narraj

Short Communication

Effect of walking and bone joint exercise on enhancing bone remodeling in menopausal women: A randomized controlled trial

Chusairil Pasa[1], Eti P. Pamungkasari[1,2*], Muchsin Doewes[1,3], Bambang Purwanto[1,4], Hartono Hartono[1,5], Risya Cilmiaty[1,6] and Paramasari Dirgahayu[1,7]

[1]Doctoral Program of Medical Science, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia; [2]Department of Public Health, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia; [3]Department of Medical Sciences, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia; [4]Department of Internal Medicine, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia; [5]Department of Physiology, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia; [6]Department of Oral Disease, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia; [7]Department of Parasitology, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia

*Corresponding author: etiponco@staff.uns.ac.id

Abstract

Osteoporosis increases fracture risk and reduces quality of life in menopausal women. Although physical activity, such as walking and bone joint exercise, is known to help maintain bone health, its effectiveness needs further examination. The aim of this study was to analyze the effects of physical activity, in particular walking and bone joint exercise, on enhancing bone remodeling in menopausal women. A randomized controlled trial was conducted among menopausal women and allocated into three groups: walking, bone joint exercise, and control groups. The intervention was provided for eight weeks, with the outcomes measured before and after the intervention. The study assessed five bone remodeling biomarkers: estrogen, parathyroid hormone (PTH), receptor activator of nuclear factor kappa-β ligand (RANKL), tumor necrosis factor-alpha (TNF-α), and bone mineral density (BMD). The paired sample student t-test and ANOVA were used to assess the effects of the interventions. The results indicated that, compared to pre-intervention, both walking and bone joint exercise significantly increased the estrogen (p=0.026 and p=0.023, respectively), decreased RANKL (p=0.019 and p=0.002, respectively), decreased PTH levels (p=0.022 and p=0.048, respectively) and increased the BMD scores (p=0.001 and p<0.001, respectively). In the control group, none of the remodeling biomarkers significantly changed except the mean level of TNF-α, which was increased significantly (p=0.001). This study highlights that structured exercise, such as walking and bone joint exercise, can significantly enhance bone remodeling markers in menopausal women. Therefore, implementing such physical activities into management may provide benefits to menopausal women.

Keywords: Menopausal, osteoporosis, estrogen, PTH, RANKL

https://narraj.org/

Introduction

Globally, the population of people aged 60 and older has grown significantly in the past ten years [1]. Among all degenerative diseases affecting the elderly, osteoporosis is the most prevalent bone and joint disease, with a prevalence of approximately 18.3% worldwide [2]. Since osteoporosis does not have any particular symptoms, it is categorized as a silent illness [3]. The Indonesian population faces a significant risk of developing osteoporosis, with 41.2% of

Received: August 12, 2024 - Accepted: October 25, 2024 - Published online: October 31, 2024

individuals aged under 55 years experiencing osteopenia, and women are six times more likely to develop osteopenia and twice as likely to develop osteoporosis compared to men [3].

Four key factors are essential in assessing bone quality, including bone density, bone turnover, bone size, and bone geometry or microarchitecture [4,5]. As bones age, they undergo remodeling, where old tissue is replaced by new. This remodeling is driven by the coordinated activities of osteoblasts (cells that form bone) and osteoclasts (cells that resorb bone), forming an anatomical structure known as the basic multicellular units (BMU). During menopause, bone loss accelerates and continues at a persistent rate [6]. One of the factors is hormonal changes, of which estrogen, a hormone crucial for maintaining the balance between bone formation and resorption, sharply declines during menopause [7]. This decrease leads to increased activity of osteoclasts and decreased activity of osteoblasts, resulting in lower bone mineral density (BMD) and a heightened risk of osteoporosis [8,9]. Additionally, the parathyroid hormone (PTH), which regulates blood calcium levels, also influences bone remodeling. In low estrogen levels, bone sensitivity to PTH increases, causing greater bone resorption and an accelerated decrease in BMD [10,11].

The formation and activation of osteoclasts are regulated by the receptor activator of nuclear factor kappa-β ligand (RANKL). During menopause, an increased level of RANKL promotes the formation of more osteoclasts, leading to increased bone resorption and a subsequent decrease in BMD [12-14]. Under normal conditions, estrogen inhibits RANKL activity; however, the reduction in estrogen levels during menopause leads to heightened RANKL activity. Additionally, osteoclast activity can be induced by tumor necrosis factor-alpha (TNF-α), a cytokine involved in inflammation. High levels of TNF-α during menopause contribute to increased bone resorption and decreased BMD, as estrogen normally inhibits TNF-α production [15,16]. In low estrogen levels, the imbalance between bone formation and resorption is mediated by increased activity of PTH, RANKL, and TNF-α, leading to decreased BMD and an increased risk of osteoporosis [15,16]. To enhance bone remodeling (bone formation) in menopausal women, it is crucial to consider the intricate interplay of these physiological processes to mitigate the risk of osteoporosis and maintain bone health [16]. The aim of this study was to analyze the molecular effects of physical activities (walking and bone joint exercise) on enhancing bone remodeling by assessing the levels of estrogen, PTH, RANKL, TNF-α and BMD in menopausal women.

Methods

Study design, setting, and sampling

A randomized controlled trial was conducted at three Community Health Centers located in Pringsewu, Gading Rejo, and Ambarawa, Lampung, Indonesia, from December 2022 to April 2023. The study involved menopausal women, who were selected through purposive sampling and randomly assigned to one of the three groups: walking group, bone joint exercise group, or control group, to evaluate the effects of physical activities on bone remodeling markers: estrogen, PTH, RANKL, TNF-α, and BMD. The levels of bone remodeling markers were conducted twice: before the intervention (pre-test) and after eight weeks of intervention (post-test).

Participants

This study included menopausal women aged 50 to 65 years old who had not experienced menstruation for at least 12 consecutive months. All menopausal women with amenorrhea due to the removal of the uterus and ovaries, as well as those with conditions such as tuberculosis, diabetes, cardiovascular disease, hypertension, thyroid disorders, long-term glucocorticoid use (over six months), or those who consumed alcohol, smoked, had a history of fractures, secondary osteoporosis, or rheumatoid arthritis were excluded from the study.

Intervention

Menopausal women were randomly assigned into three groups: walking, bone joint exercise, and control, of which each group received different interventions for eight weeks. Before the intervention started, each individual from all groups was included in an introductory meeting, during which a comprehensive technical details and study objectives were explained. The

technical aspects of the interventions, along with the preventive and promotional health benefits, were outlined to ensure clarity. A health promotion officer was present in each group and responsible for intervention monitoring.

In the walking group, the intervention involved walking at a distance of 1.6 km. Walking was conducted at the sports field in the Community Health Center working area at 7:00 AM. In the bone joint exercise group, joint movements targeting the muscles of the arms and legs were performed to enhance blood circulation and volume, as well as to stimulate a balance between osteoblasts and osteoclasts in bone tissues. Both intervention sessions were conducted three times a week for 30 minutes. When a participant missed a session, a replacement session was scheduled for the following day. In contrast, the control group did not engage in any structured physical activities.

To ensure consistency in intervention intensity, participants' performance was monitored using the SIPGAR application, a fitness assessment tool provided by the Ministry of Health of the Republic of Indonesia. The SIPGAR application provided the data or graphs of fitness measurements of the participants. In addition, participants' performance was also monitored by dedicated personnel from the Community Health Center, of which physical condition assessments were recorded.

Data collection

Data on the characteristics of the study participants, including age, weight, height, length of menopause, education, and occupation, were obtained through a general information questionnaire administered during the study. The bone remodeling biomarkers (estrogen, TNF-α, PTH, and RANKL) were measured using serum samples. Pre-intervention blood samples were collected during the introduction meeting, while post-intervention samples were collected after the intervention concluded. A 3 mL blood sample was collected from the jugular vein using a disposable syringe and immediately transferred into an ethylenediaminetetraacetic acid (EDTA) tube, where the serum was prepared and stored. After all the samples were collected, the samples were transported to the Physiology Laboratory of Universitas Brawijaya in Malang, East Java, Indonesia. Participant's BMD levels were assessed using a bone densitometer, which estimated the mineral density of the calcaneus bone via T-score measurement. BMD measurements were conducted in Pringsewu Regency, Lampung, Indonesia, concurrently with the collection of pre- and post-intervention blood samples from participants.

Measurement of estrogen, PTH, RANKL, TNF-α, and BMD

Biomarker levels were analyzed using enzyme-linked immunosorbent assay (ELISA) kits using the iMark™ Microplate Absorbance Reader (Bio-RAD, Hercules, California, USA). The specific ELISA kits utilized in this study included the CAN E-360 Human Estrogen kit (Diagnostics Biochem Inc., Ontario, Canada) for measuring estrogen levels and the E0082 Human TNF-α, E0620 Human RANKL, and E1055Hu Human PTH kits (all from Bioassay Technology Laboratory, Shanghai, China) to measure TNF-α, RANKL, and PTH, respectively. Each ELISA was performed following the manufacturer's instructions. The absorbance was measured at a wavelength of 450 nm using the ELISA reader. The estrogen and TNF-α levels were presented in ng/L while RANKL level and PTH were presented in pg/mL.

BMD measurements were conducted with participants seated, positioning their feet on the sonometer machine, Sonost 3000 Bone Densitometer (OsteoSys Co., Ltd, Seoul, Republic of Korea). Soft rubber pads were placed on both sides of the heel, and measurements were obtained by transmitting sound waves through the heel using the Sonost 3000 Bone Densitometer (OsteoSys Co., Ltd, Seoul, Republic of Korea). To ensure optimal sound wave transmission, ultrasound coupling gel was applied between the pads and the participant's skin, eliminating any air at the interface. The entire procedure, including participant positioning, was swift, taking only a few minutes. Proper leg angle was maintained by immobilizing the lower leg with an assistive device equipped with moldable foam to secure the foot. BMD outcome measurements adhered to guidelines established by the World Health Organization (WHO) and the Official Adult Position of the International Society for Clinical Densitometry 2023 [17] of which BMD levels were interpreted as follows: normal (T-score≥-1), osteopenia (-2.5<T-score<-1), and osteoporosis (T-score≤-2.5).

Statistical analysis

The normality of the data was assessed using the Shapiro-Wilk test. The paired Student t-test or Wilcoxon test was used to assess the level changes of estrogen, PTH, RANKL, TNF-α, and BMD after the intervention (between pre- and post-intervention) as appropriate. The ANOVA or Kruskal-Wallis tests were used to evaluate differences in bone remodeling marker levels (estrogen, PTH, RANKL, TNF-α, and BMD) among groups before or after the intervention. All statistical analysis was performed using SPSS version 25.0 (SPSS Inc., Chicago, USA).

Results

Characteristics of the participants

A total of 42 menopausal women were involved in this study, divided into three groups (walking, bone joint exercise, and control), each consisting of 14 participants. The detailed flow diagram of each step from recruitment to analysis is presented in **Figure 1**. The basic characteristics of the sample are presented in **Table 1**. Most of the menopausal women were in the 40–59 age category (71.4%) and were unemployed (69.0%). Normal BMI was more frequently observed in the walking and control groups. However, in the bone joint exercise group, there was an equal number of menopausal women with normal and overweight BMI. The average duration of menopause in the walking, bone joint exercise, and control groups were 6.85±4.20, 4.67±4.11, and 8.82±6.29 years, respectively (**Table 1**). Although the randomization was conducted, age, education, occupation, BMI, and body weight were significantly different among the three groups (**Table 1**).

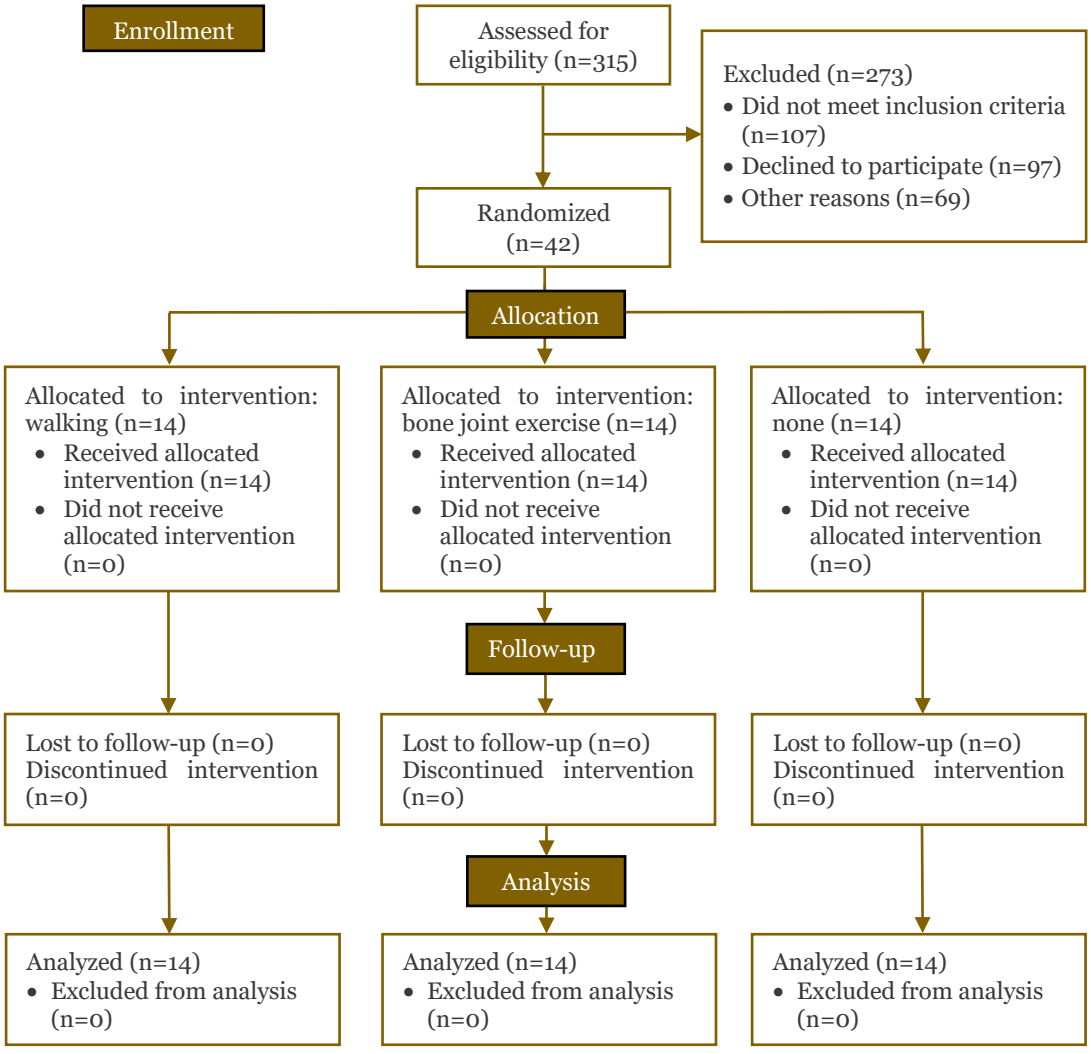

Figure 1. Consort flow diagram of the clinical trial showing each step from recruitment to analysis.

Table 1. Characteristics of the menopausal women included in each group of the study (n=42)

Characteristics	Study group			*p*-value
	Walking	Bone joint exercise	Control	
	n=14	n=14	n=14	
Age (years), n (%)				0.011
40–59	8 (57.1)	14 (100.0)	8 (57.1)	
60–69	6 (42.9)	0 (0.0)	6 (49.9)	
Education, n (%)				0.048
Low	11 (78.6)	10 (71.4)	3 (21.4)	
High	3 (21.4)	4 (28.6)	11 (78.6)	
Occupation, n (%)				0.004
Employed	1 (7.1)	5 (35.7)	7 (50.0)	
Unemployed	13 (92.9)	9 (64.3)	7 (50.0)	
Body mass index (BMI) (kg/m^2)				0.025
Underweight	1 (7.1)	0 (0.0)	0 (0.0)	
Normal	9 (64.3)	7 (50.0)	9 (64.3)	
Overweight	4 (28.6)	7 (50.0)	4 (28.6)	
Obese	0 (0.0)	0 (0.0)	1 (7.1)	
Weight (kg)				0.005
Mean±SD	53.57±6.35	62.00±5.18	60.50±7.90	
Median (min-max)	54 (41–63)	60 (56–70)	60 (49–79)	
Height (cm)				0.078
Mean±SD	154.71±5.07	157.92±3.91	154.23±4.86	
Median (min-max)	155 (145–161)	159 (150–162)	155 (146–162)	
Duration of menopause (years)				0.099
Mean±SD	6.85±4.20	4.67±4.11	8.82±6.29	
Median (min-max)	5 (1–16)	3 (1–14)	8 (0.25–21)	

Comparisons of estrogen, PTH, RANKL, TNF-α, and BMD levels among groups before and after the intervention

The comparison levels of estrogen, RANKL, TNF-α, PTH, and BMD among the walking, bone joint exercise, and control groups during pre- and post-treatment are presented in **Table 2**. The pre-intervention comparison among the three groups indicated no significant differences in estrogen levels (p=0.462), RANKL (p=0.876), TNF-α (p=0.370), and PTH (p=0.195) (**Table 2**). However, the BMD scores were significantly different (p=0.001) and post-hoc analyses indicated that the BMD scores were significantly different between the walking and control group (mean difference (MD): -0.792; 95%CI: -1.923–(-0.291); p=0.001) and between bone joint exercise and control group (MD: -0.578; 95%CI: -1.062–(-0.095); p=0.015) (**Figure 2A**). There were no significant differences in BMD scores between the walking intervention and bone joint exercise groups (MD: -0.214; 95%CI: -0.712–0.283; p=0.630).

Table 2. Comparisons of estrogen, RANKL, TNF- α, PTH, and BMD levels among groups before and after the intervention

Outcome	Group			*p*-value
	Walking (n=14)	Bone joint exercise (n=14)	Control (n=14)	
	Mean±SD	Mean±SD	Mean±SD	
Estrogen (ng/L)				
Pre-test	27.44±11.33	25.56±7.37	24.32±7.69	0.462[d]
Post-test	33.90±14.46	32.15±10.66	21.95±11.49	0.009[c*]
RANKL (pg/mL)				
Pre-test	31.79±8.56	36.44±16.62	30.26±4.01	0.876[d]
Post-test	27.86±10.26	27.26±10.14	29.85±3.95	0.076[c]
TNF-α (ng/L)				
Pre-test	35.53±17.85	37.42±15.86	29.40±8.83	0.370[d]
Post-test	30.01±17.61	32.93±12.03	30.76±7.59	0.352[c]
PTH (pg/mL)				
Pre-test	151.87±39.84	175.91±57.33	142.61±26.74	0.195[d]
Post-test	134.83±32.98	151.37±77.05	141.99±21.04	0.271[d]
BMD (score)				
Pre-test	-2.72±0.53	-2.50±0.49	-1.92±0.50	0.001[c*]
Post-test	-2.32±0.54	-2.22±0.50	-1.90±0.50	0.093[c]

BMD: bone mineral density; RANKL: receptor activator of nuclear factor kappa-β ligand; TNF-α: tumor necrosis factor-alpha; PTH: parathyroid hormone

Post-intervention analysis among the three groups revealed a significant difference in estrogen levels (p=0.009) (**Table 2**). However, no significant differences were found in the levels of RANKL (p=0.076), TNF-α (p=0.352), PTH (p=0.271), and BMD (p=0.093) (**Table 2**). Post-hoc tests for estrogen levels indicated a significant difference between the walking and control groups (median difference: 20.24; min-max: 11.29–58.54; p=0.016) and between bone joint exercise and control groups (median difference: 29.92; min-max: 15.84–54.61; p=0.004) (**Figure 2B**). There were no significant differences in estrogen levels between the walking and bone joint exercise groups.

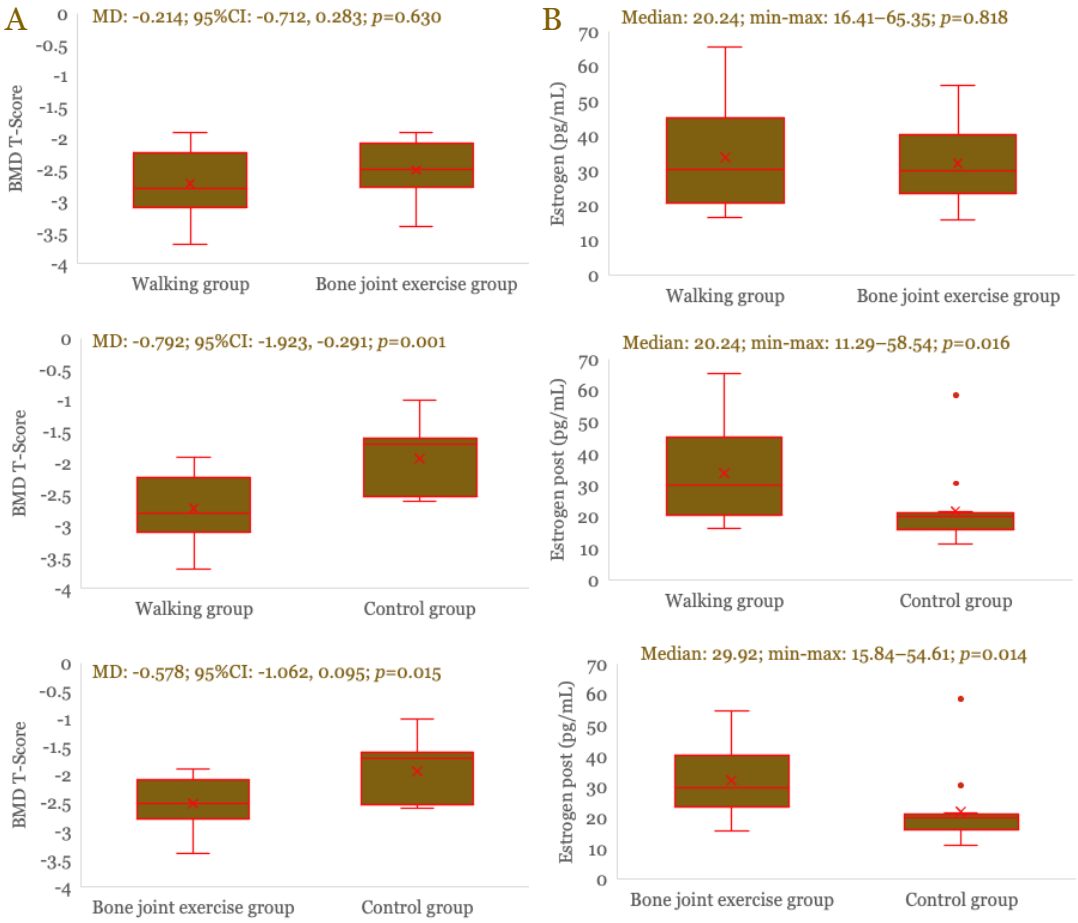

Figure 2. Post-hoc analyses of BMD and estrogen levels. (A) Post-hoc analyses depicting the comparison of different BMD levels pre-intervention between groups. (B) Post-hoc analyses depicting the comparison of different estrogen levels post-intervention between groups.

Effect of walking and exercise on estrogen, PTH, RANKL, TNF-α and BMD levels

The mean estrogen level in the walking group increased by 6.46 ng/L, from 27.44 ng/L to 33.90 ng/L (p=0.026), following the intervention (**Table 3**). Similarly, the levels also increased in the bone joint exercise group, 6.59 ng/L, from 25.56 ng/L to 32.15 ng/L (p=0.023). In contrast, the control group experienced a decrease of 2.37 ng/L from 24.32 ng/L to 21.95 ng/L, which was not statistically significant (p=0.300) (**Table 3**). The levels of RANKL after the intervention decreased by 3.93 pg/mL (p=0.019) and 9.18 pg/mL (p=0.002) in the walking and joint exercise group, respectively (**Table 3**). The control group showed a decrease of 0.41 pg/mL only from 30.26 pg/mL to 29.85 pg/mL (p=0.772) (**Table 3**). The levels of TNF-α did not decrease significantly in the walking group, from 35.53 ng/L to 30.01 ng/L (p=0.052), as well as in bone joint exercise and control groups, where TNF-α levels decreased by 4.49 ng/L (p=0.331) and 1.36 pg/mL (p=0.076), respectively (**Table 3**). The mean PTH level in the walking and bone joint exercise groups decreased by 17.04 pg/mL (p=0.022) and 4.49 pg/mL (p=0.048), respectively, while the reduction within control group was not statistically significant (p=0.925) (**Table 3**).

The BMD scores were increased significantly both in walking and bone joint exercise groups, from -2.72 to -2.32 (p=0.001) and from -2.50 to -2.22 (p<0.001), respectively (**Table 3**).

Table 3. Comparisons of estrogen, RANKL, TNF- α, PTH, and BMD levels before and after the intervention

Outcome	Group		
	Walking (n=14)	Bone joint exercise (n=14)	Control (n=14)
	Mean±SD	Mean±SD	Mean±SD
Estrogen (ng/L)			
Pre-test	27.44±11.33	25.56±7.37	24.32±7.69
Post-test	33.90±14.46	32.15±10.66	21.95±11.49
p-value	0.026 [b*]	0.023 [a*]	0.300 [b]
RANKL (pg/mL)			
Pre-test	31.79±8.56	36.44±16.62	30.26±4.01
Post-test	27.86±10.26	27.26±10.14	29.85±3.95
p-value	0.019 [b*]	0.002 [b*]	0.772 [a]
TNF-α (ng/L)			
Pre-test	35.53±17.85	37.42±15.86	29.40±8.83
Post-test	30.01±17.61	32.93±12.03	30.76±7.59
p-value	0.052 [a]	0.331 [b]	0.001 [a*]
PTH (pg/mL)			
Pre-test	151.87±39.84	175.91±57.33	142.61±26.74
Post-test	134.83±32.98	151.37±77.05	141.99±21.04
p-value	0.022 [b*]	0.048 [b*]	0.925 [b]
BMD (score)			
Pre-test	-2.72±0.53	-2.50±0.49	-1.92±0.50
Post-test	-2.32±0.54	-2.22±0.50	-1.90±0.50
p-value	0.001 [a*]	<0.001 [a*]	0.189 [a]

BMD: bone mineral density; RANKL: receptor activator of nuclear factor kappa-β ligand; TNF-α: tumor necrosis factor-alpha; PTH: parathyroid hormone
[a] Analyzed using paired sample Student t-test
[b] Analyzed using Wilcoxon test
[c] Analyzed using ANOVA test
[d] Analyzed using Kruskal-Wallis test
[*] Statically significant at p<0.05

Discussion

Our results indicated that both walking and bone joint exercise interventions significantly increased estrogen levels (**Table 3**). This suggests that moderate-intensity physical activities, such as walking, could effectively stimulate estrogen production or release, which is vital for bone health and metabolism, particularly in menopausal women [18]. Similarly, bone joint exercises led to a significant rise in estrogen levels, from an average of 25.56 ng/mL before the intervention to 32.15 ng/mL after, when performed at the same frequency and intensity as walking. Such physical activity enhances blood circulation and hormonal stimulation, thereby promoting estrogen production [18,19]. These findings align with a study that demonstrated physical activity can elevate estrogen levels and consequently improve bone density [20].

Both the walking and bone joint exercise groups in this study showed a decrease in PTH levels post-intervention (**Table 3**). These findings align with a previous study, which demonstrated that structured exercise and walking could lower PTH levels by enhancing bone sensitivity to calcium, thereby reducing the need for PTH to regulate blood calcium levels [21]. As PTH decreases, the activity of osteoclasts (cells that resorb bone) diminishes, which slows down bone mass loss [22]. This suggests that physical activity not only improves calcium sensitivity but also reduces the need for PTH, promoting bone remodeling and helping to prevent osteoporosis in menopausal women [23]. Mechanical stress, such as that induced by exercise, is a critical factor in regulating bone formation [24]. Osteocytes, the primary bone cells involved in sensing and transmitting mechanical loads, convert mechanical stimuli into intercellular signals through a specialized lacunocanalicular network. During exercise, osteocytes detect changes in mechanical stress, transmit signals to neighboring cells, and coordinate the activities of osteoblasts, osteoclasts, and the extracellular matrix within the bone microenvironment [25]. This process stimulates bone turnover and leads to bone deposition [26]. In addition to osteocytes, other bone cells, such as osteoblasts, also play a role in sensing mechanical stimuli [27].

Our study also found that the walking intervention led to a significant decrease in RANKL levels (**Table 3**), highlighting its potential as a beneficial approach for maintaining bone health and preventing osteoporosis. Similarly, bone joint exercises also showed a notable reduction in RANKL levels (**Table 3**). These findings align with a previous study, which demonstrated that both walking and bone joint exercise lowered RANKL levels by reducing RANKL expression and boosting osteoprotegerin production, thereby decreasing osteoclast activity and bone resorption [28]. Additionally, another study explained that mechanical stimulation from exercise prompts osteoblasts to form new bone, while hormonal changes elevate estrogen levels, further supporting bone formation [13]. Physical activity also reduces pro-inflammatory cytokines like TNF-α, fostering a more favorable environment for bone health [29].

In addition, walking and bone joint exercises significantly improved BMD (**Table 3**). Joint flexibility and strength exercises effectively improved BMD, indicating that structured physical activities, like bone joint exercises, may reduce the risk of bone loss and support overall bone health [30]. This aligns with a study that showed physical activity positively influences BMD by mechanically stimulating osteocytes and osteoblasts to form new bone matrix [23]. Additionally, hormonal changes, including increased estrogen and testosterone levels, further support bone formation. Physical activity also lowers pro-inflammatory cytokines like TNF-α, reduces RANKL levels, and decreases osteoclast activity, thereby enhancing BMD and promoting bone remodeling [14].

There are some limitations of this study including a relatively small sample size, which may have reduced the generalizability of the findings. A larger sample would have yielded more robust and representative results. Additionally, the eight-week intervention may not have been sufficient to observe long-term improvements in hormone balance and bone remodeling. Extending the study duration could have offered further insights into the effects of sustained physical activity. Moreover, other dietary and lifestyle factors that influenced hormone levels and bone health were not considered, although they are important variables that should have been addressed in future studies to better understand their potential impact on the outcomes.

Conclusion

Walking and bone joint exercise interventions significantly enhance bone remodeling in menopausal women. Structured physical activities, such as walking and bone joint exercises, could notably improve bone reconstruction in this population. This study illustrates how exercise contributes to increasing BMD and reducing bone resorption among menopausal women. The findings could be integrated into menopause health guidelines at hospitals and clinics, informing the development of exercise regimens and supporting ongoing monitoring to optimize outcomes for bone health. Long-term evaluations are recommended to further assess the effects of structured physical activity on hormonal balance and bone health in menopausal women, considering the influence of additional factors such as diet and lifestyle.

Ethics approval

Ethical approval has been obtained from the Health Research Ethics Committee, Universitas Malahayati, Lampung, Indonesia, No.3258/EC/KEP-UNMAL/III/2023.

Acknowledgments

We would like to thank the Pringsewu Regency Health Service, Gading Rejo Community Health Center, Wates Community Health Center, and Ambarawa Community Health Center in Pringsewu Regency, Lampung Province, Indonesia. We also extend our gratitude to the Physiology Laboratory, Faculty of Medicine, Universitas Brawijaya, and to all parties who assisted in this study.

Competing interests

The authors declare that there are no conflicts of interest.

Funding

This study was supported by a Doctoral Dissertation Research Grant from the Directorate of Research, Technology, and Community Service, Ministry of Education, Culture, Research, and Technology, as stated in Internal Contract Decree No. 1076.1/UN27.22/PT.01.03/2024.

Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

How to cite

Pasa C, Pamungkasari EP, Doewes M, *et al*. Effect of walking and bone joint exercise on enhancing bone remodeling in menopausal women: A randomized controlled trial. Narra J 2024; 4 (3): e1321 - http://doi.org/10.52225/narra.v4i3.1321.

References

1. Khavinson V, Popovich I, Mikhailova O. Towards realization of longer life. Acta Biomed 2020;91(3):e2020054.
2. Salari N, Ghasemi H, Mohammadi L, *et al.* The global prevalence of osteoporosis in the world: A comprehensive systematic review and meta-analysis. J Orthop Surg Res 2021;16(1):609.
3. Pusat Data dan Informasi Kementerian Kesehatan RI. Situasi osteoporosis di Indonesia, 2020. Jakarta: Kemenkes RI; 2020.
4. Docaj A, Carriero A. Bone health: Quality versus quantity. J Pediatr Orthop Soc N Am 2024;7:100054.
5. Wang F, Zheng L, Theopold J, *et al.* Methods for bone quality assessment in human bone tissue: a systematic review. J Orthop Surg Res 2022;17(1):174.
6. Cheng CH, Chen LR, Chen KH. Osteoporosis due to hormone imbalance: An overview of the effects of estrogen deficiency and glucocorticoid overuse on bone turnover. Int J Mol Sci 2022;23(3):1376.
7. Mills EG, Yang L, Nielsen MF, *et al.* The relationship between bone and reproductive hormones beyond estrogens and androgens. Endocr Rev 2021;42(6):691-719.
8. Chainy GBN, Sahoo DK. Hormones and oxidative stress: An overview hormones and oxidative stress: An overview. Free Radic Res 2019;54(1):1-26.
9. Lara-Castillo N. Estrogen signaling in bone. Appl Sci 2021;11(10):4439.
10. Puspitadewi SR, Kusdhany LS, Masulili SLC, *et al.* The role of parathyroid hormone in alveolar bone resorption on postmenopausal women. Open Dent J 2020;14(1):82-87.
11. Bhattarai HK, Shrestha S, Rokka K, *et al.* Vitamin D, calcium, parathyroid hormone, and sex steroids in bone health and effects of aging. J Osteoporos 2020;2020:9324505.
12. Takegahara N, Kim H, Choi Y. RANKL biology. Bone 2022;159:116353.
13. Tobeiha M, Moghadasian MH, Amin N, *et al.* RANKL/RANK/OPG pathway: A mechanism involved in exercise-induced bone remodeling. Biomed Res Int 2020;2020:6910312.
14. Amer OE, Wani K, Ansari MGA, *et al.* Associations of bone mineral density with RANKL and osteoprotegerin in Arab postmenopausal women: A cross-sectional study. Medicina 2022;58(8):976.
15. Marahleh A, Kitaura H, Ohori F, *et al.* TNF-α directly enhances osteocyte RANKL expression and promotes osteoclast formation. Front Immunol 2019;10:2925.
16. Chang X, Xu S, Zhang H. Regulation of bone health through physical exercise: Mechanisms and types. Front Endocrinol 2022;13:1029475.
17. ISCD. 2023 ISCD official positions adult. Connecticut: International Society for Clinical; 2023.
18. Elliott CG, Vidal-Almela S, Harvey P, *et al.* Examining the role of physical activity interventions in modulating androgens and cardiovascular health in postmenopausal women: A narrative review. CJC Open 2022;5(1):54-71.
19. Oizumi R, Sugimoto Y, Aibara H. The potential of exercise on lifestyle and skin function: Narrative review. JMIR Dermatol 2024;7:e51962.
20. Sipilä S, Törmäkangas T, Sillanpää E, *et al.* Muscle and bone mass in middle-aged women: Role of menopausal status and physical activity. J Cachexia Sarcopenia Muscle 2020;11(3):698-709.
21. Lombardi G, Ziemann E, Banfi G, *et al.* Physical activity-dependent regulation of parathyroid hormone and calcium-phosphorous metabolism. Int J Mol Sci 2020;21(15):1-50.

22. Martin TJ, Seeman E. Bone remodeling and modeling: Cellular targets for antiresorptive and anabolic treatments, including approaches through the parathyroid hormone (PTH)/PTH-related protein pathway. Neurospine 2023;20(4):1097-1109.
23. Jan R, Khan F, Afridi M, *et al.* Effects of physical activity on bone health: Investigate how different types of exercise influence bone density and strength. Biol Clin Sci Res J 2023;2023(1):582.
24. Liu P, Tu J, Wang W, *et al.* Effects of mechanical stress stimulation on function and expression mechanism of osteoblasts. Front Bioeng Biotechnol 2022;10:830722.
25. Hu C, Qin QH. Bone remodeling and biological effects of mechanical stimulus. AIMS Bioeng 2020;7(1):12-28.
26. Leser JM, Harriot A, Buck HV, *et al.* Aging, osteo-sarcopenia, and musculoskeletal mechano-transduction. Front Rehabil Sci 2021;2:782848.
27. Stroh AM, Stanford KI. Exercise-induced regulation of adipose tissue. Curr Opin Genet Dev 2023;81:102058.
28. Du X, Zhang C, Zhang X, *et al.* The impact of Nordic walking on bone properties in postmenopausal women with pre-diabetes and non-alcohol fatty liver disease. Int J Environ Res Public Health 2021;18(14):7570.
29. Małkowska P, Sawczuk M. Cytokines as biomarkers for evaluating physical exercise in trained and non-trained individuals: A narrative review. Int J Mol Sci 2023;24(13):11156.
30. Shojaa M, Von Stengel S, Schoene D, *et al.* Effect of exercise training on bone mineral density in post-menopausal women: A systematic review and meta-analysis of intervention studies. Front Physiol 2020;11:652.