in healthy and diseased subjects [41–45]. Biomarkers related to bone metabolism, resorption, and turnover, like osteocalcin (OC); bone specific alkaline phosphatase (s-BAP), deoxypyridinoline (DPD), and serum calcium levels significantly improved following exercise in healthy and diseased subjects [41–45].

Based on these findings, we hypothesized that high-intensity interval training (HIIT), alone or combined with vitamin D supplementations, could be an effective non-drug intervention for osteoporosis in women by enhancing BMD and bone osteogenesis. Our null hypothesis (H0) posits that HIIT, whether alone or with vitamin D supplementation, does not significantly increase BMD or bone osteogenesis in individuals with osteoporosis compared to control group. Prior studies suggest that high-intensity resistance and high-impact exercises are particularly effective in improving bone density in the lumbar spine and femur of postmenopausal women and,

that an exercise protocol including high-intensity resistance exercises and high-impact training is shown to be most effective in improving bone density and other parameters of bone health [46, 47].

Thus, this study aimed to estimate the effects of a 16-week HIIT exercise program, alone or with vitamin D supplementations on BMD and bone turnover biomarkers in women with osteoporosis.

Materials and methods

Study design

This study was based on a four-arm, pretest-posttest experimental randomized controlled trial design. The study adhered with the Consolidated Standards of Reporting Trials (CONSORT) to enhance the transparency and accuracy of reporting in research.

Study setting

Patients with osteoporosis were diagonsed with a referred medical orthopedic consultant. Based up on health electronic records, the participants were randomly enrolled to participate in this clinical trial from the outpatients of clinical rehabilitation at the College of Applied Medical Sciences, King Saud University. Enrollment took place between July 15, 2016, and May 25, 2017.

Participants

A total of 160 healthy, non-smoking premenopausal women aged 30 to 50 years, were diagnosed with osteoporosis based on clinical features and diagnostic evidence of BMD measured from both lumbar spine L2 to L4, and from the right and left sides of the hip region by Dual Energy X-ray Absorptiometry (DEXA, UNIGAMMA PLUS AC 230 V 50/60 Hz 400 w, USA) were invited to participate in this study. In addition, DEXA measurements were represented as T-scores.

Participants were required to spend most of the day indoors and maintain a sedentary lifestyle. When outdoors, they were fully clothed to minimize sun exposure, which could influence vitamin D levels during the study. Women with physical disabilities, abnormal hormonal levels, severe disease complications (such as chronic kidney or liver diseases, rheumatoid arthritis or osteoarthritis), significant overweight (BMI ≥ 25), or obesity (≥ 30 kg/m^2), as defined by the World Health Organization, were excluded. Additionally, those with a history of calcium, or multivitamin supplement use, corticosteroids, anticonvulsants, or heparin substances that could affect bone markers and BMD measurements were excluded from this study.

Only 120 women met the inclusion criteria and agreed to participate in this study after providing written informed consent, as presented in the flow chart (Fig. 1). Participants were randomly allocated to either of four groups with equal numbers (30 per group).

The 120 samples were allocated into four groups using a computer-generated random sequence with block randomization (block size 4) to ensure balanced group sizes and randomness. Each block was designed to allocate one participant to each of the four groups in a random order, ensuring equitable distribution across groups within each block. A biostatistician independent of recruitment created the sequence to maintain allocation concealment and prevent bias. The sequence was securely stored and accessed only after confirming eligibility, ensuring unbiased and methodologically rigorous distribution of 30 samples per group. Participants and assessors were blinded to group allocation for the intervention assignments.

During the data collection period, participants were instructed to maintain their usual eating habits. Based on exercise and vitamin D intake, patients were classified into four groups (HIIT exercise group, vitamin D group, concurrent group, and control group), 30 patients in each group; Control group (C), patients with normal eating habits and routine daily activities; HIIT exercise group (HIIT), HIIT-exercise 40 min/3 times/week for16 weeks; vitamin D group (VD), patients receiving vitamin D supplements 800IU/ day for 16 weeks; and concurrent group (HIIT-VD), patients who participated in HIIT exercise and received vitamin D supplements 800IU/ day for 16 weeks. The demographic and clinical data of the participants are in Table (1).

Anthropometric measurements

Height, weight, and BMI were evaluated as described previously [46]. All patients underwent anthropometric measurements using a tape measure and calibrated Salter Electronic Scales (Digital Pearson Scale; ADAM Equipment Inc., Columbia, MD, USA) using a standardized procedure [46].

Vitamin D administration

To study the effect of vitamin D on osteoporosis, participants received a supplement of 400 IU of vitamin D3 taken twice daily (Calcigran Forte®, Nycomed, Norway) to reach to the proposed vitamin D dose of 800 IU /day as previously reported [47], and the vitamin was taken during the experiment for 16 weeks.

Exercise Training program

Using an electronic treadmill (Vegamax, Taiwan), a high-intensity interval training (HIIT) program was performed for 40 min / 3 sessions/week for 16 weeks. HIIT program proceeds in 4 × 4 min intervals at 80–85% of HRmax, with 3-min active recovery at 70% of HRmax between intervals. First, the participants were started

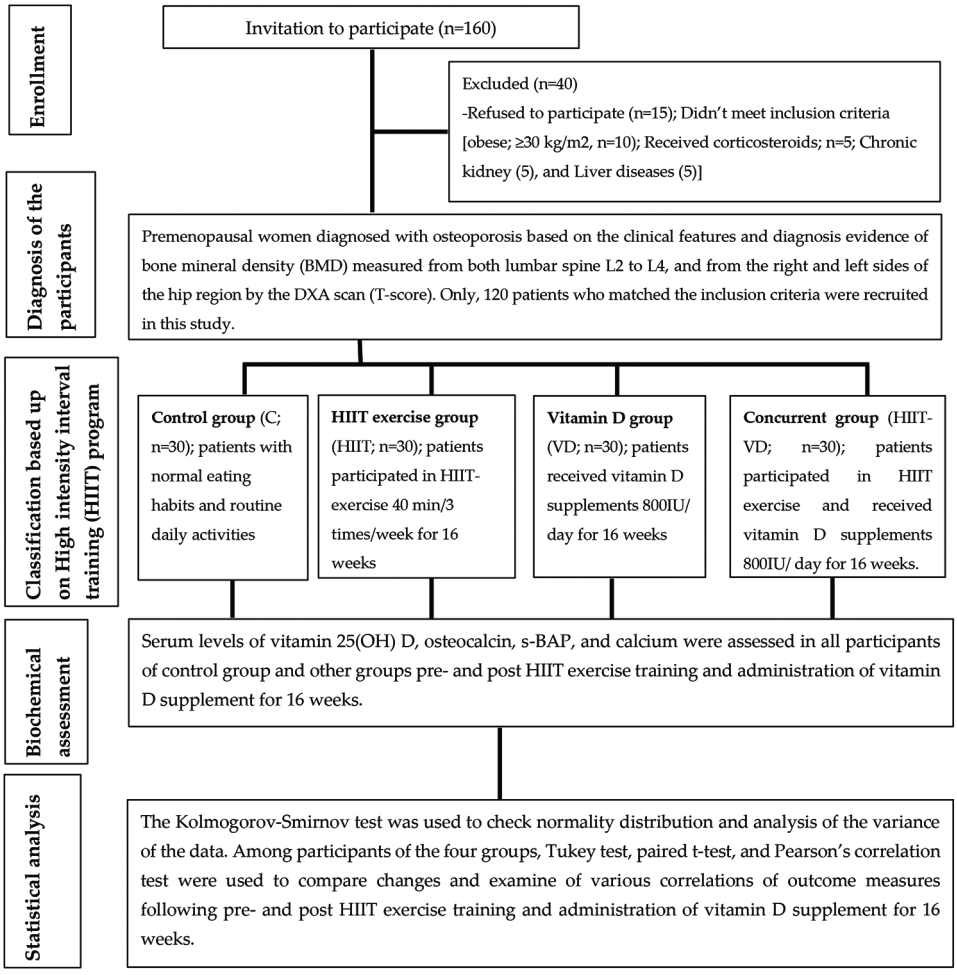

Fig. 1 Outline of study procedures

Table 1 Demographic and some clinical parameters of BMD at baseline of women with osteoporosis

Characteristic	Mean ± SD				
	C	HIIT	VD	HIIT + VD	*P*-value
Number	30	30	30	30	-
Mean age (years)	43.5 ± 3.7	41.8 ± 3.9	41.2 ± 3.75	41.9 ± 3.85	N.S.
BMI (kg/m^2)	22.9 ± 2.6	23.9 ± 3.9	24.1 ± 3.8	23.7 ± 1.7	N.S.
WHR	0.85 ± 0.05	0.79 ± 0.06	0.80 ± 0.07	0.78 ± 0.09	N.S.
Body fat (%)	36.9 ± 4.2	34.7 ± 2.9	34.2 ± 4.6	33.6 ± 3.5	N.S.
25OH-D (ng/ml)	17.9 ± 6.75	28.8 ± 9.5	26.60 ± 13.16	18.80 ± 10.4	**0.010**
Osteocalcin(ng/ml)	28.5 ± 3.7	21.7 ± 3.7	21.6 ± 6.8	18.5 ± 3.8	**0.010**
T-Calcium (mg/dl)	17.8 ± 3.4	16.6 ± 5.1	18.3 ± 4.3	15.6 ± 5.8	**0.010**
sBAP (U/l)	32.3 ± 4.8	26.4 ± 2.6	25.9 ± 8.6	28.6 ± 6.1	**0.020**
Right hip BMD (T-score)	-1.20 ± 0.68	-0.65 ± 0.52	-1.31 ± 0.86	-1.11 ± 0.87	**0.001**
Left hip BMD (T-score)	-2.61 ± 0.48	-2.85 ± 0.38	-2.89 ± 0.34	-2.71 ± 0.32	**0.001**
Lumbar spine (L2-L4) BMD (T-score)	-0.14 ± 0.72	-0.56 ± 0.89	-0.31 ± 0.91	-0.26 ± 0.95	**0.010**

Data expressed as mean ± SD, Standard deviation (SD); body mass index (BMI); waist to hip ratio (WHR); 25-hydroxyvitamin D (25OH-D); bone mineral density (BMD); serum bone alkaline phosphatase (s-BAP); high intensity interval training (HIIT); Control group (C-group); high intensity interval training (HIIT group), high intensity interval training-vitamin D intake (HIIT-VD group); vitamin D (VD group). Not significant (N.S.); Significance of bold values ($p < 0.05$)

the warm-up stage for 10 min at 50% of maximal heart rate (HRmax), followed by 5 min cool-down before initial HIIT sessions, as previously reported [48]. Both heart rate and the Borg scale of perceived exertion, as well as adjustment of the treadmill speed were monitored during the training to ensure that all subjects exercised at their corresponding intensity and to avoid training adaptations during the entire training program.

Assessments of bone mineral density (BMD)

Before and after training, along with vitamin D supplements, BMD of the lumbar spine (L2-L4) and hip of the participants in the control and treated groups were estimated using Dual Energy X-ray Absorptiometry (DEXA, UNIGAMMA PLUS AC 230 V 50/60 Hz 400 w, USA). The BMD of the lumbar spine was measured from L2 to L4, whereas in the hip region, BMD was analyzed from the right and left sides. DEXA measurements were represented as T-scores. Osteoporosis was diagnosed among participants using the DEXA method according to T-score; Normal (0 to–0.99); Osteopenia (low bone density) (–1 to – 2.49); Osteoporosis (≤–2.5); Severe or established osteoporosis (≤ – 2.5 with fracture) [45].

Assessments of bone serum markers and vitamin 25(OH) D

On the fifth day of the female monthly period (8–10 h fasting), blood samples were taken from all participants after overnight fasting and within 48 h before starting the test, just following a 16-week exercise training and receiving vitamin D supplements. To obtain serum, blood samples from each patient were centrifuged. The separated serum samples were stored in small capped vials for long-term use at -20°C until reused for analysis.

Serum levels of vitamin 25(OH) D, osteocalcin, s-BAP, and calcium were assessed in all participants before and after exercise training, according to a previously reported methodological analysis [45–50]. Vitamin 25(OH) D levels in all serum samples were estimated using ELISA and immunoassay kits (IDS, Tyne& Wear, UK). Serum osteocalcin (ng/mL) levels were determined using a MicroVue Osteocalcin enzyme immunoassay (QUIDEL Corporation, San Diego, CA) [45, 49, 50]. In addition, MicroVue BAP immunoenzymetric assay (QuidelCorporation, San Diego, CA, USA) was used to evaluate serum BAP concentrations (U/L) in all patients. Calcium in patient serum samples was estimated using commercially available kits (Hoffman-LaRoche Ltd., Basel, Switzerland) and a Cobas Integra colorimetric analyzer [45, 49, 50].

Sample size calculation

The power of the sample size was estimated by using the G ∗ Power program for Windows (version 3.1.9.7). A sample comprising 120 subjects were included in this study. Using the T-test analyses (two–tallied) with a significance level of 0.05, the total sample of 119 achieves an actual power of 90% with effect size dz of 0.30, Df = 118.0, critical t = 1.98, and noncentrality -α = 3.27.

Statistical analysis

Outcome measures were analyzed using SPSS 20 and Excel 2010. Descriptive statistics were used to analyze the means and standard deviations of the data. The Kolmogorov-Smirnov test was used to check normality of the distribution and analyze the variance of the data. Post-hoc analysis (Tukey's test) was used to compare outcome measures among participants of the four groups; however, within group changes were compared using a paired t-test. In addition, Pearson's correlation tests were performed to examine various correlations. Data were considered statistically significant at $P \leq 0.05$.

Results

A total of 120 women aged from 30 to 50 years, diagnosed with osteoporosis, participated in this study. Basic demographic and bone biochemical markers, along with BMD indicators were estimated for all patients. No significant correlations were observed between these parameters in the basic state (Table 1).

The effect of HIIT alone or in combination with vitamin D intake for 16 weeks on osteoporosis was significant in all groups.

The data showed that the levels of serum 25OH-D and BMD indicators measured as T-score in the right and left hip, and both sides of lumbar spine L2 to L4, were significantly improved ($p = 0.010$) in patients in the HITT group and patients in the vitamin D supplementation group ($p = 010$), following HIIT exercise training or vitamin d supplementation for 16 weeks, compared to the control non-exercised patient group (Table 2). However, in patients in the concurrent group (HIIT + vitamin D), the levels of both 25OH-D and BMD indicators were significantly improved ($p = 0.001$) compared to those in the HIIT, vitamin D, and control non-exercised group as well (Table 2).

Similarly, bone markers such as osteocalcin, total calcium, and s-BAP in patients in the HIIT training, vitamin D intake, and HIIT + Vitamin D intake groups were significantly improved ($p = 0.001$) following HIIT and/or vitamin D interventions for 16 weeks compared to the control non-exercised group, as shown in Table 3 and Fig. (2 A, B, C, and D).

In addition, DEXA scan measurements showed that the changes in hip BMD values (right and left) and lumbar spine BMD in studied patients of HIIT training, vitamin D intake, and HIIT + Vitamin D intake groups were significant (Right: $p < 0.001$, $p < 0.010$, $p < 0.001$; left: $p < 0.001$, $p < 0.010$, $p < 0.001$; lumbar spine: $p < 0.001$,

Table 2 Comparison of clinical BMD indicators and the level of 25OH-D among studied groups after 16-weeks HIIT and /or vitamin D interventions using one-way ANOVA and Tukey post hoc test

Groups	Clinical parameters											
	25OH-D (ng/ml)			Right hip BMD (T-score)			Left hip BMD (T- score)			Lumbar spine (L2-L4) BMD (T-score)		
	MD	SD	*P*	MD	SD	*P*	MD	SD	*P*	MD	SD	*P*
C	-21.1	3.600	-	-0.600	0.090	-	−0.660	0.050	-	-0.426	0.160	-
HITT	-13.8	2.950	**0.010**	-0.340	0.085	**0.010**	-0.160	0.032	**0.010**	-0.044	0.150	**0.010**
VD	-16.90	3.420	**0.010**	-0.330	0.075	**0.010**	-0.440	0.025	**0.010**	-0.390	0.146	**0.010**
HITT-VD	-3.100	3.240	**0.001**	-0.010	0.064	**0.001**	-0.440	0.046	**0.001**	-0.390	0.149	**0.001**

Data expressed as mean ± SD, 25-hydroxyvitamin D (25OH-D); bone mineral density (BMD); high intensity interval training (HIIT), Control group (C-group); high intensity interval training (HIIT group), high intensity interval training-vitamin D intake (HIIT-VD group); vitamin D (VD group); Significance of bold values ($p < 0.05$)

$p < 0.010$, $p < 0.001$, respectively) as shown in Fig. (3 A, B, and D).

Moreover, significant correlations between BMD, vitamin status, and the related bone reformation markers S-BAP (U/l), Osteocalcin (ng/ml), and calcium (mg/dl) were estimated in patients with osteoporosis after 16 weeks of concurrent HIIT training alone or in combination with vitamin D consumption. The data showed that BMD status and vitamin D levels correlated positively with serum levels of osteocalcin and total calcium and negatively with BMI and s-BAP, as shown in Table (4).

Discussion

In the older population, osteoporosis is a major medical condition that frequently contributes to hip fractures via a low-trauma mechanism [51]. Compared to men, residual lifetime risks such as, loss of function, severe pain, stiffness, and bone injuries resulting from osteoporosis are approximately four times higher in women aged 50 years [52]. In addition, the incidence of hip fractures is expected to increase to ≥6 million by 2050 [53]. Moreover, the American Society of Anesthesiologists Schaumburg IL scores have reported that frail patients who need to undergo hip replacements represent a high-risk category for morbidity and mortality due to their associated pathological conditions [54]. Thus, the potential risk factors, prevention measures, and management strategies were narratively overviewed to gather a series of experience that may aid medical staff in the development of diagnostic and therapeutic protocols, especially in surgical techniques used for patients with some high-risk complications, like hip replacement [55].

In addition, vitamin D levels and good physical fitness have played significant roles in new trials for the prevention and treatment of osteoporosis [12, 13]. Vitamin D deficiency and low physical activity accelerate bone loss through secondary hyperparathyroidism and obesity-related syndromes [26–30, 56–59]. Improvement in BMD following exercise training is related to the activity of osteocytes, which provides a balance between bone resorption and formation. Positive effects on BMD were observed after exercise training programs with long and adequate mechanical loads to provide adequate pressure [60], stimulate osteoblast activity and new bone formation [61, 62].

This study evaluated the influence of concurrent HIIT and vitamin D consumption on some indices of BMD and bone markers; OC, Ca, and s-BAP were evaluated in women with osteoporosis. The data obtained showed that combination trials of both concurrent HIIT and Vitamin D for 16 weeks positively affected BMD and bone markers in young women with osteoporosis compared to separate trials of ordinary vitamin D consumption or concurrent training.

Table 3 Changes in bone markers of osteoporotic patients following 16-weeks of HIIT-training and /or vitamin D interventions (no = 120)

Groups	Clinical parameters								
	Osteocalcin (ng/ml)			T-Calcium (mg/dl)			S-BAP (U/l)		
	MD	SD	*P*	MD	SD	*P*	MD	SD	*P*
C	-21.100	4.350	-	-24.700	0.960	-	-9.700	2.700	-
HITT	-10.500	4.100	**0.001**	-15.700	0.915	**0.001**	-6.700	2.530	**0.001**
VD	-12.900	3.850	**0.001**	-6.400	0.895	**0.001**	-4.000	2.617	**0.001**
HITT-VD	-12.900	3.980	**0.001**	-24.400	0.932	**0.001**	-7.100	2.694	**0.001**

Data expressed as mean ± SD, serum bone alkaline phosphatase (s-BAP); high intensity interval training (HIIT); Control group (C-group); high intensity interval training (HIIT group), high intensity interval training-vitamin D intake (HIIT-VD group); vitamin D (VD group). analysis estimated by using one-way Anova and Tukey post hoc test; Significance of bold values ($p < 0.05$)

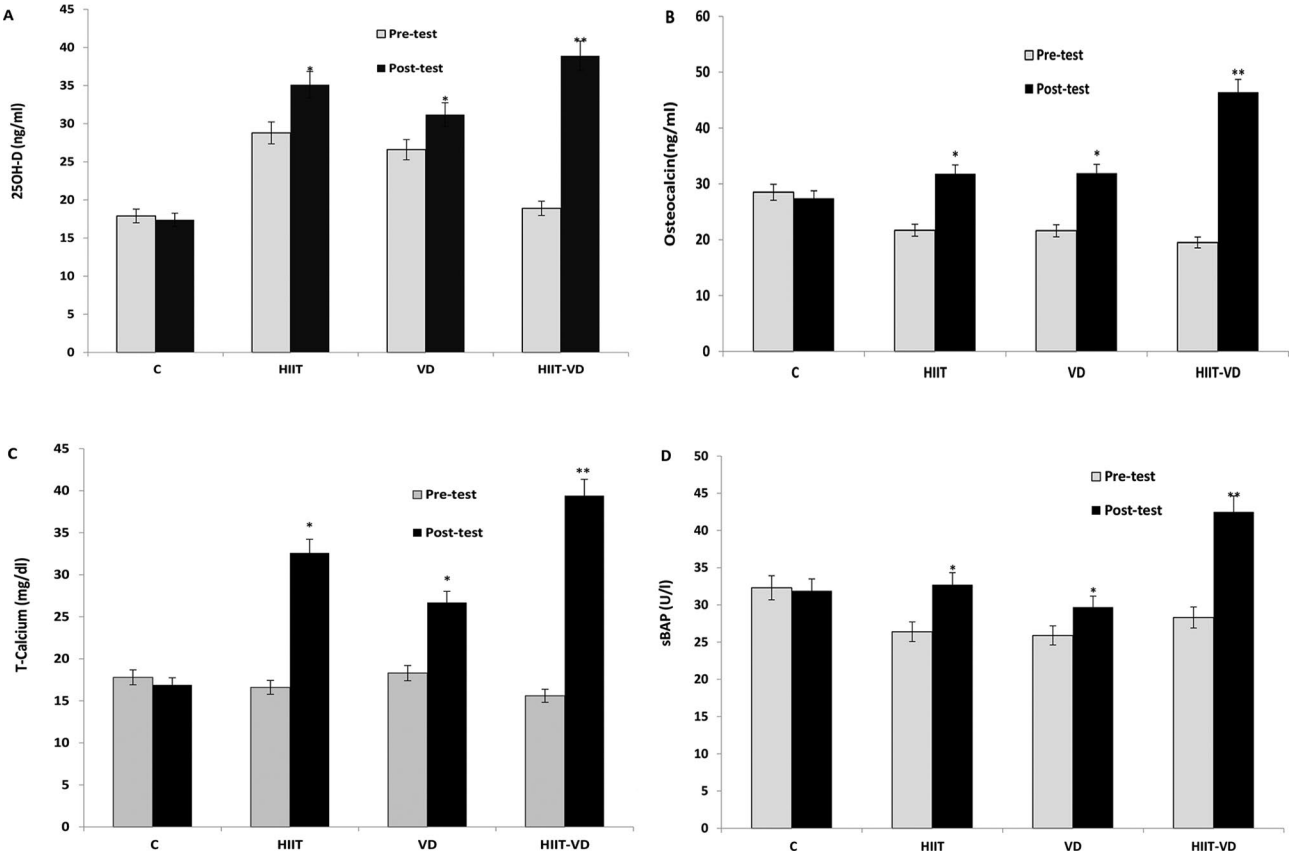

Fig. 2 Changes in 25OH-D (**A**), Osteocalcin(ng/ml) (**B**), T-Calcium (mg/dl) (**C**), sBAP (U/l) (**D**) following 16 weeks of HIIT training and VD interventions (mean ± SD). *($p \leq 0.01$), **($p \leq 0.001$), denotes significant differences between baseline and post training values. Standard deviation (SD); 25-hydroxyvitamin D (25OH-D); serum bone alkaline phosphatase (s-BAP); Total-calcium (T-calcium); high intensity interval training (HIIT); Control group (C-group); high intensity interval training (HIIT group), high intensity interval training-vitamin D intake (HIIT-VD group); vitamin D (VD group)

In the present study, patients who participated in the HIIT concurrent training program along with vitamin D consumption for 16 weeks showed a significant increase in serum vitamin D levels compared to those in the vitamin D and training groups. In addition, BMD showed significant changes or improvements in hip BMD values (right and left) and lumbar spine BMD as measured by DEXA.

Exercise has been reported as a pivotal non-drug strategy for preventing osteoporosis [28], whereas bone gain in participants was frequently observed in load-bearing bone sites following physical exercise [26, 27]. Thus, exercise is considered a useful means to prevent osteoporosis, in both childhood growths [28, 29], by increasing the peak of bone mass and in the elderly by decreasing the rate of bone loss [30].

The impact of concurrent training on BMD has been investigated in a few studies, with the main target being to focus on the effects of aerobic and resistance activities separately. In aerobic exercise models, a weak effect on

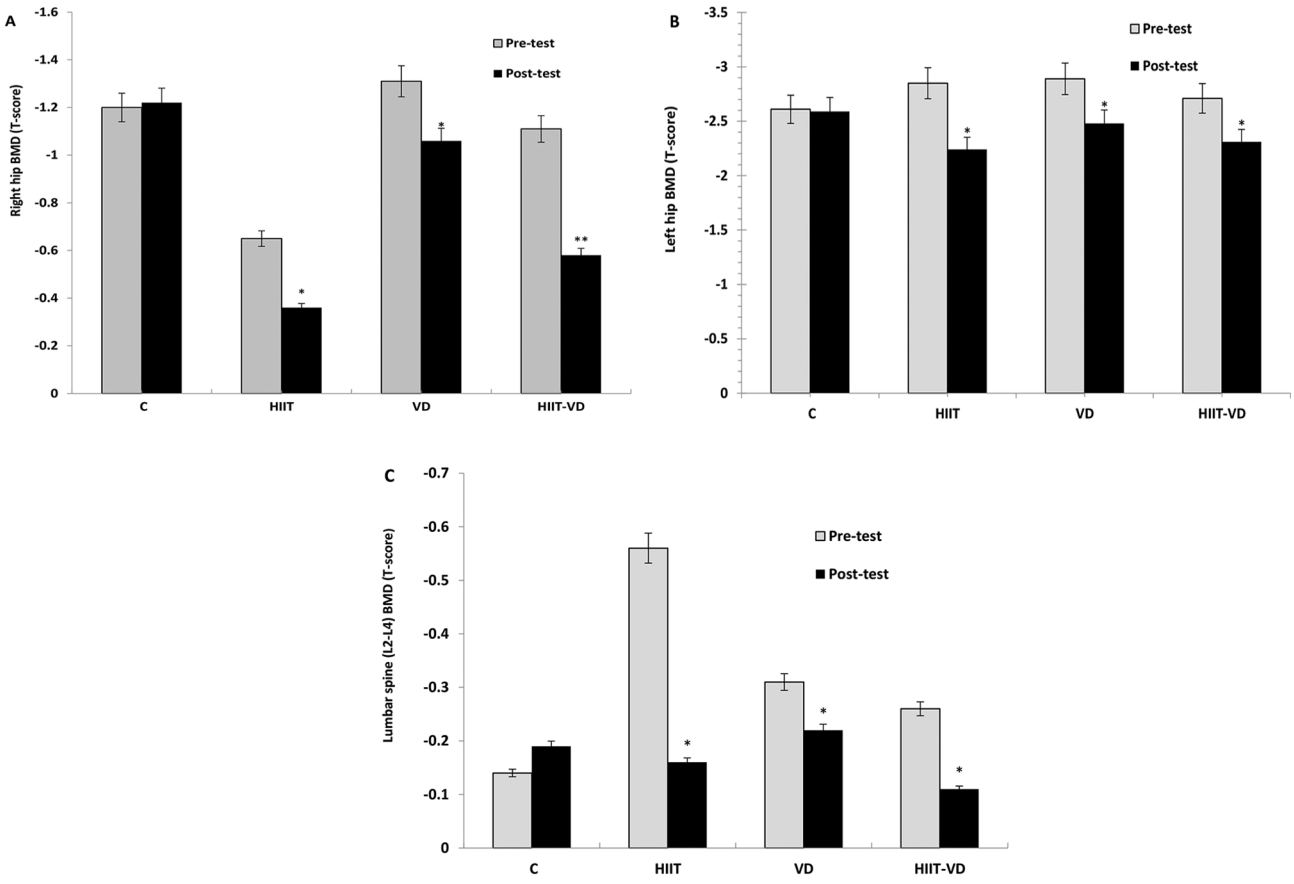

Fig. 3 Changes in right hip BMD (**A**), left hip BMD (**B**), and lumbar spine (**C**) following 16 weeks of HIIT training and VD interventions (mean ± SD). *($p \leq 0.01$), **($p \leq 0.001$), denotes significant differences between baseline and post training values. Standard deviation (SD); intensity interval training (HIIT); Control group (C-group); high intensity interval training (HIIT group), high intensity interval training-vitamin D intake (HIIT-VD group); vitamin D (VD group)

BMD has been reported in adults, and controversial evidence for the effectiveness of HIIT concurrent training programs on age-related bone loss has been previously reported [63, 64]. In postmenopausal women, bone density in the femoral neck was increased by 2% after walking for 24 weeks. This aerobic training program usually includes walking without lateral or twisting movements, which are insufficient for improving bone density [65].

The slight improvement in BMD in women with osteoporosis may be related to the low exercise intensity of walking, which exerts lower pressure on the body and may lead to weak osteogenic stimulation compared with running programs [66]. Thus, both concurrent walking and running programs are helpful to women after the postmenopausal period [67]. In addition, high-intensity exercise, which falls within the physiological range, provides a noticeable increment in physical function compared to low-intensity exercise [31, 32].

Thus, in this study, a higher-intensity interval training program was conducted for 16 weeks, along with vitamin D intake. The data obtained were in line with other studies that reported that exercise programs with dynamic loading have a greater effect on BMD than those with static loading [22] and that greater osteogenic effects were reported following high impact-related mechanical strain compared to muscle action alone [33, 34]. Similarly, experimental analysis in rats showed that high-intensity treadmill training programs influence bone metabolism and exert more BMD gain than low-intensity running programs [35, 36]. Consistent with our results, lumbar spine and femoral neck bone densities improved after high-intensity training [31]. These results showed that HIIT training improves the rate of force development training, which increased bone density by 2.9 for the lumbar spine and 4.9% for the femoral neck [31]. In young women before menopause, high-impact exercise with high pressure on the skeleton is recommended as a strategy to increase bone mass providing greater osteogenic effects and activating bone formation [68].

Regarding the effect of vitamin D intake, our results match with those who reported positive effects on femoral BMD in patients with osteoporosis following the

Table 4 Correlation between bone markers, BMI, BMD status, and levels of 25OH-D vitamin of osteoporotic patients following 16-weeks of HIIT-training ($n = 120$)

Characteristic	HIIT				HIIT-VD				VD			
	BMD		25OH-D		BMD		25OH-D		BMD		25OH-D	
	R	*P*-value	*R*	*P*-value	*R*	*P*-value	*R*	*P*-value	*R*	*P*-value	*R*	*P*-value
BMI	-0.78	**0.010**	−0.42	**0.001**	−0.38	**0.001**	−0.35	**0.001**	-0.33	**0.010**	-0.53	**0.010**
S-BAP (U/l)	-0.27	**0.010**	-0.32	**0.001**	-0.45	**0.001**	−0.76	**0.001**	-0.37	**0.010**	-0.25	**0.010**
Osteocalcin (ng/ml)	0.85	**0.010**	0.65	**0.001**	0.57	**0.001**	0.25	**0.001**	0.52	**0.010**	0.72	**0.010**
T-Calcium (mg/dl)	0.39	**0.010**	0.71	**0.001**	0.39	**0.001**	0.95	**0.001**	0.65	**0.010**	0.48	**0.010**

Data presented as coefficient (R); Results denotes significance at <0.05; Significance of bold values ($p < 0.05$)

administration of vitamin D, alone or with calcium [12–16]. Clinical trials have shown that vitamin D supplementation with or without calcium intake significantly reduces secondary hyperparathyroidism, slows bone turnover, retard bone loss, and increases areal BMD [69–73].

The beneficial effects that appear on bone density in women following vitamin D intake may be related to a reduction in the bone remodeling space that, in turn, leads to a decline in the number of remodeling sites of the activated bone, leading to a reduction in the process of bone resorption [74].

In a previously published study, vitamin D insufficiency was shown to be linked with higher bone resorption and inversely correlated with bone formation markers such as serum alkaline phosphatase (ALP) levels which may lead to increased bone loss, osteoporosis, and increased bone turnover, which appears to increase fracture risk. Thus, serum 25(OH) D levels of 50 nmol/L should be maintained to minimize the occurrence of fractures in older adults [75].

Finally, the data of our study showed that in women with osteoporosis, BMD status correlated positively with the serum levels of vitamin 25(OH) D, osteocalcin, and total calcium, and negatively with BMI and s-BAP following 16 weeks of concurrent HIIT training alone or in combination with vitamin D consumption. Previously, in a double-blind, randomized, controlled trial, positive effects on BMD were demonstrated in young adult women with peri- and post-menopausal status following calcium and Vitamin D supplementation [76].

Similarly, regular impact exercise training achieved bone benefits, whereas serum basal PTH levels were significantly lowered, which probably supports the superior alteration between basal PTH and transient exercise-induced PTH peaks leading to osteogenic effects and subsequently greater improvements in BMD [77]. In addition, it has been reported that physical exercise training with appropriate mechanical loading elicits advantageous adaptations in both bone mass and geometric orientations at load-bearing bone sites [78–80], and that increases in 25OHD values were found in patients following impact exercise training [41–45].

Strength and limitations of the study

The strength of our research is that combining vitamin D with HIIT further enhances bone health because vitamin D supplementation provides the necessary building blocks for bone, while HIIT stimulates the mechanical processes that encourage bone strengthening, improves BMD, and enhances muscle strength in premenopausal women, particularly for managing or preventing osteoporosis.

Our study has several limitations. First, we were unable to perform a sex-comparison analysis of the data, because the recruited bone tissue samples were from female patients. Second, the study lacked a healthy control group, which is considered a major weakness, as it led difficulty in observing long-lasting changes in BMD and related bone markers following exercise interventions. Finally, the small sample size of the current study leads to the interpretation that our results as preliminary findings, and more studies are needed to understand the potential association and establishment of HIIT/Vit D interventions for improving BMD and related bone markers among women with premenopausal osteoporosis.

Conclusions

Our results demonstrated that HIIT and vitamin D consumption combination trials for 16 weeks significantly added more benefits to the BMD of young women with osteoporosis than separate vitamin D consumption or HIIT training. Therefore, concurrent training and consumption of vitamin D may be recommended as strategic options to prevent BMD reduction with aging or to slow its reduction rate.

Abbreviations

SD	Standard deviation
BMI	Body mass index
WHR	Waist-to-hip ratio
25OH-D	25-hydroxyvitamin D
BMD	Bone mineral density
s-BAP	Serum bone alkaline phosphatase
HIIT	High-intensity interval training
C-group	Control group
HIIT group	High-intensity interval training
HIIT-VD group	High-intensity interval training-vitamin D intake
VDgroup	Vitamin D
DEXA	Dual-energy x-ray absorptiometry
HR max	Heart rate maximum

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Author contributions

Conception: A.H.A, S.A.G, and A.I.; Methodology: S.A.G and A.H.A.; Data curation: S.A.G.; Data analysis and interpretation: S.A.G and A.I.; Preparation of the manuscript: A.H.A, S.A.G, and A.I.; Revision for intellectual content: A.H.A, S.A.G, and A.I.; Supervision: A.H.A. All authors read, understood, and approved the manuscript's final version to be published.

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Data availability

All related data has been presented within the manuscript.

Declarations

Ethics statement and consent to participate

The study protocol was reviewed and approved by the Ethics Sub-Committee, King Saud University, Kingdom of Saudi Arabia, under file ID: RRC-2016-028. The study was performed according to the ethical guidelines of the Declaration of Helsinki (1975). The study protocol was retrospectively registered to the 'ClinicalTrials.gov PRS' under a trial identifier: NCT06624657 dated: 1/10/2024. Before data collection, written informed consent was obtained from all participating patients.

Competing interests

The authors declare no competing interests.

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