

ORIGINAL ARTICLE

Effect of a vigorous aerobic regimen on physical performance in breast cancer patients — a randomized controlled pilot trial

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Abstract

This randomized, controlled pilot trial was carried out to assess the feasibility and efficacy of an aerobic exercise in enhancing physical performance of breast cancer patients after adjuvant treatments. The potential of the training regimen to prevent accompanying bone loss was also assessed. Thirty patients, 41–65 years of age, were randomly assigned into training or control groups shortly after adjuvant chemo- or radiotherapy. The 12-week training included a guided aerobic exercise session once a week (the effective part being either step aerobic- or circuit-training in alternate weeks) and similar home exercise sessions twice a week. Adherence to the guided sessions was 78%, while home training was performed an average 2.1 times per week. Agility assessed with figure-8 running test and peak jumping power showed significant between-group treatment-effects (~5% and ~10%, respectively). Judged from the accelerometer data, reaction forces up to six times body weight occurred during the training, which implies that the training could also have potential to affect bone mass. The present exercise regimen turned out to be feasible and effective among breast cancer patients in terms of physical performance. Large controlled trials are necessary to confirm these findings.

Breast cancer is the most common malignant disease of women in Western countries. The incidence of breast cancer has significantly increased during the last few decades in all industrialized countries. In some countries the peak incidence has already been reached, while in many other countries the incidence is still increasing. In Finland, the incidence of breast cancer has increased almost fourfold during the last four decades, from less than 1000 new cases per year in the 1960's to about 4000 at present. However, the mortality has changed only marginally. The improved survival in breast cancer is related to early diagnosis and better therapeutic results. At present, there are approximately 40 000 women in Finland living with a history of breast cancer from whom the majority have underwent the adjuvant treatments. Of those, a half are less than 60 years old and still working. While the number of survivors has increased, the long-term adverse effects of adjuvant treatments have become a more central issue.

Besides the intended treatment effect, adjuvant treatments of breast cancer can cause multiple adverse effects. As chemotherapy causes ovarian failure in two-third of premenopausal women, most of the long-term adverse effects are related to oestrogen deficiency like menopausal symptoms, weight gain, fatigue and impaired quality of life. Antiestrogens, in turn, have both oestrogen agonistic and antagonistic effects depending on target organ and menopausal status, and aromatase-inhibitors decrease the oestrogen-level in postmenopausal women. One of the anticipated adverse effects is thus the bone loss in the majority of patients [1–5] that may increase the risk of osteoporosis and related fractures. Consequently, antiresorptive medication is often prescribed as a counter-measure against bone loss [6–8]. However, such a medication does not help compensate other adverse effects such as declined physical performance, postmenopausal symptoms and possibly increased body weight

[9–13]. In this context, dedicated exercise regimens may complement the rehabilitation of breast cancer survivors in a holistic fashion.

Despite the fact that breast cancer survivors seldom receive any exercise guidance or counseling, regular exercise has been suggested as a potential method to stimulate their recovery after completed adjuvant chemotherapy [9]. Exercise can indeed increase physical performance, prevent bone loss, promote weight control, have a positive effects on quality of life and decrease fatigue [10–13], while it has been reported to cause only a few, if any, complications among breast cancer survivors. Further corroborating this view, Holmes et al. [14] reported recently encouraging results concerning higher survival rate of more active breast cancer survivors than sedentary ones. However, when tailoring rehabilitative exercise programs for these patients, both the efficacy and the feasibility of the training need to be carefully considered. Although the training at light intensity is apparently feasible [15], a more vigorous aerobic exercise may provide a more efficient option to enhance physical performance [16–19], not to mention the evident exercise-induced benefits in bone mass [20,21]. However, the possibility that such a high intensity aerobic exercise might be too fatiguing for the breast cancer survivors and compromise their healing process cannot be ruled out.

The present pilot study was therefore carried out to assess the feasibility and efficacy of a vigorous aerobic exercise in breast cancer patients shortly after the adjuvant treatments. Besides the primary assessment of training effects on patients' physical performance, the secondary goal of the present study was, through estimating the loading (body reaction forces) during the training sessions, to preliminarily evaluate the potential of the present training regimen to affect bone mass.

Material and methods

Participants

A total of 30 breast cancer patients, aged from 41 to 65 years, receiving adjuvant treatments such as chemotherapy, radiotherapy, endocrine therapy, or their combination participated in this 12 week, randomized controlled exercise intervention trial. Participants were recruited from the Department of Oncology in Tampere University Hospital, Tampere, Finland. Inclusion criteria were histologically proven invasive breast cancer, adjuvant chemotherapy within six months or duration of endocrine therapy no more than six months, aged from 35 to 65 and signed informed consent.

Exclusion criteria were hematogenous metastases, no systemic adjuvant therapy, pregnancy or lactation, severe cardiac disease (NYHA class III or more), myocardial infarction within 12 months, uncontrolled hypertension, verified osteoporosis, other serious illness or medical condition, which could be contraindication for exercise, patients not capable of training (severe knee arthrosis, ligament or cartilage injuries at lower extremities), residence more than one hour from the exercise center and competitive athlete. After having given the informed consent, the participants were stratified by age and then randomly assigned into exercise and control groups. The ethical committee of Tampere University Hospital approved the study protocol.

Description of the intervention

The exercise group attended guided aerobic exercise sessions once a week. The guided training session comprised 10-minute warm-up and cool-down periods, with an intermediate 30 to 40 minute effective period. In alternate weeks, the effective part of the guided training was based either on step aerobics or circuit training. In total, the planned weekly exercise program was intended to consist of the above mentioned guided training session and at least two home training sessions (three home sessions were recommended, but two sessions were considered sufficient in the study protocol). During the first two weeks, intensity of the training was kept moderate (11 in terms of self-rated perceived exertion, RPE [22]), while it was increased gradually from moderate to somewhat hard or hard levels (from 14 to 16 in overall assessed RPE scale) during 12-week exercise period. During the guided training sessions, the training intensity was occasionally monitored with heart rate measurements in order to ensure the consistency between self-rated and actual exertion levels. The guided training was intended to be near to the anaerobic threshold but mostly aerobic. However, individuals' anaerobic threshold could have been exceeded temporarily during the training.

Step aerobics consisted of several, typical step movements resulting in a total of 150 to 180 jumps and leaps to diverging directions during each session. Circuit-training consisted of three rounds of 8 to 10 different vigorous movements such as rope-jumping and skate-jumping resulting in a total of 100 to 150 jumps and leaps during each session. Duration of each circuit training movement varied from 20 to 40 seconds with a similar resting period between consecutive movements. The home training session consisted of about 100 leaps and jumps similar to those employed in the circuit training-program. In addition, endurance training (walking, cycling,

swimming etc.) performed at the same RPE was recommended to complement the home training session in terms of total duration.

The control group was advised to continue their normal daily routines and activities during the 12-week follow-up period.

Measurements

Physical performance was assessed with figure-8 running (a measure of dynamic agility), counter movement jump (a measure of dynamic muscle performance), maximal isometric muscle force of leg extension and elbow flexion tests in all participants at baseline before randomization and after the 12-week intervention. The figure-8 running test [23] was performed by running around two poles placed 10 m apart. The participant was asked to run or walk two laps of the course as fast as possible. The running time was measured using a stop-watch. This test has been found sensitive to show training-related effects in physical performance among pre- and postmenopausal women [20,24]. Dynamic maximal take-off force and power were measured with a force-plate (Kistler Ergojump 1.04, Kistler Instrumente AG, Winterthur, Switzerland) during counter movement jump with a precision of about 3% [25]. Maximal isometric leg extension and arm flexion strength values were measured with isometric leg press (Tamtron, Tampere, Finland) and arm (Digitest, Muurame, Finland) dynamometers with a precision of about 5% and 10%, respectively [21,25]. Two-kilometer walking time (a measure of cardiorespiratory fitness) was assessed with the two kilometer walk test (UKK walk test, Tampere, Finland) with a precision of 2.2% [26]. In order to determine the activity level of the participants in general, number of walking steps was measured during one week before and in the middle of the 12-week intervention with a pedometer (Yamax Digiwalker, DW 700, Tokyo, Japan).

Distribution of relative ground reaction forces in multiples of body weight (i.e., in vertical accelerations expressed in multiples of *g* above the normal Earth's gravity) were measured from three participants with a physical activity recorder based on triaxial accelerometers (Newtest Oy, Oulu, Finland) during the guided step-aerobics and circuit training sessions as well as during home training sessions during last two weeks (weeks 11 and 12) of the training intervention [27]. These three participants were subjectively selected on the basis of their apparent skills and preferred intensity in jumping and were accordingly classified as jumper, mediocre and non-jumper.

Statistical analysis

Analysis was done with SPSS statistics software (version 11.0). Means and standard deviations (SD) were given as descriptive statistics. On the intention-to-treat basis (all subjects with follow-up measurements were included, despite their adherence to or compliance with the exercise regime), analysis of covariance (ANCOVA) with age, days since the completed chemotherapy treatment and baseline values as covariates, was used to evaluate the treatment effect between the groups during the training intervention. A *p*-value less than 0.05 was considered statistically significant.

Results

Clinical and physical performance characteristics of the training and control group at baseline and at the end of 12-week exercise intervention are shown in Table I. The group characteristics were similar at the baseline. Body weight did not change in either group. Typical heart rate during the exercise training was between 150 and 170 beats according to heart rate monitoring. Mean number (SD) of daily walking steps per day in the training and control groups were 7852 (2318) and 9122 (3220) at baseline, and 8674 (1237) and 8809 (3181) in the middle of the intervention, respectively.

Compliance and adherence to the training

One participant withdrew from the study before randomization due to family reasons. Another participant, suffering from epilepsy related sketching disorder, withdrew from the intervention group before starting the training. In addition, one participant underwent elective operation unrelated to breast cancer or training and was thus able to attend only three training sessions in the end of the intervention. Ignoring these three participants, the adherence to the weekly-supervised training sessions was 78%. The most common reasons for not attending the session were a holiday trip or flu. Home training program was performed 2.1 times per week on average, complying fully with the study protocol. As regards the contents of home training sessions, the mean duration was 21 minutes including 86 leaps and jumps on average in addition to endurance activities, the number of jumps and leaps being in fully line with what was intended in the study protocol.

Training-effects on physical performance

Time of figure-8 running and peak power during counter movement jump take-off showed a signifi-

Table I. Clinical characteristics and physical performance at baseline and at 12-week follow-up, and the observed treatment effect.

Group	Training (n = 14)		Control (n = 14)		Treatment effect ^a	
	Baseline Mean (SD)	12 week Mean (SD)	Baseline Mean (SD)	12 week Mean (SD)	Mean (95% CI)	p-value
Age, years	52.5 (6.4)		51.3 (7.3)			
Weight, kg	74.6 (12.8)	73.5 (13.3)	75.4 (12.0)	75.5 (12.8)	-0.4 (-1.6 to 0.8)	0.484
Body Mass Index	27.4 (5.4)	26.9 (5.6)	27.6 (4.6)	27.7 (4.9)	-0.2 (-0.6 to 0.3)	0.449
Height, cm	165 (5)		165 (6)			
<i>Adjuvant treatment</i>	Training (n = 14)		Control (n = 14)			
Chemotherapy (C)		5		2		
Endocrine therapy (E)		2		4		
Combination (C + E)		7		8		
<i>Physical Performance</i>						
8-figure running, sec	16.1 (1.6)	15.7 (1.3)	16.9 (2.0)	16.7 (1.4)	-0.8 (-1.5 to -0.2)	0.017*
counter movement jumping force, N	1576 (324)	1579 (274)	1663 (389)	1615 (379)	84 (-143 to 310)	0.445
counter movement jumping power, W/kg	31.0 (6.4)	31.8 (5.8)	31.1 (5.1)	30.5 (4.2)	3.6 (1.1 to 6.1)	0.007*
isometric leg extension force, N	1246 (177)	1305 (177)	1383 (284)	1393 (275)	39 (-49 to 137)	0.358
isometric elbow flexion force, N	127 (18)	131 (20)	130 (30)	129 (28)	14 (-2 to 28)	0.082
2-km walk time, min	17.9 (1.5)	17.6 (1.3)	17.8 (1.5)	17.2 (1.4)	0.55 (-0.004 to 1.1)	0.051

^aAbsolute treatment effect between the training and the control group (*p < 0.05) at follow-up (covariance analysis, age, days since the completed chemotherapy and baseline value were used as covariates).

cant treatment-effect between the trainees and controls (Table I). Otherwise the changes in physical performance values did not differ between the groups, the 2-km walking time excluded, indicating a borderline trend in favor of the control group.

Training induced accelerations of the body

Estimated mean ground reaction force distributions of the three selected participants (a jumper, mediocre and non-jumper) during a step aerobics, circuit-training and home training session are shown in Figure 1. Acceleration profiles were distinctly different not only between individuals but also between different training modes. More intensive jumping in step-aerobics, as one could expect, resulted in higher accelerations (up to 6 times of body weight), while the profiles during the circuit training were surprisingly similar irrespective of the participant. Particularly noteworthy is that the home training was able to result in at least as comparable acceleration profiles as were the guided sessions.

Discussion

We were one of the first groups to investigate the effects of a relatively vigorous aerobic exercise regimen among breast cancer survivors after recently completed adjuvant chemotherapy while endocrine therapies were still continuing. There was an indication of somewhat improved physical performance in both groups, although the trend was more consistent in the training group. The

common trend for improvement was most likely attributable to overall recovery process of the patients after the heavy treatments and severe disease. The actual positive training-induced effects were seen in the agility and lower extremity muscle power. From the clinical perspective, this is relevant since a good dynamic muscle performance is not only necessary for high bone mass but also for good body balance, both factors being associated with reduced risk of osteoporosis-related bone fractures in later life.

This present training performed mostly at somewhat hard or hard level between 14 and 16 in the RPE scale, increasing the heart rate over 80% of the maximum and producing several high ground impacts, was tolerated surprisingly well. Fatigue could well have limited their participation in the training sessions, but participants committed themselves both to the guided and home training despite the relatively high physical demands of the regimen. According to the word of participants, the similar background of the trainees and the small training group seemed to facilitate the adherence to the training. The run-in period at lower intensity in the beginning and relatively slow progression in the training intensity may also have contributed to good compliance. As regards the overall feasibility, it is stressed that the home training was accomplished very satisfactorily, too. This observation supports the notion that the breast cancer survivors are highly motivated to pay attention to health enhancing issues, including physical activity.

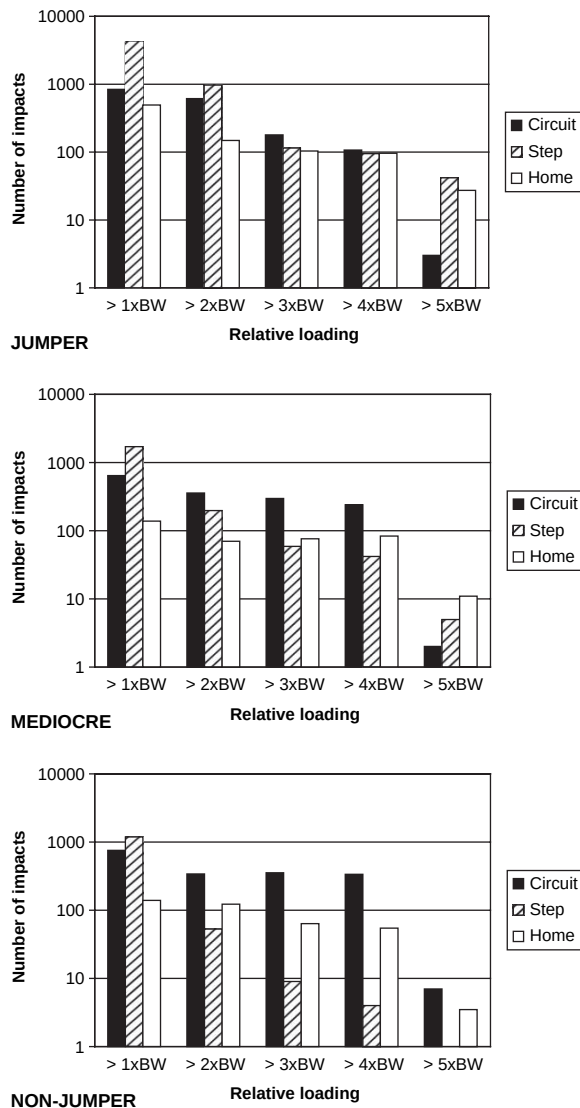


Figure 1. Acceleration profiles in three subjects during circuit training (black bar), step-aerobics (striped bar), and home training (white bar) sessions. The x-axis denote the categories of reaction forces, expressed in multiples of body weight (BW) (*i.e.*, between $1 \times$ (standing) and less than $2 \times$ BW, between $2 \times$ and $3 \times$ BW etc.), while the y-axis denote the total number of recorded within the particular category. The subjects were classified in terms of their jumping skills and preferred intensity as jumper (upper panel), mediocre (middle panel) and non-jumper (lower panel). Of note, the non-jumpers' step aerobic training was compromised due to leg pain during the particular test session.

In addition to good adherence to the training, the average number of walking steps around 9000 per day soon after heavy adjuvant treatments corresponds to an amount of quite an active person, even among healthy persons. Such a large amount of walking demonstrates patients' will to be engaged in feasible physical activity. The study participants including the control patients were allowed to keep the pedometers over the entire 12-week intervention period and this may also have motivated the control

subjects to walk. In line with the above, the 2-km walking time actually seemed to improve more in the control group than in the training group. Trainees, however, perceived a considerable proportion of these steps in intervention related activities, which were more vigorous in nature.

Regarding the intended ability of the present exercise regimen to prevent treatment related bone loss; the present results were very promising. The trainees tolerated the versatile jumping and leaping exercises well and the magnitude of loading, as obtained from the accelerometers, reached and exceeded the level, (*i.e.*, four times of body weight or more) which is known to be effective in increasing bone mass [20,27]. In addition, the total daily number of sufficiently high impacts needs not to be very high for its efficacy—most likely some 50 of such impacts would suffice [28]. The three patients with apparently different skills in jumping achieved adequate number of stimuli in their training. It is important, however, that the contents of training are sufficiently varying while the magnitude and number of specific loading stimuli is kept adequate. The experience and competence of the exercise instructors can be particularly crucial in planning the training sessions, and attention should be paid to this topic. The role of local cancer societies may turn out to be central in developing, and particularly in organizing customized exercise classes for breast cancer survivors' to promote their healing process.

It is recognized that the sample size of breast cancer survivors was small in this study, the duration of the intervention was relatively short, and the study addressed only a very narrow segment of this pertinent health problem. Nevertheless, this pilot exercise intervention trial clearly showed that relatively vigorous and versatile training performed at high heart rate is feasible among breast cancer survivors, and it is able to result in improved dynamic muscle performance.

In summary, the intense aerobic exercise appeared to be well-tolerated and effective training mode among breast cancer survivors, who had recently completed heavy adjuvant treatments such as chemotherapy. Significant training effects were observed in lower limb dynamic performance. These findings, in conjunction with the fact that the magnitude of incident loading during the training sessions seemed to be sufficiently high to increase bone mass in different subjects, suggest that this kind of vigorous training regimen is feasible among breast cancer survivors and could have a potential to prevent bone loss accompanying the adjuvant treatments of breast cancer. Large prospective controlled trials are needed to confirm these findings.

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References

- [1] Baum M, Budzar AU, Cuzick J, Forbes J, Houghton JH, Klijn JG, et al. Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early breast cancer: First results of the ATAC randomised trial. *Lancet* 2002;359: 2131–9.
- [2] Bines J, Oleske DM, Cobleigh MA. Ovarian function in premenopausal women treated with adjuvant chemotherapy for breast cancer. *J Clin Oncol* 1996;14:1718–29.
- [3] Plowman PN. Tamoxifen as adjuvant therapy in breast cancer. Current status. *Drugs* 1993;46:819–33.
- [4] Powles TJ, Hickish T, Kanis JA, Tidy A, Ashley S. Effect of tamoxifen on bone mineral density measured by dual-energy x-ray absorptiometry in healthy premenopausal and postmenopausal women. *J Clin Oncol* 1996;14:78–84.
- [5] Saarto T, Blomqvist C, Valimaki M, Makela P, Sarna S, Elomaa I. Chemical castration induced by adjuvant cyclophosphamide, methotrexate, and fluorouracil chemotherapy causes rapid bone loss that is reduced by clodronate: A randomized study in premenopausal breast cancer patients. *J Clin Oncol* 1997;15:1341–7.
- [6] Ettinger B, Black DM, Mitlak BH, Knickerbocker RK, Nickelsen T, Genant HK, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: Results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. *JAMA* 1999;282:637–45.
- [7] Lamont EB, Lauderdale DS. Low risk of hip fracture among elderly breast cancer survivors. *Ann Epidemiol* 2003;13: 698–703.
- [8] Liberman UA, Weiss SR, Broll J, Minne HW, Quan H, Bell NH, et al. Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis. The Alendronate Phase III Osteoporosis Treatment Study Group. *N Engl J Med* 1995;333:1437–43.
- [9] Jones LW, Courneya KS. Exercise discussions during cancer treatment consultations. *Cancer Pract* 2002;10:66–74.
- [10] Courneya KS. Exercise in cancer survivors: An overview of research. *Med Sci Sports Exerc* 2003;35:1846–52.
- [11] Galvao DA, Newton RU. Review of exercise intervention studies in cancer patients. *J Clin Oncol* 2005;23:899–909.
- [12] Penedo FJ, Schneiderman N, Dahn JR, Gonzalez JS. Physical activity interventions in the elderly: Cancer and comorbidity. *Cancer Invest* 2004;22:51–67.
- [13] Stevinson C, Lawlor DA, Fox KR. Exercise interventions for cancer patients: Systematic review of controlled trials. *Cancer Causes Control* 2004;15:1035–56.
- [14] Holmes MD, Chen WY, Feskanich D, Kroenke CH, Colditz GA. Physical activity and survival after breast cancer diagnosis. *JAMA* 2005;293:2479–86.
- [15] Ott CD, Lindsey AM, Waltman NL, Gross GJ, Twiss JJ, Berg K, et al. Facilitative strategies, psychological factors, and strength/weight training behaviors in breast cancer survivors who are at risk for osteoporosis. *Orthop Nurs* 2004;23:45–52.
- [16] Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: Cardiopulmonary and quality of life outcomes. *J Clin Oncol* 2003;21: 1660–8.
- [17] Fairey AS, Courneya KS, Field CJ, Bell GJ, Jones LW, Mackey JR. Randomized controlled trial of exercise and blood immune function in postmenopausal breast cancer survivors. *J Appl Physiol* 2005;98:1534–40.
- [18] Kolden GG, Strauman TJ, Ward A, Kuta J, Woods TE, Schneider KL, et al. A pilot study of group exercise training (GET) for women with primary breast cancer: Feasibility and health benefits. *Psychooncology* 2002;11:447–56.
- [19] Segal R, Evans W, Johnson D, Smith J, Colletta S, Gayton J, et al. Structured exercise improves physical functioning in women with stages I and II breast cancer: Results of a randomized controlled trial. *J Clin Oncol* 2001;19:657–65.
- [20] Heinonen A, Kannus P, Sievanen H, Oja P, Pasanen M, Rinne M, et al. Randomised controlled trial of effect of high-impact exercise on selected risk factors for osteoporotic fractures. *Lancet* 1996;348:1343–7.
- [21] Heinonen A, Oja P, Sievanen H, Pasanen M, Vuori I. Effect of two training regimens on bone mineral density in healthy perimenopausal women: A randomized controlled trial. *J Bone Miner Res* 1998;13:483–90.
- [22] Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14:377–81.
- [23] Tegner Y, Lysholm J, Lysholm M, Gillquist J. A performance test to monitor rehabilitation and evaluate anterior cruciate ligament injuries. *Am J Sports Med* 1986;14:156–9.
- [24] Uusi-Rasi K, Kannus P, Cheng S, Sievänen H, Pasanen M, Heinonen A, et al. Effect of alendronate and exercise on bone and physical performance of postmenopausal women: A randomized controlled trial. *Bone* 2003;33:132–43.
- [25] Torvinen S, Sievanen H, Jarvinen TA, Pasanen M, Kontulainen S, Kannus P. Effect of 4-min vertical whole body vibration on muscle performance and body balance: A randomized cross-over study. *Int J Sports Med* 2002;23: 374–9.
- [26] Oja P, Laukkanen R, Pasanen M, Tyry T, Vuori I. A 2-km walking test for assessing the cardiorespiratory fitness of healthy adults. *Int J Sports Med* 1991;12:356–62.
- [27] Vainionpää A, Korpelainen R, Vihriala E, Rinta-Paavola A, Leppaluoto J, Jamsa T. Intensity of exercise is associated with bone density change in premenopausal women. *Osteoporos Int* 2006;17:455–63.
- [28] Turner CH. Three rules for bone adaptation to mechanical stimuli. *Bone* 1998;23:399–407.