Original Research

What Effect Do Different Training Environments Have on Femoral Bone Density in Premenopausal Women?

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ABSTRACT

Considering that maintaining the optimal level of bone mineral density during premenopausal period is important in reducing the risk of osteoporosis and subsequent fractures during postmenopausal period, the aim of the present study was to evaluate the effect of different training environments on femoral bone density in premenopausal women. In this quasi-experimental study with a pretest-posttest design, 40 premenopausal women aged between 40 to 45 years were divided in four groups, 10 people in each group (exercise group in water, land, combined and control). Exercise groups performed 12 weeks of exercise three times a week 70 minutes per session. The subjects’ femoral bone density was measured before and after 12 weeks by DEXA bone density measurement device. Data were analyzed using descriptive statistics, one-way analysis of variance, analysis of covariance and LSD post hoc test at a significance level of P≤0.05, using SPSS software version 24. Femoral bone density showed a significant increase in the combined exercise group (P <0.05) but in the control group a decrease in bone density was observed (P <0.05). Total bone density of hip and femoral neck showed statistical differences in water exercise group, land exercise group and combined exercise group in comparison with control group (P <0.05). Given this there was no difference between the exercise groups in water and land environment, exercise in any environment is recommended for premenopausal women. Because weight training exercises in all three types of training environments prevent the progression of bone mineral density in premenopausal ages.

Keywords: Knee, Bone density, Water-based exercise, Land-based exercise, Combined exercise, Premenopause.
Introduction

Osteoporosis is the most common metabolic bone disease that results in decreased bone density and destruction of bone structure and it is determined as a result of increased bone fragility and fracture sensitivity, especially in the wrist, spine and femoral head, which is cancellous bone (1). Osteoporosis is defined as a decrease in bone density to the extent of 2.5 standard deviation from the mean maximum density in young and normal people in the community, and it happens as a result of a negative balance between bone absorption and reabsorption (2).

The prevalence of osteoporosis and its related fractures is 8 times higher in women than men (1). Osteoporosis is not specific to the elderly; as it is shown, the prevalence of osteoporosis and osteopenia in premenopausal women is 5% and 15%, respectively (3) and BMD decreases is reported between 2.5 and 1% per year in these individuals (4). It is estimated that about 200 million people worldwide suffer from this disease, which due to the high cost of treatment of fractures caused by this disease, appropriate strategies to prevent osteoporosis is required (4). Maximum bone density depends mainly on a person’s genetic background, but calcium intake, vitamin D and exercise are also effective (5, 6). The decrease in density in both genders is started from about 35 to 45 years of age, so that from about 40 years of age in both sexes it is decreased by 0.5 to 1% per year and it will be continued until the end of life, which will be more severe in women after menopause (7). Factors such as body mass index (BMI), smoking, alcohol and inactivity are effective in accelerating this process (6).

Studies have shown that maintaining optimal levels of bone mineral density during the premenopausal period reduces the risk of osteoporosis and subsequent fractures during the postmenopausal period, is important which increases the relative risk by 1.5 to 3 times (3).

A number of researches have been done on the effects of exercise in various age groups and on different variables in a variety of exercise environments and time periods (8-11). However, in the field of bone density, most studies have examined the effect of exercise in postmenopausal women with osteoporosis (12, 13), while today osteoporosis is not the problem of only postmenopausal women, rather, many young women are exposed to the disease for a variety of reasons. Therefore, it is necessary to study the prevention of this phenomenon at a younger age. Little research has been done in this field, some of which have pointed to the positive effect of exercise on BMD and some have shown the opposite. For example, Kelley et al. (2013), in their meta-analysis research, supported the positive effects of exercise on BMD in premenopausal women (14).

On the other hand, Habibzadeh (2010) investigated the effect of walking exercises in the prevention of osteoporosis on bone density in healthy girls aged 20 to 35 years and did not observe a significant effect on femoral and lumbar BMD (15). Nichols et al. (1995) examined the effect of 12 months of weight-bearing exercise on 34 postmenopausal women with a history of physical activity and did not observe a difference in density between the patient and control groups (16). Bassey and Ramsdale (1995) studied the effect of high and low intensity weight-bearing exercise on 44 postmenopausal women for one year and did not observe a significant difference in bone mineral density (17). Lau et al. (1992) examined the effect of 10 months of weight-bearing exercise in 50 postmenopausal women and did not observe any effect on the mineral density of the femoral neck and lumbar vertebrae (18).

As a result of exercise, the pressures on the bone changed its curvature, increase the convexity of the bone surface and, ultimately, stimulate the activity of osteoblasts (19). Exercises that are not stressful in nature are less effective or completely ineffective than weight-bearing exercises such as running and jumping (20). The results of conducted research on pharmacological methods for the treatment or prevention of osteoporosis have shown that these methods, in addition to their benefits, can cause cardiovascular disease, breast cancer and increased risk of stroke in the long-run, while physical activity without any side effects has shown its positive effects in preventing a decrease in bone density (21). To what extent this goal can be achieved depends on various factors such as the type of exercise program and the age of onset of exercise. Therefore, in recent years, the use of exercise-therapy to treat or prevent osteoporosis has been considered by many researchers.

Among the types of exercise, the effect of water exercise on bone density and its comparison with exercise in a land environment has been less studied. While water is an environment that puts the necessary resistance on the body according to each person’s needs, hence, it causes muscle activity and involvement of larger muscle groups to overcome resistance, and it can increase mechanical pressure on the bones, it is very useful in stimulating bone formation, increases people’s ability to maintain balance to reduces the risk of falls and
fractures in individuals (22). Also, due to its higher viscosity, water has a higher resistance than air, which causes slower movements and, as a result, people have more time to respond and show reaction (23). A study conducted by Kun et al. (2001) showed bone mineral density is higher in organs that bear the weight of the body (24). Bravo et al. (1996) examined the effect of one year of weight-bearing exercises on bone density in 124 postmenopausal women with osteoporosis and concluded that such exercises reduce the rate of bone loss and lumbar pain. (25).

A review of the researches show that studies are often conducted in an environment (land or water) and show sometimes contradictory results (26). On the other hand, most research has been done in the postmenopausal women community, while the World Health Organization (WHO) has identified osteoporosis as the third most common health problem in the world, after heart disease and various types of cancer that is called silent epidemic (1). It seems that the most appropriate approach is to perform the effect of exercise related to bone density increase from premenopausal ages and with the aim of preventing osteoporosis in order to achieve the desired training strategies in this field in which environment (land, water or combined) exercise is more appropriate. Therefore, the aim of the present study was to investigate the effect of different training environments on femoral bone density in premenopausal women.

Material and Methods
Subjects
The present study was a quasi-experimental, pretest-posttest design and applied type. The statistical population of the study consisted of premenopausal women aged 40 to 45 years. The research protocol was approved by the Research Ethics Committee with the abbreviation number of IR.UMSHA.REC.1394.421 and informed consent was obtained from the individuals. A questionnaire was distributed including age, height, weight, history of fractures during life, drug use, calcium intake, physical activity, number of giving birth, onset of menstrual age, pregnancy and disease. From those who refer to doctor, 40 people who were qualified for the research entered the study voluntarily. Inclusion criteria were the following items, no rheumatoid arthritis, hypothyroidism or hyperthyroidism, parathyroid and adrenal, diabetes mellitus, renal failure, advanced liver failure, cardiorespiratory disease, neurological disorders, concussion, trauma, menopause, fractures, any kind of cancer, menstrual irregularities starting after the age of 18, permanent menopause or miscarriage in the last trimester, less than 6 months of menstruation in the past year, removal of the ovary under menopause and infertility or pregnancy or breastfeeding while studying, drug addiction, spinal deformity, hospitalization due to illness during the two weeks before the study, complete bed rest for three consecutive months, taking estrogen drugs progesterone had a T-score of less than 2.5, calcium tablets intake, multivitamins and vitamin D, and vitamin D3 ampoules (26). Using G*Power software, total sample size for ANCOVA analysis, significance level 0.05, power 0.80 and effect size 0.5 was 40 people for groups (27). Purposefully subjects were divided into four groups of 10, including water exercise, land exercise, combined and control group, while each group was unaware of the intervention of the other group (one blind). The exercise groups exercised for 12 weeks, three times a week, and each session lasted for 70 minutes (with at least one day of rest between each session), while the control group did no exercise for 12 weeks.

Exercise protocols
Water exercise protocol: Water temperature varied between 29 and 30 °C and water height varied from the seventh vertebra of the neck (first month), xiphoid appendix (second month) to the anterior superior iliac spine (third month) (18). When entering the water, warm-up and stretching exercises (20 minutes) were in the muscles of the lumbar region and lower limbs. Resistance exercises (20 minutes) were performed in the first four weeks without training aids and in the second and third weeks using waterproof equipment. From bars, dumbbells and barbells for upper body resistance exercises (chest press, back rotation, flexion and lumbar extension) and from sponge pads for lower body resistance exercises (plantar and dorsiflexion ankle, leg press, knee flexion and extension, hip abduction and adduction and hip extension flexion) were used. These equipment created resistance when moving in water, which due to the physical properties of water, the resistance increased with increasing speed, so the subjects performed the exercises in full range of motion and as fast as possible. In order to control the
intensity of exercise, heart beat rate was measured in each session. Endurance exercises (20 minutes) included walking, rocking and jumping in different directions in the water. Cooling exercises included exercises for relaxation of muscles in water in a floating and stretching position (23, 24).

**Land exercise protocol:** Warming up for 10 minutes included walking and running at a slow speed and stretching. Strength training (35 minutes) consisted of 50% in the open movement chain and 50% in the closed movement chain and consisted of 8 movements (latissimus stretch, knee flexion, standing leg press, trunk extension, sitting knee press, knee extension, sitting leg press and sit-up) (25, 28, 29). The first four weeks consisted of 1-2 sets of ten with an intensity of 60-65% 1RM. In the second four weeks, 3 sets with 8 repetitions and an intensity of 70-75% 1RM and in the third four weeks, 3 sets with 10 repetitions and an intensity of 75-80% 1RM continued to practice (25, 28). There was a minute rest between sets. In addition to determining 1RM before exercise, 1RM was repeated on the first of each month. Endurance training (15 minutes) included walking at 60-65% of maximum heart rate on the treadmill (30 seconds between each set) and cooling down (10 minutes) included relaxation and stretching.

**Combined exercise protocol:** It included 6 weeks of training in water and 6 weeks of training on land. The classification of this type of exercise was based on the first two weeks, the second two weeks and the third two weeks instead of the first, second and third four weeks, they were both according to the training protocols mentioned in the water and land was done.

**Data collection tools and methods**

To measure height (cm), standing gauge with an accuracy of 1 mm (after a normal exhalation) and weight (kg) were used by a digital scale with an accuracy of 0.01 kg with a minimum of clothing and without shoes. Bone density in proximal femur areas (Figure 1), by Dexa X-ray bone density measuring device, model Dextra-T, OSTEOSYS Company, made in South Korea, and was evaluated by a specialist physician. To measure bone density by the central device, after gaining weight, the subject lay on the back of the device, the receiver of the device was placed on the hip area in the pelvis and the X-ray was directed towards it. This method is simple, fast, non-invasive and painless and does not require anesthesia to perform the test and measures bone density in a short time between 20 to 30 minutes. Before people enter the research in relation to the density measuring device and possible losses of it, was explained to all subjects. Bone mineral density was calculated in grams per square centimeter and the results were immediately prepared by a computer connected to the device. All bone density tests were analyzed before and after a 12-week training period (48 to 72 hours after the last exercise session was performed).

![Figure 1. Bone density in proximal femur areas](image-url)

**Statistical analysis**
For statistical analysis, mean and standard deviation were used to describe the data, Kolmogorov-Smirnov was used to test the hypothesis of normality of the measured parameters, parametric one-way analysis of variance, analysis of covariance and LSD post hoc test were used to evaluate the difference between groups. To perform analysis of covariance, the assumptions of the analysis were first examined. Therefore, to ensure that the data of this study estimate the underlying assumptions of analysis of covariance, the four assumptions of analysis of covariance, including the normal distribution of scores ($P \geq 0.05$), homogeneity of variances ($P \geq 0.05$), homogeneity regression slope ($P \geq 0.05$) and linearity of pretest correlation and dependent variable ($P \leq 0.05$) were investigated and confirmed and LSD post hoc test was used to compare the groups. The tests were analyzed at a significance level of 0.05, using SPSS software version 24.

Results

As can be seen in the table of mean and standard deviation of demographic characteristics of the subjects (table 1), one-way analysis of variance showed that the participating groups were homogeneous in terms of age, height, weight and body mass index.

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>Water</th>
<th>Land</th>
<th>Combined</th>
<th>Control</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.64±43.30</td>
<td>2.20±42.20</td>
<td>1.72±42.50</td>
<td>1.84±43.50</td>
<td>11</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>3.62±158.11</td>
<td>7.87±158.10</td>
<td>6.52±160.72</td>
<td>6.46±160.53</td>
<td>0.66</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>11.09±75.53</td>
<td>6.83±72.68</td>
<td>9.13±71.02</td>
<td>11.60±71.07</td>
<td>0.51</td>
</tr>
<tr>
<td>Body Mass Index* (kg / m²)</td>
<td>4.07±30.17</td>
<td>3.74±29.24</td>
<td>3.44±27.74</td>
<td>4.73±27.68</td>
<td>0.34</td>
</tr>
</tbody>
</table>

*Body Mass Index (BMI): Weight to height ratio

The results of analysis of covariance (table 2) for total hip and femoral neck variables in three exercise groups of water, land, combined and control group after 12 weeks showed that the amount of these variables by adjusting on pre-test variables, statistically the difference is significant in total hip and femoral neck ($P < 0.05$).

<table>
<thead>
<tr>
<th>area</th>
<th>Sources</th>
<th>Total squares type III</th>
<th>Degrees of freedom</th>
<th>$F$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Total Hip) (g/cm²)</td>
<td>constant</td>
<td>0.001</td>
<td>1</td>
<td>0.140</td>
<td>0.710</td>
</tr>
<tr>
<td></td>
<td>pretest</td>
<td>0.001</td>
<td>1</td>
<td>0.207</td>
<td>0.652</td>
</tr>
<tr>
<td></td>
<td>group</td>
<td>0.095</td>
<td>3</td>
<td>11.451</td>
<td>0.001</td>
</tr>
<tr>
<td>(Femoral Neck) (g/cm²)</td>
<td>constant</td>
<td>0.001</td>
<td>1</td>
<td>0.251</td>
<td>0.620</td>
</tr>
<tr>
<td></td>
<td>pretest</td>
<td>0.001</td>
<td>1</td>
<td>0.187</td>
<td>0.668</td>
</tr>
<tr>
<td></td>
<td>group</td>
<td>0.056</td>
<td>3</td>
<td>5.728</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Pair comparison of groups (LSD) in table 3 shows that in the total hip area (Total Hip), water group ($P = 0.001$), land group ($P = 0.001$) and combined group ($P = 0.001$) showed a significant difference in comparison with the control group; in comparison with other groups, no difference was observed between the other training groups in this variable ($p > 0.05$). In the femoral neck area, the water group ($P = 0.021$), land group ($P = 0.001$) and combined group ($P= 0.001$) showed a significant difference in comparison
with the control group and no difference was observed between the other training groups in this variable \((p > 0.05)\).

### Table 3. Results of pairwise comparison of groups in LSD post hoc test

<table>
<thead>
<tr>
<th>Areas of bone density</th>
<th>Groups</th>
<th>Mean difference</th>
<th>Standard error</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Total Hip) (g/cm²)</td>
<td>Control</td>
<td>Water -0.101</td>
<td>0.024</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Land -0.111</td>
<td>0.025</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Combined -0.129</td>
<td>0.024</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>Water</td>
<td>Land -0.009</td>
<td>0.024</td>
<td>0.697</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Combined -0.027</td>
<td>0.024</td>
<td>0.252</td>
</tr>
<tr>
<td></td>
<td>Land</td>
<td>Combined -0.018</td>
<td>0.024</td>
<td>0.454</td>
</tr>
<tr>
<td>(Femoral Neck) (g/cm²)</td>
<td>Control</td>
<td>Water -0.062</td>
<td>0.026</td>
<td>0.021*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Land -0.092</td>
<td>0.026</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Combined -0.091</td>
<td>0.026</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>Water</td>
<td>Land -0.035</td>
<td>0.026</td>
<td>0.189</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Combined -0.029</td>
<td>0.026</td>
<td>0.265</td>
</tr>
<tr>
<td></td>
<td>Land</td>
<td>Combined 0.006</td>
<td>0.026</td>
<td>0.822</td>
</tr>
</tbody>
</table>

*Significant difference in level \(p \leq 0.05\)

### Discussion

The aim of this study was to determine the effect of different training environments on femoral bone density in premenopausal women. The results showed that 12 weeks of training in all three environments increased femoral bone density, while the results of two-way test did not show a statistical difference between the training groups. The results of the study were consistent with the study of Kun et al. (2001), who reported higher density in weight-bearing limbs (24). In the present study, it seems that exercise with mechanical pressure on the femur increased density. Simas et al (2017), in meta-analysis that all participants were postmenopausal women, compared Water-based exercise (WBE) to land-based exercise (LBE). Meta-analyses revealed significant differences between WBE and control group in favor of WBE for changes in bone mineral density (BMD) at the lumbar spine and femoral neck. Significant differences were also revealed between WBE and LBE in favor of LBE for changes in lumbar spine BMD. However, there was no significant difference between WBE and LBE for changes in femoral neck BMD (30). The results of the exercise group showed a significant increase in the femur that there were similarities according to the findings of Mulhim (2004), whose exercises were performed in a similar period to this study and the age of the subjects was 25 to 50 years (29). Kelly et al. (2001) showed the positive effect of stretching exercises on the lumbar vertebrae (14), which were pursuant to the findings of the present study, except that the statistical sample was postmenopausal women and the type of exercises was stretching. The results of the study of Chien et al. (2000) were in congruence with the results of this study (31) with the difference that the duration of their training was twice the present study and was performed on postmenopausal women, while this study took less time and applying more pressure on younger people that showed positive results. The results of this study were in compliance with the results of the study of Mousavian et al. (2015) which was similar to the present study for 12 weeks (32) but their exercises were Pilates in a land environment with women 60 to 65 years old. However, present study was performed in three training environments and on younger age groups.

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In the present study, the results of the water exercise group showed a significant increase in the femur area compared to the control group. This was in line with the study of Vanaky et al. (2014) which was carried out in water for 12 weeks and weight-bearing (33). With the difference that Vanaky research subjects were sedentary women aged 50 to 70 years. But the subjects of this study were younger than their subjects and also, they observed a significant effect on the lumbar vertebrae while, exercises in the water group in this study had a positive effect on the thigh. Tofoghi and Hefzollesan (2011) in their study examined the effect of 12 weeks of aerobic and water resistance training on the lumbar vertebrae and femur that observed a significant increase in femoral bone density (34) but did not observe significant difference in lumbar vertebrae. Their study was performed on obese postmenopausal women, which was different from our study. The results of this study were inconsistent with the study of Mohammadi et al. (2013) which was performed on osteoporosis of postmenopausal women for 8 weeks in land and water environment (35). In their study, exercise in water was more effective than to exercise on land, while in the present study, no statistical difference was observed between the training environment in water and on land. In this study, a significant increase in all variables was observed in relation to the exercise group in a combined environment compared to the control group, but we did not find a similar study. The results of this study were inconsistent with the study of Habibzadeh et al. (2010), so that they did not see a significant effect on lumbar bone density in fat and thin girls (15). Possible reasons for the mismatch may be due to shorter time (two months) or lower intensity of exercise (walking at 50 to 75% of heart rate) or younger age and lower weight of subjects compared to the present investigation. The results of this study were inconsistent with the study of Smitd et al. (1992) and Bassey and Ramsdell (1995) (17, 36). It seems that this difference is probably due to the difference in the intensity of exercise and the age of the subjects (in their study, postmenopausal women were studied). The study conducted by Bravo et al. (1997) was also inconsistent with our study, which found that 12 weeks of weight-bearing exercise in water reduced bone density in postmenopausal women (25). The mismatch of this study may be due to menopause and its negative effects on bone density. Goldstein et al. (1994), who studied the effect of five months of water and land exercise on postmenopausal women’s bone density, found that the water exercise group had a more significant increase in radius and wrist bone density than the land exercise group (28). Generally, the comparison of the present study with previous researches was inconsistent in some areas and types of exercises and inconsistent in some variables and the general reason may be that in previous studies, more attention has been paid to the community of postmenopausal women. More importantly, most of the researches were conducted regarding to the comparison of one or two environments (water and land).

Conclusion
According to the research findings, it can be said that all three training environments (water, land and combined) affect bone density. But in some bone areas, the effect of exercise was better and in some areas it was less effective. On the other hand, the results compared to previous studies showed that the statistical population of previous studies was more postmenopausal women with osteoporosis, while there were very few studies on premenopausal exercise. The findings of the present study and similar studies emphasize that exercise is a suitable and harmless method to prevent bone loss in old age and the least effect it can have is to prevent bone loss due to aging. On the other hand, contrary to previous opinions that indicate the effect of exercise on bone density, only in a land environment, this study showed that according to the conditions of each person, exercise in any environment (water, land or combined) is effective to prevent the process of decreasing bone density during menopause.

According to the findings of the present study, although the training environment (water, land or combined) and the study area (femur) are the factors affecting the significance of bone density, but in general, exercise has positive effects on bone density. Therefore, the least effect that exercise can have is to prevent a decrease in bone density at near menopausal ages.

Acknowledgements
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چکیده فارسی

محیطهای تمرینی مختلف چه تاثیری بر تراکم استخوان فمور زنان پریمنوپوز دارند؟

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گروه مدیریت ورزشی، دانشکده علوم ورزشی، دانشگاه اراک، اراک، ایران.

با توجه به اینکه حفظ سطح بهینه استخوان در طی دوران پریمنوپوز در کاهش خطر ابتلا به پوکی استخوان و شکستگی‌ها معنادار است، هدف از انجام تحقیق حاضر اثر محیطهای تمرینی مختلف بر تراکم استخوان ران زنان پریمنوپوز بود. در این تحقیق نیمینه آزمایشی با طرح پیوستگی آزمون-پسآزمون، ۴۰ زن پریمنوپوز ۴۰ تا ۵۵ سال در چهار گروه ۱۰ نفره (گروه تمرین در آب، خشکی، ترکیبی و کنترل) تحقیم شدند. گروههای تمرینی ۱۲ هفته فعالیت ورزشی را در هفته و هر جلسه ۷۰ دقیقه انجام دادند. اجرای تحقیق و آمار توصیفی، تحلیل واریانس یک راهه، تحلیل کوواریانس و آزمون تعقیبی LSD در سطح معناداری ۰.۰۵ با استفاده از نرم‌افزار SPSS نسبت به تراکم استخوان ران در گروه تمرین ترکیبی افزایش معناداری نشان داد (P<0.۰۵). مقدار Tراکم استخوان کل هیپ و گردن فمور در گروه تمرین در آب، گروه تمرین در خشکی و گروه تمرین ترکیبی در مقایسه با گروه کنترل اختلاف آماری نشان داد (P<0.۰۵). با توجه به اینکه تحولات در بین گروههای تمرینی در محیط آب و خشکی مشاهده نشد، تمرین در هر محیطی به زنان پریمنوپوز توصیه می‌شود. زیرا تمرینات تحمیل وزن در هر سه نوع محیط تمرینی باعث جلوگیری از پیشروی کاهش تراکم استخوان در سنین پریمنوپوز می‌شود.

واژه‌های کلیدی: تراکم استخوان، تمرین در آب، تمرین در خشکی، تمرین ترکیبی، پریمنوپوز.