# Treadmill weight-bearing exercise versus electromagnetic field on bone mineral density in women with osteoporosis secondary to aromatase inhibitors: A randomized controlled trail

激

**Haidy Nadi Ashem1, Amira Hussein Draz2, Amr Almaz Abdel-aziem3, Marwa Esmael Hasanin4, Mohamed Abdelrahman5**

1Department of Physical Therapy for Surgery, Faculty of Physical Therapy, Cairo University
2Department of basic science, Faculty of Physical Therapy, Cairo university
3Department of Biomechanics, Faculty of Physical Therapy, Cairo University
4Department of Physical Therapy for Woman's Health, Faculty of Physical Therapy, Cairo University
5Department of Clinical Oncology, Faculty of Medicine, Cairo University

## Abstract

Background and objective. Aromatase inhibitor therapy for postmenopausal women with breast cancer is associated with a decrease in bone mineral density (BMD). Both Pulsed electromagnetic fields (PEMFs) and treadmill walking exercises have a positive effect on bone osteoporosis. So, this study aimed to evaluate the effect of PEMFs and treadmill weight bearing exercises on the BMD of the lumbar spine in women with osteoporosis secondary to adjuvant hormonal treatment with aromatase inhibitor.

Methods. A total of 45 female breast cancer patients with osteoporosis secondary to adjuvant aromatase inhibitor were randomly assigned into three equal groups. The control group received only pharmacological treatment (Bisphosphonates, Calcium and Vitamin D). In the other 2 groups, the same drug therapy was consolidated by a program of treadmill weight bearing exercises (treadmill exercise group; 30 min/session, 3 sessions/week), and PEMFs (PEMFs group; 30 min/session, 3 sessions/week). The BMD of the spinal vertebrae was assessed before and after 3 months of intervention by using the Dual energy X-rays (DEXA).

Results, The post value of the PEMFs group was significantly higher than those of the treadmill exercise group and the control group ($p = 0.002$, 0.001 respectively), and the post value of the treadmill exercise group was significantly higher than that of the control group ($p= 0.001$), The post values of the three groups were higher than pre values ($p = 0.001$).

Conclusion. Both treadmill weight bearing exercises and PEMFs were effective in improving the BMD. Moreover, the BMD response to PEMFs was better than treadmill weight bearing exercise.

## Key words:

Bone mineral density, weight bearing exercise, pulsed electromagnetic field, breast cancer, aromatase

## 摘要

## 关键词：

## Introduction

Aromatase inhibitors of third generation is now a standard of care for postmenopausal women with hormone receptor positive early stage and metastatic breast cancer [1,2]. It is associated with a decrease in bone mineral density (BMD), and increasing the fracture risks [3]. By stopping the conversion of androgens to estrogens in peripheral tissue, they have proven to suppress plasma and tissue estrogen level by > 98% in vivo. Furthermore, it is well known that estrogens have a positive effect on bone metabolism by stimulating bone growth and inhibiting bone resorption. So, their depletion in patients with endocrine responsive breast cancer leads to increased bone demineralization and finally osteoporosis occurs [4–6].

Due to the association of aromatase inhibitors and decreased BMD, practical guidelines have been developed for the management of these important side effects. Firstly, it is well accepted that all postmenopausal women, initiating therapy with aromatase inhibitors should receive calcium and vitamin D supplements [7]. Recently, Hong et al. [8] reported that the long-term adjuvant aromatase inhibitors treatment negatively influenced bone quality in addition to BMD in patients with breast cancer. They suggested that early monitoring and management are needed in patients with breast cancer who are starting aromatase inhibitors.

The risk of bone fractures increases in patients with osteoporosis, which are associated with increased mortality and lower quality of life. Protein and calcium intakes, and vitamin D supplies, together with regular weight-bearing physical exercise are the corner stone of fracture prevention [9]. Weight-bearing exercise is one where bones and muscles work against the force of gravity. This is any exercise in which our feet and legs carry our weight. Activities like walking, jogging, aerobics, dancing, stair climbing and skating are all examples of weight-bearing exercise. If one has osteoporosis, one should walk preferable, at least a mile a day [10].

Benedetti et al. [11] showed that walking alone did not appear to improve bone mass; however it is able to limit its progressive loss. In fact, to make the weight-bearing exercises effective, they must reach the mechanical intensity useful to determine an important ground reaction force. In subjects with osteoporosis, addition of weight-bearing exercise program to medical treatment increases BMD more than non weight-bearing exercise [12]. The treadmill walking exercises stimulate bone synthesis and decrease bone resorption in postmenopausal women with osteoporosis [13]. Moreover, the mechanism for the positive response of lumbar BMD to moderate walking exercise in women with osteopenia/osteoporosis appears to be the suppression of bone turnover [14].

The pulsed electromagnetic fields (PEMFs) technologies are a useful therapies for the treatment of delayed-union fractures and chronic wounds. It generates short bursts of electrical current in injured tissue without producing heat or interfering with nerve or muscle function [15]. The physical PEMFs stimulation begins to send cascades of signals, which effectively improve osteogenesis and angiogenesis in an coordinated spatiotemporal manner and ultimately enhance the self-repair capability of bone tissues [16].

At the beginning, the PEMFs was applied in treating patients with delayed fracture healing and non-unions, and later, it turned out to be a potential and effective therapy for postmenopausal osteoporosis. It can enhance osteoblastogenesis and inhibit osteoclastogenesis, thus contributing to an increase in bone mass and strength [17]. So, it has been recently employed as an effective method to enhance bone repair because of their non-invasiveness, safety, lack of side effects, convenience, and superior treatment prospects in several refractory bone diseases, such as non-unions and delayed healings of fractures [18,19], osteoporosis [20,21] and osteonecrosis of the femoral head [22].

To the best of our knowledge, there are no studies comparing between the effect of treadmill exercises and PEMFs on the BMD of women with osteoporosis due to aromatase inhibitor therapy. Moreover, Bosco [23] found a lack of the recommendations in order to prevent osteoporosis related to the administration of aromatase inhibitors. So, this study was conducted to evaluate the effect of the PEMFs and treadmill weight-bearing exercises on the BMD of the lumbar spine in women with osteoporosis secondary to adjuvant hormonal treatment by aromatase inhibitor post mastectomy.

## Patients and methods

### Participants

Of the 50 women with osteoporosis secondary to aromatase inhibitor hormonal treatment post mastectomy (After 6 months of starting aromatase inhibitor), 45 were enrolled in the study, aged 45-55 years. They participated in the study after signing a written informed consent form before data collection, their Dual energy X-ray absorptiometry (DEXA) was more than -2.5. Women with cardiopulmonary disorders, chronic hypertension or had any contraindication for PEMFs as implanted device, pacemaker, active tuberculosis, acute viral conditions, severe atherosclerosis, neurological diseases with seizure, hyperthyroidism and viral infections were excluded from the study.

This was a randomized, controlled study conducted in the outpatient clinics of the Cairo University hospital, Egypt. The participants were randomly assigned in to three groups (treadmill exercises, PEMFs and control groups) by an independent person who was blinded to the research protocol and not involved in the study procedure. He selected numbers from sealed envelopes containing the numbers of the participants. The study was performed in accordance with the Declaration of Helsinki and approved by the local institutional review board (P.T.REC/012/002227) and a written consent form was signed by each participant. Flow of participants through the stages of the study is shown in (Fig. 1).

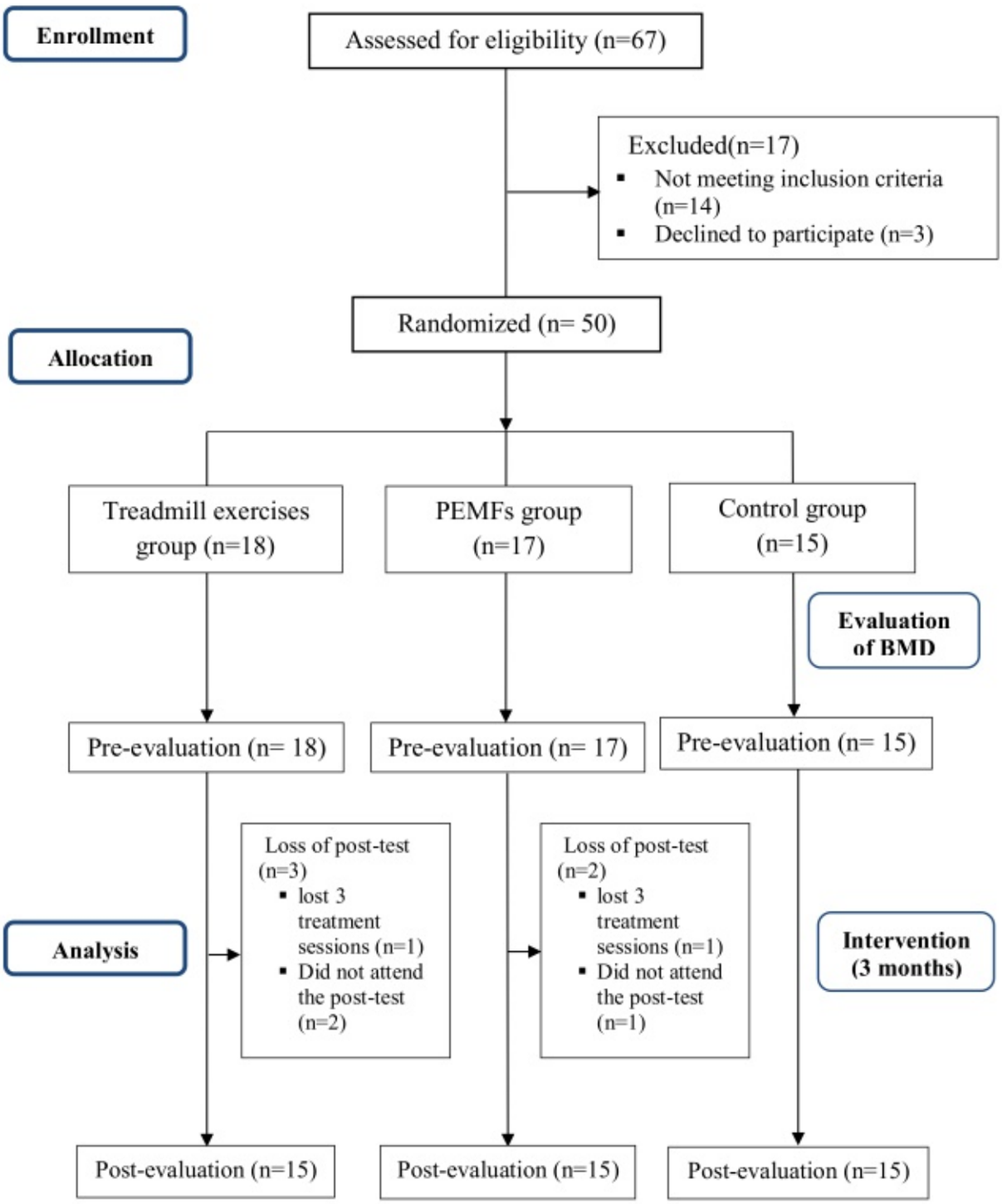


**Figure 1. Flowchart of the study processes. BMD indicates bone mineral density**

**Procedures**

The BMD of the lower lumbar spine was evaluated by using the DEXA (GE Lunar iDXA with encore 12.0 software, GE Healthcare Lunar, Madison, USA) before and after 12 weeks of treatment, the average BMD of the four lumbar vertebrae (L1-L4) will be extracted.. The DEXA is one of the most accurate methods to assess the BMD measured at the spine, hip or total body [24].

The three groups received the same pharmacological therapy; Bisphosphonate (Zodronic acid 3mg/dl), calcium (1-1.2 mg), and vitamin D (0.5 mg/day). Control group (n = 15), "drugs-only". The other 2 groups were additionally received the following types of intervention: The treadmill exercise group (n = 15) received a treadmill weight-bearing exercises for 30 minutes (3 sessions/week), the treatment protocol was achieved by using an electronic treadmill Kettler- marathon model; 7899-800, Germany. The treadmill weight-bearing exercises was consisted of 5 minutes warm up, twenty minutes walking on treadmill (moderate phase according to the Borg scale). Walking on the treadmill with moderate speed and increase speed gradually as the patient can and increase inclination of the treadmill gradually and five minutes cool

down. The patients were instructed to avoid vigorous activities or running [25], while those assigned to the PEMFs group (n = 15) received PEMFs (30 min/session, 3 sessions/week) with the frequency set at 72Hz [26], by using the PEMFs device (MAS Mini Maximum power: 100 Gauss, Frequency: 50-100Hz, 10 mTesla, Austria), while they were lying supine on the PEMF mat fully clothed, without any metal objects. The PEMFs was delivered perpendicular to the lumbar spine. All participants were asked to refrain from seeking any other physical therapy or medications throughout the study period.

**Statistical analysis**

Data were analyzed using SPSS Statistics for Windows, Version 20.0 (Armonk, NY: IBM Corp). Analysis of variance (ANOVA) was used to compare between the treadmill weight-bearing exercises, PEMF, and routine medical treatment on the BMD of the lumbar spine. The parametric analysis of the data was conducted as the results of the Shapiro-wilk test showed that the data were normally distributed ($p > 0.05$). The least significant difference was used to determine the source of difference with $p < 0.05$.

## Results

There was no significant difference between groups regarding the age, height, weight and body mass index (BMI) ($p = 0.457, 0.184, 0.106, 0.442$ respectively) as shown in table 1. Regarding the lumbar vertebrae BMD, there was no significant difference between the pre values of the three groups ($p = 0.600$). However, there was a significant difference between the post values of the three groups ($p = 0.001$). The post value of the pulsed electromagnetic group was significantly higher than those of the treadmill exercise group and the control group ($p = 0.002, 0.001$ respectively), and the post value of the treadmill exercise group was significantly higher than that of the control group ($p = 0.001$), The post values of the three groups were higher than pre values ($p = 0.001$), as shown in table 2.

**Table 1. Demographic data of the participants**

| Characteristics | Treadmill exercise group, n=15 | Pulsed electromagnetic group, n=15 | Control group, n=15 | p value |
|---|---|---|---|---|
| Age (years) | 53.87 ± 6.90 | 54.67 ± 6.48 | 56.67 ± 5.26 | 0.457 |
| Height (cm) | 161.13 ± 3.80 | 159.33 ± 3.75 | 158.73 ± 3.37 | 0.184 |
| Weight (kg) | 75.13 ± 3.34 | 73.53 ± 4.39 | 71.93 ± 4.28 | 0.106 |
| BMI (kg/m$^2$) | 28.93 ± 0.49 | 28.62 ± 0.86 | 28.54 ± 1.16 | 0.442 |

*Data are presented as mean ± standard deviation, BMI; body mass index, p> 0.05 means non significant difference*

**Table 2. The lumbar spinal bone mineral density (g/cm2)**

| Lumbar BMD | Treadmill exercise group, n=15 | Pulsed electromagnetic group, n=15 | Control group, n=15 | p value |
|---|---|---|---|---|
| Pre | 0.48 ± 0.09 | 0.48 ± 0.08 | 0.46 ± 0.08 | 0.600 |
| Post | 0.66 ± 0.09 | 0.73 ± 0.05 | 0.51 ± 0.07 | 0.001 |
| p-value | 0.001 | 0.001 | 0.001 | |

*Data are presented as mean ± standard deviation, BMD: bone mineral density, p< 0.05 means significant difference*

## Discussion

The results of the current study revealed that the treadmill weight-bearing exercises and PEMFs were effective in improving the BMD of the lumbar spine. Moreover, the PEMFs was more effective than the treadmill weight-bearing exercise in women with osteoporosis secondary to aromatase inhibitors. Osteoporosis primarily occurs due to hormonal imbalances which interfere with osteoblastic activity that requires progesterone to remain healthy and youthful also estrogen is needed to stimulate skeletal growth and maintain healthy bone. However, treatment with synthetic progesterone or estrogen therapy have a risk of developing uterine and breast cancer [27].

The improvement of the BMD of the treadmill weight-bearing exercises group concurs with the findings of Rafiq et al. [28] who concluded that weight-bearing exercises combined with medication was more effective than medication alone in improving the post-menopausal osteoporosis. Moreover, the premenopausal women who participated in a low to moderate intensity exercise regimen had higher bone mineral densities than women who were not exercising regularly [29]. Also, the current finding agrees with a study which stated that "T-score" of the neck of the femur, significantly increased after the application of combined weight- and non weight-bearing exercise programs, suggesting that exercises can be effective in decreasing bone loss and main-

taining good bone quality after menopause. The significant positive changes of "T-score" in the weight-bearing exercise group than the non weight-bearing exercises, indicated that weight-bearing had more influence on BMD especially on weight-bearing bones. The mechanical loads of weight-bearing activities are transmitted to the skeleton by muscle pull and gravitational forces where the bone cells selectively respond to different mechanical stresses to increase or decrease BMD [30].

Weight-bearing and resistance exercises that improve muscle strength are essential for preserving the health of the musculoskeletal system [31]. Roghani et al.[13] concluded that the submaximal aerobic exercise with and without external loading stimulate bone synthesis and decrease bone resorption in postmenopausal women with osteoporosis, which is coincident with the increase in BMD of the treadmill exercise group. Moreover, Gombos et al.[32] examined the direct effects of a single session of resistance exercise or walking on biochemical markers of bone metabolism in patients with low bone mass. They found that the resistance exercise influenced the serum concentrations of carboxy-terminal cross-linked telopeptide of type I collagen, a marker of bone resorption, but walking did not. However, 60-minute, middle intensity training and the brisk walking have an immediate effect on bone metabolic markers [33] which support the result of the treadmill weight-bearing exercise group.

The improvement of the PEMFs group is supported by Wang et al.[34] who reported that PEMFs promote bone formation by activating soluble adenylyl cyclase (sAC), cyclic adenosine monophosphate (cAMP), protein kinase A (PKA), and cAMP response element-binding protein (CREB) signaling pathways of osteoblasts directly or indirectly. Furthermore, the PEMFs could accelerate fracture healing and enhance bone mass by stimulating the osteoblastic functions and, hence, regulates downstream osteogenesis-associated gene/protein expressions [35].

In addition, Li et al. [36] found that the PEMFs therapy improves BMD, increase growth of osteoblasts and positively influence bone remodeling via cytokines, prostaglandins and cell growth factors. Moreover, Jing et al. [37] reported that the electromagnetic stimulation has been documented to treat recalcitrant problems of the musculoskeletal system. It was also suggested that the PEMFs therapy may be used in early stages of bone regeneration to enhance callus formation, providing earlier stabilization and better bone unions for bone grafts [37].

It is noticed that the improvement of PEMFs group was higher than that of the treadmill weight-bearing exercises that is consistent with the findings of Elsisi et al.[38] who concluded that the low-frequency, low-intensity PEMFs and circuit weight training programs are effective modalities in increasing BMD especially in elderly women. Moreover, a 10-min exposure to low-intensity PEMFs showed a significant increase in self-selected gait speed and stride length from baseline in older adults (≥ 70 years) with low bone mineral density [39]. However, resistance training for 30-40 minutes is effective for improving bone formation and joint function in severe haemophilia A patients with osteoporosis compared to 60 minutes of PEMFs [40].

Tabrah et al. [26] examined the effect of PEMFs with a frequency similar to that used in this study (72Hz) on bone density of women with osteoporosis. They concluded that the PEMFs was useful in the prevention and treatment of osteoporosis. In spite of the high frequency and intensity of the PEMFs therapy that used in the current study, the result of PEMFs group is consistent with the findings of previous studies [38,39] that adopted low-frequency, low-intensity PEMFs and the study of Yan et al. [21] who used moderate frequency and different intensities PEMFs. However, Wang et al.[41] reported that the clinicians should be careful about the safety of PEMF treatment and strictly choose the frequency and intensity of PEMFs in preventing or treating the osteoporosis of the patients after resection of ovarian cancer.

This study also had a number of limitations. It examined only the BMD of the participants without consideration of markers of bone formation. The sample size was small that may inversely affect on the generalization of the study's findings. There was no follow up assessment of the BMD to illustrate the sustained effect of the treadmill weight bearing exercises and PEMFs. The current study was conducted on women with osteoporosis secondary to aromatase inhibitors hormonal treatment post mastectomy. So, further studies are needed to clarify the effects of the treadmill weight-bearing exercises and PEMFs on elderly women (above 65 years) with osteoporosis due to other causes. More research work is required to examine the effects of both interventions on the overall functional capacity, body balance and gait abilities. Finally, according to the recommendation of Wang et al. [41] the effect of different frequencies and intensities of PEMFs on secondary osteoporosis should be examined in the future researches.

## Conclusion

The findings of the current study displayed that both treadmill weight-bearing exercise and PEMFs were effective in improving the lumbar spine BMD in breast cancer female suffering from osteoporosis secondary to aromatase inhibitors hormonal treatment post mastectomy. Moreover, the PEMFs was more effective in improving the BMD than the treadmill weight-bearing exercise.

Acknowledgements: The researchers wish to acknowledge our gratitude to participants for their patience during conduction of this study.

Adres do korespondencji / Corresponding author

**Amira Hussein Draz**

E-mail: amira.draz@pt.cu.edu.eg

## Piśmiennictwo/ References


1. Burstein HJ, Prestrud AA, Seidenfeld J, Anderson H, Buchholz TA, Davidson NE, et al. American Society of Clinical Oncology clinical practice guideline: Update on adjuvant endocrine therapy for women with hormone receptor-positive breast cancer. J Clin Oncol 2010;28:3784–96. doi:10.1200/JCO.2009.26.3756.
2. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thürlimann B, Senn HJ. Progress and promise: Highlights of the international expert consensus on the primary therapy of early breast cancer 2007. Ann Oncol 2007;18:1133–44. doi:10.1093/annonc/mdm271.
3. Y I. [Secondary osteoporosis. Cancer treatment-induced bone loss.]. Clin Calcium 2018;28:1665–70. doi:CliCa181216651670.
4. Ghazi M RC. Hormonal deprivation therapy-induced osteoporosis in postmenopausal women with breast cancer. Best Pr Res Clin Rheumatol 2009;23:805–11.
5. McCaig FM, Renshaw L, Williams L et al. A study of the effects of the aromatase inhibitors anastrozole and letrozole on bone metabolism in postmenopausal women with estrogen receptor-positive breast cancer. Breast Cancer Res Treat 2010;119:643–51.
6. Folkestad L, Bjarnason NH, Bjerregaard JK et al. The effect of aromatase inhibitors on bone metabolism. Basic Clin Pharmacol Toxicol 2009;104:3–10.
7. Markopoulos C, Tzoracoleftherakis E, Polychronis A, Venizelos B, Dafni U, Xepapadakis G, et al. Management of anastrozole-induced bone loss in breast cancer patients with oral risedronate: Results from the ARBI prospective clinical trial. Breast Cancer Res 2010;12:R24. doi:10.1186/bcr2565.
8. Hong AR, Kim JH, Lee KH, Kim TY, Im SA, Kim TY, et al. Long-term effect of aromatase inhibitors on bone microarchitecture and macroarchitecture in non-osteoporotic postmenopausal women with breast cancer. Osteoporos Int 2017;28:1413–22. doi:10.1007/s00198-016-3899-6.
9. R R. Postmenopausal osteoporosis: Assessment and management. Best Pr Res Clin Endocrinol Metab 2018;32:739–57.
10. Bassey EJ. Exercise for prevention of osteoporotic fracture. Age Ageing 2001;30:29–31. doi:10.1093/ageing/30.suppl_4.29.
11. Benedetti MG, Furlini G, Zati A MG. The effectiveness of physical exercise on bone density in osteoporotic patients. Biomed Res Int 2018;2018. doi:org/10.1155/2018/4840531.
12. Shanb A, Youssef E. The impact of adding weight-bearing exercise versus nonweight bearing programs to the medical treatment of elderly patients with osteoporosis. J Fam Community Med 2014. doi:10.4103/2230-8229.142972.
13. Roghani T, Torkaman G, Movasseghe S, Hedayati M, Goosheh B, Bayat N. Effects of short-term aerobic exercise with and without external loading on bone metabolism and balance in postmenopausal women with osteoporosis. Rheumatol Int 2013;33:291–8. doi:10.1007/s00296-012-2388-2.
14. Yamazaki S, Ichimura S, Iwamoto J, Takeda T TY. Effect of walking exercise on bone metabolism in postmenopausal women with osteopenia/osteoporosis. Metab, J Bone Min 2004;22:500–8.
15. Aaron RK, Ciombor DMK, Simon BJ. Treatment of Nonunions with Electric and Electromagnetic Fields. Clin Orthop Relat Res 2004;419:21–9. doi:10.1097/00003086-200402000-00005.
16. Yuan J, Xin F, Jiang W. Underlying Signaling Pathways and Therapeutic Applications of Pulsed Electromagnetic Fields in Bone Repair. Cell Physiol Biochem 2018;46:1581–94. doi: 10.1159/000489206.
17. Zhu S, He H, Zhang C, Wang H, Gao C, Yu X HC. Effects of pulsed electromagnetic fields on postmenopausal osteoporosis. Bioelectromagnetics 2017;38:406–24.
18. Selvamurugan N, He Z, Rifkin D, Dabovic B, Partridge NC. Pulsed Electromagnetic Field Regulates MicroRNA 21 Expression to Activate TGF- β Signaling in Human Bone Marrow Stromal Cells to Enhance Osteoblast Differentiation. Stem Cells Int 2017. doi:10.1155/2017/2450327.
19. Streit A, Watson BC, Granata JD, Philbin TM, Lin HN, O'Connor JP, et al. Effect on Clinical Outcome and Growth Factor Synthesis with Adjunctive Use of Pulsed Electromagnetic Fields for Fifth Metatarsal Nonunion Fracture: A Double-Blind Randomized Study. Foot Ankle Int 2016;37:919–23. doi:10.1177/1071100716652621.
20. Zhu S, He H, Zhang C, Wang H, Gao C, Yu X HC. Effects of pulsed electromagnetic fields on postmenopausal osteoporosis. Bioelectromagnetics 2017;38:406–24.
21. Yan JL, Zhou J, Ma HP, Ma XN, Gao YH, Shi WG, et al. Pulsed electromagnetic fields promote osteoblast mineralization and maturation needing the existence of primary cilia. Mol Cell Endocrinol 2015;404:132–40. doi:10.1016/j.mce.2015.01.031.
22. Leo M, Milena F, Ruggero C, Stefania S, Giancarlo T. Biophysical stimulation in osteonecrosis of the femoral head. Indian J Orthop 2009;43:17–21. doi:10.4103/0019-5413.45319.
23. Bosco D. Osteoporosis and aromatase inhibitors: Experience and future prospects. Clin Cases Miner Bone Metab 2012.
24. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis Prevention, Diagnosis, and Therapy. JAMA J Am Med Assoc 2001. doi: 10.1001/jama.285.6.785.
25. Turner CH, Robling AG. Designing exercise regimens to increase bone strength. Exerc Sport Sci Rev 2003;31:45–50. doi:10.1097/00003677-200301000-00009.
26. Tabrah F, Hoffmeier M, Gilbert F, Batkin S, Bassett CAL. Bone density changes in osteoporosis-prone women exposed to pulsed electromagnetic fields (PEMFs). J Bone Miner Res 1990;5:437–42. doi:10.1002/jbmr.5650050504.
27. Schwartz Z, Fisher M, Lohmann CH, Simon BJ, Boyan BD. Osteoprotegerin (OPG) production by cells in the osteoblast lineage is regulated by pulsed electromagnetic fields in cultures grown on calcium phosphate substrates. Ann Biomed Eng 2009. doi:10.1007/s10439-008-9628-3.
28. Junaid Ijaz M, Rafiq S, Zia S, Anjum Shahid H, Adeel M. Role Of weight-bearing exercises In the treatment of post-menopausal osteoporosis. J Coll Physicians Surg Pakistan 2018;28:122–5. doi:10.29271/jcpsp.2018.02.122.
29. Hartard M, Haber P, Ilieva D, Preisinger E, Seidl G, Huber J. Systematic strength training as a model of therapeutic intervention: A controlled trial in postmenopausal women with osteopenia. Am J Phys Med Rehabil 1996;75:21–8. doi:10.1097/00002060-199601000-00006.
30. Meyer K, Leblanc MC. Aquatic therapies in patients with compromised left ventricular function and heart failure. Clin Investig Med 2008;31:E90-7.
31. Drootin M. Summary of the updated american geriatrics society/british geriatrics society clinical practice guideline for prevention of falls in older persons. J Am Geriatr Soc 2011;59:148–57. doi:10.1111/j.1532-5415.2010.03234.x.
32. Gombos GC, Bajsz V, Pék E, Schmidt B, Sió E, Molics B, et al. Direct effects of physical training on markers of bone metabolism and serum sclerostin concentrations in older adults with low bone mass. BMC Musculoskelet Disord 2016;16. doi:10.1186/s12891-016-1109-5.
33. Gombos Császár G, Bajsz V, Sió E, Steinhausz Tóth V, Schmidt B, Szekeres L, et al. The direct effect of specific training and walking on bone metabolic markers in young adults with peak bone mass. Acta Physiol Hung 2014;101:205–15. doi:10.1556/APhysiol.101.2014.001.
34. Wang YY, Pu XY, Shi WG, Fang QQ, Chen XR, Xi HR, et al. Pulsed electromagnetic fields promote bone formation by activating the sAC–cAMP–PKA–CREB signaling pathway. J Cell Physiol 2019;234:2807–21. doi:10.1002/jcp.27098.
35. Zhai M, Jing D, Tong S, Wu Y, Wang P, Zeng Z, Shen G, Wang X, Xu Q LE. Pulsed electromagnetic fields promote in vitro osteoblastogenesis through a Wnt/β-catenin signaling-associated mechanism. Bioelectromagnetics 2016;73:152–62.
36. Li JKJ, Lin JCA, Liu HC, Chang WHS. Cytokine release from osteoblasts in response to different intensities of pulsed electromagnetic field stimulation. Electromagn Biol Med 2007;26:153–65. doi:10.1080/15368370701572837.
37. Jing D, Cai J, Shen G, Huang J, Li F, Li J, et al. The preventive effects of pulsed electromagnetic fields on diabetic bone loss in streptozotocin-treated rats. Osteoporos Int 2011;22:1885–95. doi:10.1007/s00198-010-1447-3.
38. Elsisi HFEM, Mousa GSM, ELdesoky MTM. Electromagnetic field versus circuit weight training on bone mineral density in elderly women. Clin Interv Aging 2015;9:539–47. doi: 10.2147/CIA.S78485.
39. Giusti A, Giovale M, Ponte M, Fratoni F, Tortorolo U, De Vincentiis A, et al. Short-term effect of low-intensity, pulsed, electromagnetic fields on gait characteristics in older adults with low bone mineral density: A pilot randomized-controlled trial. Geriatr Gerontol Int 2013;13:393–7. doi:10.1111/j.1447-0594.2012.00915.x.
40. Parhampour B, Torkaman G, Hoorfar H, Hedayati M, Ravanbod R. Effects of short-term resistance training and pulsed electromagnetic fields on bone metabolism and joint function in severe haemophilia A patients with osteoporosis: A randomized controlled trial. Clin Rehabil 2014;28:440–50. doi:10.1177/0269215513505299.
41. Wang Q, Wu W, Chen X, He C, Liu X. [Effect of pulsed electromagnetic field with different frequencies on the proliferation, apoptosis and migration of human ovarian cancer cells]. Sheng Wu Yi Xue Gong Cheng Xue Za Zhi 2012;29:291–5.