

Original Article

Bone turnover markers response to aerobic versus resistance exercise among postmenopausal Saudi women

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Abstract:

BACKGROUND: Menopause is characterized by low bone turnover biomarkers (BTMs), leading to a faster reduction in bone mass and an increased risk of fractures. Osteoporosis is a major health concern among postmenopausal women in Asia. Physical exercise is widely recognized as an effective method for both the primary and secondary prevention of osteoporosis-related fractures. However, our understanding of the most effective exercise training program to prevent osteoporosis in postmenopausal women remains incomplete. **OBJECTIVE:** The present study was designed to examine the effects of aerobic versus resisted exercise training on markers of bone turnover in postmenopausal Saudi women, including serum osteoprotegerin (OPG), receptor activator of nuclear factor kappa B ligand (RANKL), and the OPG/RANKL ratio. **MATERIALS and METHODS:** One hundred Saudi postmenopausal women, aged 50 to 58 years, participated in the study. Participants enrolled in two groups: Group (A) received treadmill aerobic exercises where, group (B) received resistance exercise training for 6 months. **RESULTS:** There were significant improvement in six-minute walking test and hand grip strength and significant reduction in serum osteoprotegerin (OPG), receptor activator of nuclear factor kappa B ligand (RANKL) and OPG/receptor activator of nuclear factor kappa B ligand (OPG/ RANKL) ratio in group A compared to group B. **CONCLUSION:** Six months of resisted exercise is superior to aerobic exercise in modifying bone turnover markers and functional ability among postmenopausal women.

Keywords: Aerobic Exercise; Bone Turnover Markers; Resistance Exercise; Menopause.

Introduction

Menopause is characterized with low bone turnover biomarkers (BTMs), leading to faster reduction of bone mass and higher fracture risk [1,2]. Among Asian subjects, osteoporosis is a common medical problem as it is expected to cause about 50% of hip fractures among Asian population in 2050 [3]. Reduction in bone mass

and strength leads to an increased risk of fractures [4]. Bone mineral density (BMD) is the usual method for measuring bone strength [4,5] which gradually reduced from the 4th decade and accelerates in early years of postmenopausal period [6–8]. This increases the risk of fracture especially spinal, forearm and hip fractures [4,9]. Approximately 200 million women worldwide have osteoporosis [9], and about 6% of men and 21% of women in Western countries suffer from osteoporosis [4].

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Bone turnover biomarkers (BTMs) refers to resorption and formation of bone which reflect the remodeling status of bones [10]. Diabetes mellitus adversely affects remodeling of bone as biomarkers of both bone resorption and formation are reduced [11-14]. Despite increased bone marrow density, diabetic patients suffer from high fracture risk [15,16]. Therefore, BTMs are considered more sensitive than BMD in determining the fracture risk in diabetic patients [17,18].

Bone turnover biomarkers (BTMs) can be considered as possible osteoporosis predictors [19-24] and a measure for hip fracture risk [25-27]. Independent of BMD, several studies considered BTMs as predictors for fractures [21, 28,29].

Physical exercise is an accepted method for both primary and secondary prevention of fractures related to osteoporosis [4,9]. Aerobic walking exercise can improve bone density and as a result reduce fracture risk [30-34]. Previous studies proved that different exercise programs positively affect bone density among postmenopausal women [4-7].

Decreased bone density, abnormal bone metabolism, and reduced muscle strength can be improved through aerobic and resisted exercise training. Therefore, the present study was designed to examine the effects of aerobic versus resisted exercise training on markers of bone turnover in postmenopausal Saudi women after 6 months.

Materials and Methods

Subjects

One hundred postmenopausal Saudi women aged 50-58 years. The inclusion criteria were: menopause onset more than 10 years ago, non-smokers, no alcohol consumption, and no use of hormone replacement therapy. The exclusion criteria included diabetes, hypertension, cardiac, musculoskeletal, or endocrine disorders, as well as the use of medications that may affect bone metabolism. All participants signed the consent form prior to their participation. Participants were divided into two groups. Group A received treadmill exercise training, while Group B received resisted exercise training.

Measurements

A. Bone turnover biochemical markers measurement: Overnight fasting venous blood samples were collected, centrifuged, and stored at -70°C to measure bone turnover and bone resorption biomarkers. These included serum osteoprotegerin (OPG) and receptor activator of nuclear

factor kappa B ligand (RANKL), which were determined using commercial sandwich enzyme-linked immunosorbent assays (ELISA) according to the manufacturers' protocols (Immunodiagnostic Systems Ltd, Boldon, UK and Cusabio Biotech, China). The same serum samples used for RANKL measurements were also used for OPG measurements, and the assay was performed blinded to the subject group [35].

B. Hand Grip Strength: Hand dynamometer (Jamar, Sammons Preston Rolyan, Cedarburg, WI, USA) was used in assessment of grip strength. The mean value of two measurement trials was taken, with the elbow joint flexed at a right angle and without any part of the body in close contact [36].

C. Six Minute Walk Test (6MWT): The mean distance walked by each participant within 6 minutes in two different days was analyzed [37].

All assessments of handgrip strength, the six-minute walk test, OPG, RANKL, and the OPG/RANKL ratio were taken before the start of the training program and after its completion.

Procedures

All participants were randomly enrolled in two equal groups as following:

Group (A): Training program included range of motion and stretching exercises as a warming-up for five minutes, treadmill aerobic exercise for 30 minutes and 10 minutes of cooling down. Participants completed a 6-months treadmill aerobic exercise, three sessions weekly [38].

Group (B): The training program included resistance exercises on various resistance machines, with three sessions per week for 6 months. The program consisted of a 5-minute warm-up with range of motion and stretching exercises, followed by 30 minutes of resistance training targeting the upper limbs, lower limbs, and trunk muscles, and concluding with a 10-minute cool-down [39].

Statistical analysis

The mean values of the investigated parameters obtained before and after six months in both groups were compared using paired "t" test. Independent "t" test was used for the comparison between the two groups ($P < 0.05$).

Results

Table 1 shows the baseline characteristics of the participants who entered the trial. There were no significant differences in baseline characteristics between the two groups.

TABLE 1: BASELINE AND DEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS.

Characteristic	Group (A)	Group (B)	p-value
Age (years)	56.64 ± 4.27	57.21 ± 5.36	> 0.05
BMI (kg/m ²)	23.82 ± 4.54	24.37 ± 4.18	> 0.05
SBP (mm Hg)	131.46 ± 9.25	132.15 ± 8.39	> 0.05
DBP (mm Hg)	84.62 ± 6.12	86.24 ± 4.55	> 0.05
BMD of lumbar spine (mg/cm ³)	127.28 ± 8.54	125.79 ± 8.11	> 0.05
BMD of tibia (mg/cm ³)	266.18 ± 10.67	263.94 ± 11.24	> 0.05
BMD of radius (mg/cm ³)	270.76 ± 10.42	268.34 ± 9.23	> 0.05
Serum Calcium (mg/dl)	8.53 ± 2.23	8.26 ± 2.12	> 0.05
Parathyroid Hormone (pg/ml)	13.74 ± 3.12	14.29 ± 3.25	> 0.05

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

The mean values of six-minute walking test and hand grip strength were significantly increased, while the mean values of the serum osteoprotegerin (OPG), receptor activator of nuclear factor kappa B ligand (RANKL) and OPG/receptor activator of nuclear factor kappa B ligand (OPG/ RANKL) ratio were significantly decreased in the both groups at the end of the study (table 2 and 3). Additionally, there were significant differences between the mean levels of the investigated parameters in Group A and Group B at the end of the study, with greater changes observed in patients who received resisted exercise training (tables 4). These results confirm that resisted exercise is more effective than aerobic exercise training in modulating bone turnover markers and improving functional ability in postmenopausal women.

Discussion

Changes in the musculoskeletal system following menopause are significant health concerns due to their serious complications, which increase morbidity and mortality among affected individuals. Decreased bone density, abnormal bone metabolism and decreased general muscle strength can be corrected by aerobic and resisted exercise training. Therefore, the present study was designed to evaluate the effects of aerobic versus resisted exercise training on bone turnover markers in postmenopausal Saudi women over a 6-month period. Our principal finding in the present study was that six months of resisted exercise is more effective than aerobic

TABLE 2: MEAN VALUE AND SIGNIFICANCE OF HANDGRIP STRENGTH, SIX-MINUTE WALK TEST, OPG, RANKL AND OPG/RANKL OF GROUP (A) BEFORE AND AT THE END OF THE STUDY.

	Mean +SD		T-value	p-value
	Pre	Post		
Hand grip strength (mmHg)	149.31 ± 17.27*	170.54 ± 19.28	3.42	< 0.05
Six minute walk test (meter)	322.53 ± 24.64*	381.41 ± 28.13	3.77	< 0.05
OPG (pg/mL)	507.16 ± 35.83*	462.25 ± 32.42	4.18	< 0.05
RANKL (pg/mL)	28.17 ± 7.94*	25.33 ± 6.21	3.26	< 0.05
OPG/ RANKL	29.23 ± 9.15*	23.82 ± 8.16	3.34	< 0.05

OPG: Serum osteoprotegerin; RANKL: Receptor activator of nuclear factor kappa B ligand; (*) indicates a significant difference, P < 0.05.

TABLE 3: MEAN VALUE AND SIGNIFICANCE OF HANDGRIP STRENGTH, SIX-MINUTE WALK TEST, OPG, RANKL AND OPG/RANKL OF GROUP (B) BEFORE AND AT THE END OF THE STUDY.

	Mean +SD		T-value	p-value
	Pre	Post		
Hand grip strength (mmHg)	147.25 ± 18.91*	193.61 ± 21.43	7.38	< 0.05
Six minute walk test (meter)	318.24 ± 26.12*	436.17 ± 30.29	8.45	< 0.05
OPG (pg/mL)	512.55 ± 38.74*	423.42 ± 31.65	9.16	< 0.05
RANKL (pg/mL)	29.32 ± 8.11*	22.85 ± 6.73	6.57	< 0.05
OPG/ RANKL	30.56 ± 9.63*	19.71 ± 7.82	7.14	< 0.05

OPG: Serum osteoprotegerin; RANKL: Receptor activator of nuclear factor kappa B ligand; (*) indicates a significant difference, P < 0.05.

exercise in modifying bone turnover markers and enhancing functional ability among postmenopausal women. These findings are consistent with previous research.

TABLE 4: MEAN VALUE AND SIGNIFICANCE OF HANDGRIP STRENGTH, SIX-MINUTE WALK TEST, OPG, RANKL AND OPG/RANKL OF GROUP (A) AND GROUP (B) AT THE END OF THE STUDY.

	Mean +SD		T-value	p-value
	Group (A)	Group (B)		
Hand grip strength (mmHg)	170.54 ± 19.28*	193.61 ± 21.43	3.22	< 0.05
Six minute walk test (meter)	381.41 ± 28.13*	436.17 ± 30.29	3.45	< 0.05
OPG (pg/mL)	462.25 ± 32.42*	423.42 ± 31.65	4.23	< 0.05
RANKL (pg/mL)	25.33 ± 6.21*	22.85 ± 6.73	3.39	< 0.05
OPG/RANKL	23.82 ± 8.16*	19.71 ± 7.82	3.43	< 0.05

OPG: Serum osteoprotegerin; RANKL: Receptor activator of nuclear factor kappa B ligand; (*) indicates a significant difference, P < 0.05.

Our findings confirmed that both resisted and aerobic exercises significantly improved patients' functional ability with greater significant results in the resisted exercise training group. Schmitt et al. (2009) reported that two prospective cohort studies demonstrated a negative relationship between hip fracture risk and physical activity, as evidenced by a slowing of bone loss and improved bone density associated with physical activity in postmenopausal women [40]. Similarly, another study that implemented a combined aerobic and resisted exercise training program over 12 months found a reduction in the rate of bone loss, along with improvements in maximum isometric strength in postmenopausal women [41]. Moreover, Küçükçakır et al. (2013) demonstrated that Pilates exercises, performed twice a week for 12 months, are an effective and safe alternative treatment for improving quality of life and functional status in postmenopausal women with osteoporosis [42]. Marques et al. (2013) conducted a study with forty-seven healthy older adults who engaged in resistance and weight-bearing exercises. The findings demonstrated that exercise training significantly improved bone mineral density (BMD), lower limb strength, balance performance, and modulated inflammatory biomarkers [43].

In the present study, both six months of resisted and aerobic exercise training significantly increased serum osteoprotegerin (OPG) levels and the OPG/RANKL ratio,

while also reducing serum RANKL levels, with more pronounced changes observed following the resisted exercise training program. These results agreed with Kim et al. (2006) who stated that mechanical stimulation inhibits osteoclastogenesis that resulted from dynamic flow-induced shear stress through increased level of OPG and reduced levels of RANKL [44]. Similarly, Saunders et al. (2006) reported increased levels of OPG following mechanical stimulation through substrate deformation [45]. However, more intense training via long-distance running significantly improved values of BMD [46]. Esen et al. (2009) proved that ten weeks of high intensity walking training program resulted in significant reduction in the level of RANKL in middle-aged men [47]. However, Marques et al. (2013) reported that both aerobic and resisted exercise training had little effect on bone metabolism markers included RANKL and OPG [43]. Conversely, Marques et al. (2011) reported that muscle strength and BMD, along with OPG and RANKL levels, significantly improved after 8 months of resistance exercise, showing more favorable changes compared to aerobic exercise [48].

Conclusion

Six months of resisted exercise is superior to aerobic exercise in modifying bone turnover markers and functional ability among postmenopausal women.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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استجابة علامات دوران العظام للتمارين الهوائية مقابل التمارين المقاومة بين النساء السعوديات بعد انقطاع الطمث

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المستخلص:

الخلفية: يتميز انقطاع الطمث بانخفاض المؤشرات الحيوية لدوران العظام (BTMs) مع تقليل أسرع في كتلة العظام وارتفاع خطر الكسر. تعتبر هشاشة العظام مشكلة صحية رئيسية بين النساء الآسيويات بعد انقطاع الطمث. التمرين البدني هو وسيلة مقبولة في كل من الوقاية الأولية والثانوية من الكسور المرتبطة بهشاشة العظام. ومع ذلك، فإن فهمنا لأفضل برنامج تدريبي للوقاية من هشاشة العظام بين النساء بعد انقطاع الطمث غير مكتمل. **الهدف:** تم تصميم الدراسة الحالية لفحص تأثيرات التدريب الهوائي مقابل التدريب المقاوم على علامات دوران العظام لدى النساء السعوديات بعد انقطاع الطمث، والتي تشمل أوستيوبوروتيجيرين (OPG) في المصل، ومنتش مستقبلات العامل النووي كابا ب (RANKL) ، ونسبة OPG/منتش مستقبلات العامل النووي كابا ب (OPG/RANKL) **المواد والأساليب:** مائة امرأة سعودية بعد انقطاع الطمث، تتراوح أعمارهن بين 50-58 عامًا. تم تسجيل المشاركين في مجموعتين: المجموعة (أ) تلقت تمارين هوائية على جهاز المشي حيث تلقت المجموعة (ب) تدريبات على تمارين المقاومة لمدة 6 أشهر. **النتائج:** كان هناك تحسن معنوي في اختبار المشي لمدة ست دقائق وقوة قبضة اليد وانخفاض معنوي في مصل أوستيوبوروتيجيرين (OPG) ، ومنتش مستقبلات العامل النووي كابا ب (RANKL) و OPG / منتش المستقبل للعامل النووي كابا ب (OPG / RANKL) نسبة الترابط الناتج عن العامل النووي كابا ب (OPG / RANKL) بعد التدريب في كلتا المجموعتين مع وجود فروق ذات دلالة إحصائية بين المجموعتين. **الخلاصة:** ستة أشهر من التمارين المقاومة تتفوق على التمارين الهوائية في تعديل علامات دوران العظام والقدرة الوظيفية لدى النساء بعد انقطاع الطمث.

الكلمات الدالة: التمارين الهوائية. علامات دوران العظام. تمرين المقاومة. سن اليأس.

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