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Osteoporosis and Arterial Stiffness: Effects of Exercise Training

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1. Introduction

In addition to menopause and advanced age, risk factors for atherosclerosis are also associated with osteoporosis. Osteoporosis and atherosclerosis are major public health problems that lead to increased rates of morbidity and mortality. Because these diseases progress with aging and share common risk factors, both seem to correlate with aging. Although historically considered as independent conditions, clinical and epidemiological studies indicate that common pathophysiological mechanisms underlie these diseases. Physical activity is of primary importance to reach optimal peak bone mass and decrease arterial stiffness, an independent risk factor of atherosclerosis. Exercising that incorporates levels of whole body accelerations exceeding 3.9 g at a frequency of 100 per day has been shown to have positive effects on cardiovascular fitness, femoral bone density and balance (Jämsä et al, 2006; Vainionpää et al, 2006; Heikkinen et al, 2007). These acceleration levels are normally reported in activities such as running or jumping, which may be appropriate for middle aged and younger individuals, but may be more difficult for many older people or those with chronic lower limb injuries to achieve. This chapter explains the effect of exercise on osteoporosis and arterial stiffness.

2. Arterial structure

Arteries are flexible, muscular blood vessels that carry blood from the heart and oxygenated blood to tissues throughout the body (Murray, TD. & Murray JM. 1998). The arterial wall comprises three layers (Fig. 1). The outermost adventitia primarily consists of connective tissue made of collagen, a structural protein that helps to maintain vessel integrity and provide flexibility. The elastin media is the middle layer, which mostly comprises smooth muscle tissue that confers the ability to contract and relax. This helps to regulate the size of the vessel lumen and thus alter blood pressure and flow. The inner intima layer comprises smooth epithelial tissue that facilitates blood flow. This layer includes the endothelium, which is the inner arterial wall.

3. Collagen and elastin on bone and arteries

About 80% of the total protein in bone consists of collagen, about 95% of which is type I. Bone strength depends on the orientation of osteons (and thus collagen fibers) within

cortical bone. Various determinants of bone quality are interrelated, especially minerals and collagen (Viguet-Carrin et al, 2007).

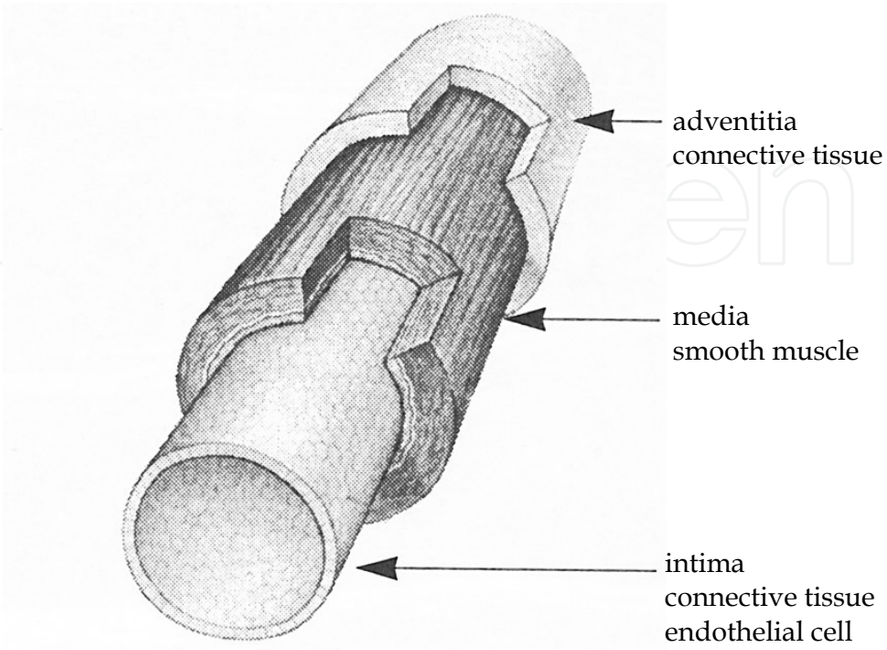

Fig. 1. Arterial structure

Collagen and elastin are two vital components of blood vessels (Greenwald, 2007). Elastic arterial fibers comprise 90% elastin, which enables tissues to resume shape after stretching or contraction (Milewicz et al, 2000). Collagen is the most common protein in mammals (25% to 35% of total body protein content) as it is the main component of connective tissue. Elastin and collagen play crucial roles in arterial remodeling. Moreover, arterial stiffness depends upon the composition of the elastin and collagen, and the calcium content of elastin. As collagen ages, specific physical and biochemical changes reduce extensibility and increase rigidity. Thus, aging increases the diameter of collagen fibers in various tissues. Fibrils also become more crystalline, which strengthens intermolecular bonds and increases resistance to further deformation. Furthermore, aging is believed to be associated with an increased number of intramolecular and intermolecular cross-links that restrict the ability of collagen molecules to glide past each other. Collagen fibers are only slightly extensible but are very resistant to tensile stress. Therefore, they are the main constituents of structures such as ligaments, tendons and arteries that are subjected to pulling forces. As a result of aging, elastic fibers lose resilience and undergo various other changes, including fragmentation, fraying, classification and other types of mineralization and increased cross-linkages (Knott et al. 1997).

4. Osteoporosis and arterial stiffness

The multifactorial and degenerative entities of osteoporosis and atherosclerosis are major public health problems. These diseases accompany the aging process and share common risk factors. Increased arterial stiffness independently predicts cardiovascular and

cerebrovascular events in healthy populations. Several studies have examined associations between atherosclerosis at different sites and osteoporosis or low bone mineral density (BMD) in women, and the findings suggest that the development of osteoporosis is a risk for advanced atherosclerosis after menopause (Hak et al, 2000; Sanada et al, 2004). The Osteo Sono-Assessment Index, which reflects elastic properties of bone tissues, negatively correlates with pulse wave velocity (PWV) in both sexes; this association is more prominent in females than in males and becomes even closer in post-menopausal females (Hirose et al, 2003, Fig. 2).

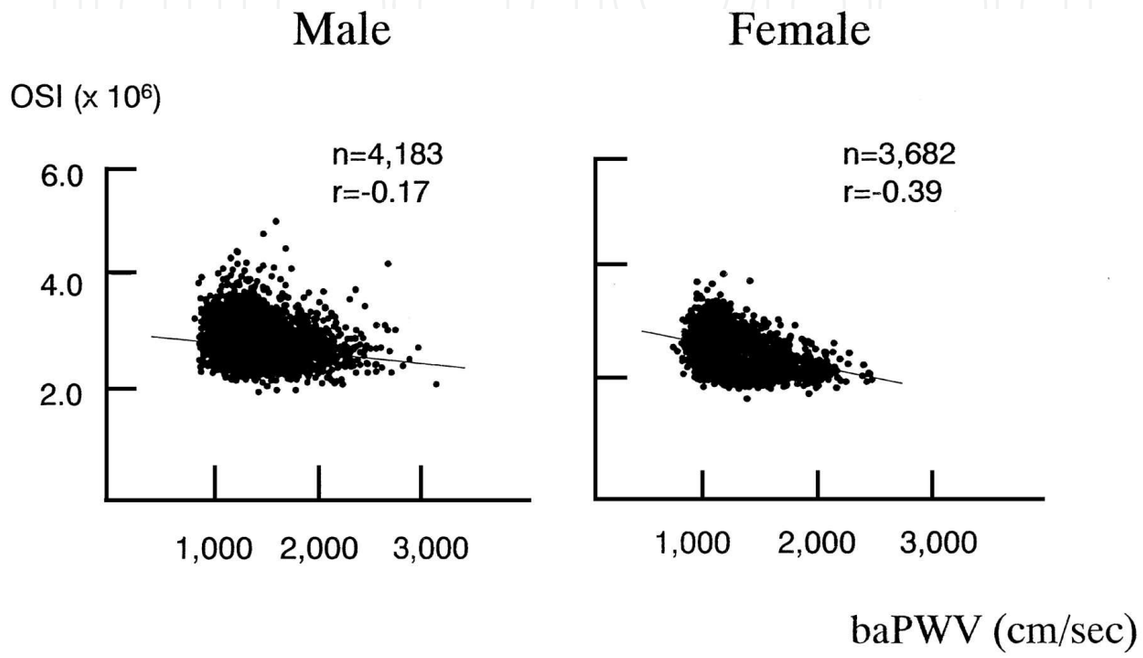

Fig. 2. Correlation between osteo-sono assessment index (OSI) and brachial-ankle pulse wave velocity (baPWV) in both genders (Quotation from Hirose et al, 2003).

Increased central arterial stiffness reduces the arterial buffering function of the pulsation of blood pressure and blood flow, which contributes to increases in systolic blood pressure and in pulse pressure. Increased arterial stiffness alters the cyclical dynamics of arterial wall connective tissues, promotes vascular remodeling, and increases arterial wall thickness and plaque formation. Patients with osteoporosis have the most arterial stiffness. The reciprocal association between osteoporosis and arterial stiffness is supported by the relationship between bone mineral loss and each of vascular calcification, atherosclerosis and cardiovascular disease (CVD). Arterial calcification leading to increased arterial stiffness, a powerful risk factor for CVD, might underlie the association between osteoporosis and CVD in post-menopausal women. Osteoprotegerin might be a molecular link between bone loss and vascular calcification. In fact, intimal calcification is associated with advanced atherosclerosis. In addition, Frost et al. (2008) suggested that decreased BMD is associated with arterial calcification and stiffening and raised the possibility that osteoprotegerin is a marker of arterial stiffening, independently of any association with BMD. Osteoporotic postmenopausal women free of CVD and risk factors had increased augmentation index, a measure of wave reflections and arterial stiffness, and central aortic systolic and pulse

pressures, which show a higher estimated aortic PWV indicating a stiffer aorta (Mangiafico et al, 2008, Tab. 1). Such alterations may increase the risk of CVD in postmenopausal osteoporosis. Therefore, the prevention and treatment of increased arterial stiffness and/or osteoporosis are important.

Parameter	Patients n=182	Controls n=160	P value
Brachial SBP (mmHg)	123.7±11.8	122.2±12.3	0.17
Brachial DBP (mmHg)	75.8±8.5	74.2±7.4	0.12
Brachial PP (mmHg)	47.9±11.4	48.0±10.8	0.77
Aortic SBP (mmHg)	117.5±12.1	111.4±12.2	<0.0001
Aortic DBP (mmHg)	76.9±8.4	74.9±8.0	0.28
Aortic PP (mmHg)	40.5±10.3	36.4±8.1	0.0007
Heart rate (beats/minutes)	71.9±7.6	73.6±12.9	0.80
Ejection duration (ms)	317.3±29.9	321.0±24.4	0.58
Augmentation (mmHg)	15.3±5.4	11.0±3.7	<0.0001
Augmentation index (%)	37.2±7.0	29.6±9.2	<0.0001
Timing of reflected wave (ms)	122.0±11.5	130.6±13.6	<0.0001
Subendocardial viability ratio (%)	134.6±14.5	134.9±30.5	0.28

SBP = systolic blood pressure; DBP = diastolic blood pressure; PP = pulse pressure; ms = milliseconds.

Table 1. Peripheral and central haemodynamic parameters of osteoporotic patients and control subjects (Quotation from Mangiafico et al, 2008)

5. Effects of aging on osteoporosis and arterial stiffness

In addition to menopause and advanced age, risk factors for CVD such as obesity and diabetes are also associated with osteoporosis. Thus, osteoporosis and atherosclerosis seem to correlate with aging. Osteoporosis-related fractures represent a major health concern, particularly among elderly populations. Post-menopausal osteoporosis in women with increased availability of circulating osteoprogenitor cells has a detrimental influence on arterial compliance. Lifestyle modification includes measures to reduce falls and bone loss such as participating in exercise, adequate dietary calcium intake and avoiding smoking and excessive alcohol consumption. Osteoporosis is characterized by the progressive loss of bone tissue and micro-architectural deterioration that reduces the quality of life for the elderly and thus it is a persistent public health issue. BMD at the femoral neck and spine in aging women decreases by 1 - 2 % per year (Finkelstein et al, 2008). Decreasing estrogen concentrations after menopause can cause a decline in BMD, which leads to osteoporosis. Epidemiological data suggest that estrogen deficiency is a risk factor for CVD and osteoporosis.

Changes in arterial function with age include a decrease in major artery compliance and increased arterial stiffness will result in an increase in resting and exercise blood pressure. Large arteries that convey blood at high pressure have relatively thick walls. Arterial stiffness, an independent risk factor for CVD, increases with advancing age (Tomiyama et al, 2003, Fig. 3). This age-related increase is greater in post-menopausal women, which increases their vulnerability to CVD. The cause of progressive age-related stiffness is the obviously increased thickness of the artery walls and interstitial collagen. Vessel structure also changes when an increase in blood pressure augments vascular tension. Increased arterial stiffness might be due to age-associated structural changes in the arterial walls. Aging is associated with a decrease in elastin and a concomitant increase in collagen and connective tissues in the arterial walls and an increase in arterial stiffness due to menopause.

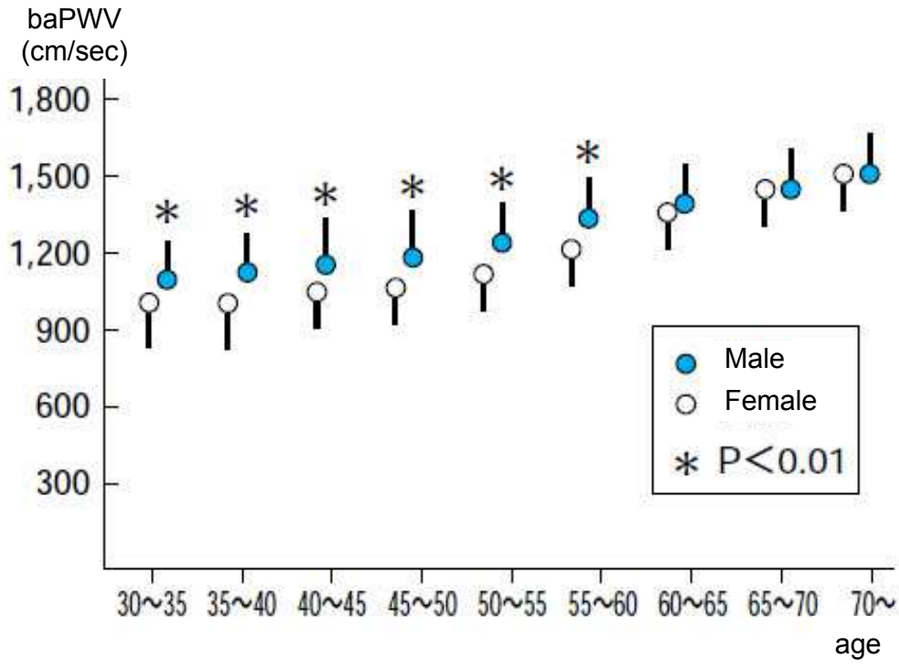

Fig. 3. Chronological changes in brachial-ankle pulse wave velocity (baPWV) in healthy men and women (Quotation from Tomiyama et al, 2003).

6. Exercise

Health organizations such as the American Heart Association (AHA) and the American College of Sports Medicine (ACSM) recommend habitual exercise to prevent and treat CVD and frailty associated with aging. In contrast to age, regular physical exercise in general, and aerobic exercise/fitness in particular, are associated with enhanced vascular function and a reduced risk of CVD. However, in contrast to the beneficial effects of aerobic exercise, high-intensity resistance training increases arterial stiffness in young and middle-aged healthy men and in pre-menopausal women.

To date, the predominant medical strategies to prevent and/or treat post-menopausal bone loss have focused on antiresorptive medications (i.e., bisphosphonates). However, these treatments might be limited due to adverse side effects, questionable compliance and long-term safety concerns. Various types of exercise, such as walking, jogging or resistance training, could provide an important role in maintaining and/or increasing bone density in women. Therefore, implementing non-pharmacological treatment strategies such as exercise that have few or no inherent side effects is critical. Exercise plays an important role in maintaining or increasing bone density. Physical activity increases growth in the width and mineral content of bones in girls and adolescent females, particularly when initiated before puberty, carried out in volumes and at intensities seen in athletes, and accompanied by adequate caloric and calcium intake. The differences are regularly the largest in gymnasts whose hip and spine BMD values are 30% – 40% higher than those of long-distance runners (Robinson et al, 1995); a plausible explanation for this is the greater magnitude of impact forces generated in gymnastic movements (10- to 12-fold body weight) compared with

running (3- to 5-fold body weight) (Duncan et al, 2002). Moreover, not only are high-impact sports associated with a greater BMD, but athletes involved in high-impact sports also have a greater section modulus (a predictor of strength in bending) (Nikander et al, 2005, Fig. 4). Since the two mechanisms that principally determine adult bone health are peak BMD at skeletal maturity and the rate of bone loss with advancing age, maximizing pre-menopausal BMD is a critical strategy for preventing osteoporosis and resultant fractures later in life.

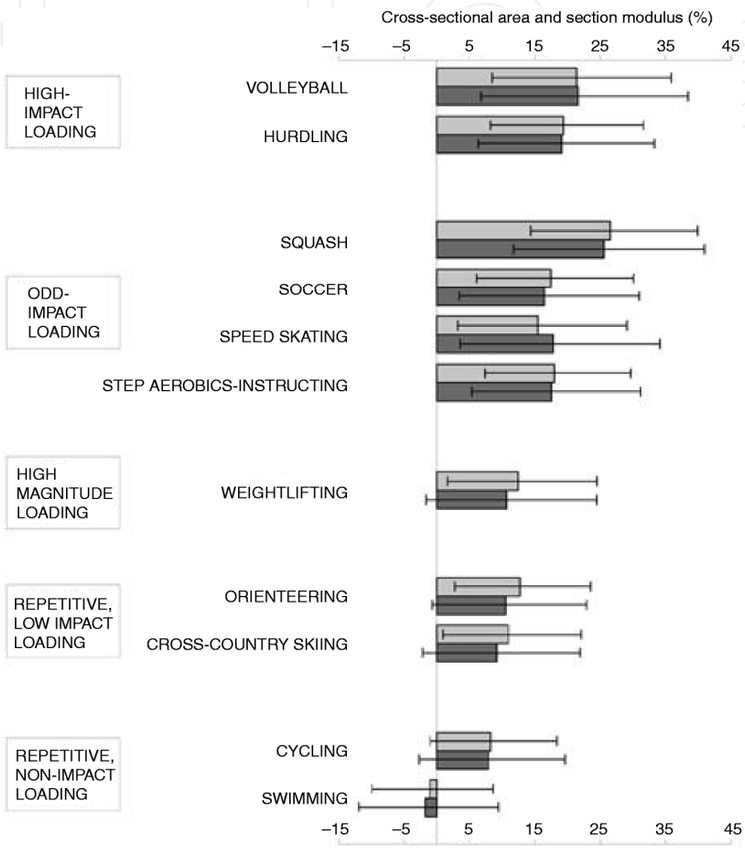

Fig. 4. Differences in cross-sectional area and section modulus (a predictor of strength in bending; between athletes participating in sports of different loading modalities and controls. Values are means and 95% confidence interval (CI) represented by horizontal bars. Where the 95% CI does not cross the zero line (the value for the controls) the difference was significant (P<0·05) (Quotation from Nikander et al, 2005) .

6.1 Aerobic exercise and arterial stiffness

Physical activity can be used as a prophylactic tool against osteoporosis and to improve skeletal resistance to bone fractures. A physically active lifestyle is associated with a 30% to 50% decrease in the risk of vertebral or hip fractures. Aerobic exercise positively affects blood pressure and arterial stiffness. Regular aerobic exercise is recommended to prevent and treat CVD and the frailty associated with aging. Regular aerobic exercise is beneficial for reversing arterial stiffening in middle-aged and older adults (Tanaka et al, 2000, Fig. 5). Moderate, short-term aerobic exercise could restore carotid arterial compliance in previously sedentary post-menopausal women taking hormone replacement therapy (Moreau et al, 2002).

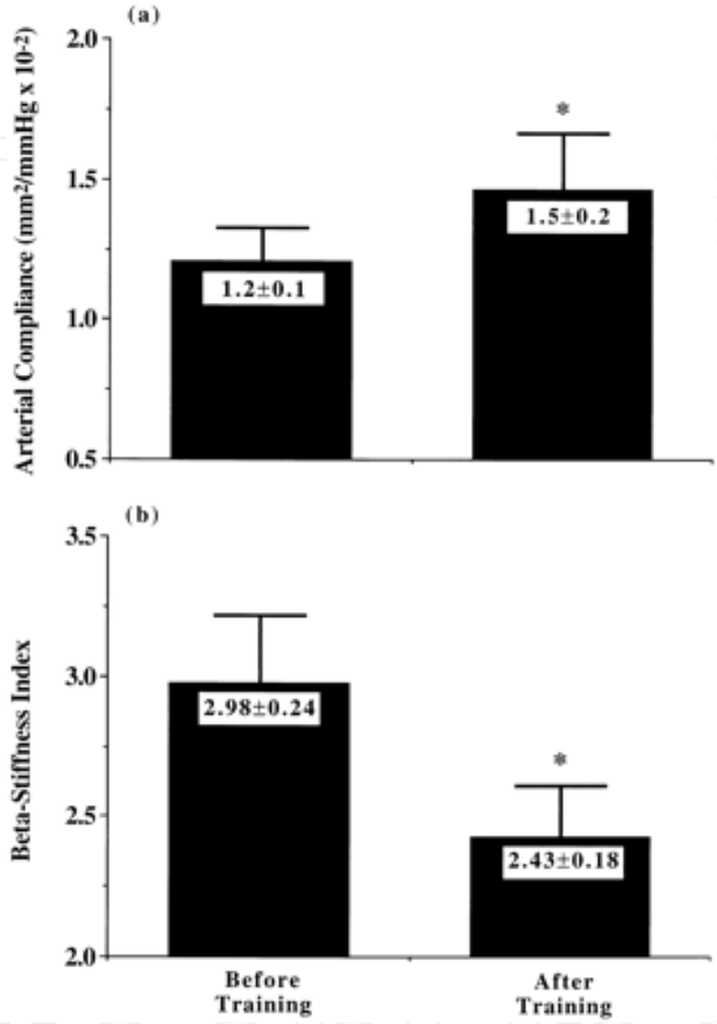

Fig. 5. Arterial compliance (a) and ß-stiffness index (b) before and after aerobic exercise intervention. *P<0.01 vs before training. (Quotation from Tanaka et al, 2000)

The ACSM position on physical activity and bone health recommends regular weight-bearing endurance activities, including jogging and jumping to preserving bone mass during adulthood. Moreover, although vascular function is not improved by aerobic exercise before resistance training, aerobic exercise thereafter can prevent vascular function from deterioratin (Okamoto et al. 2007, Fig. 6). Adaptive bone responses might require dynamic, rather than static mechanical stimulation. Aerobic exercise combined with high-impact exercise training seems to be effective against osteoporosis and/or for improving vascular health.

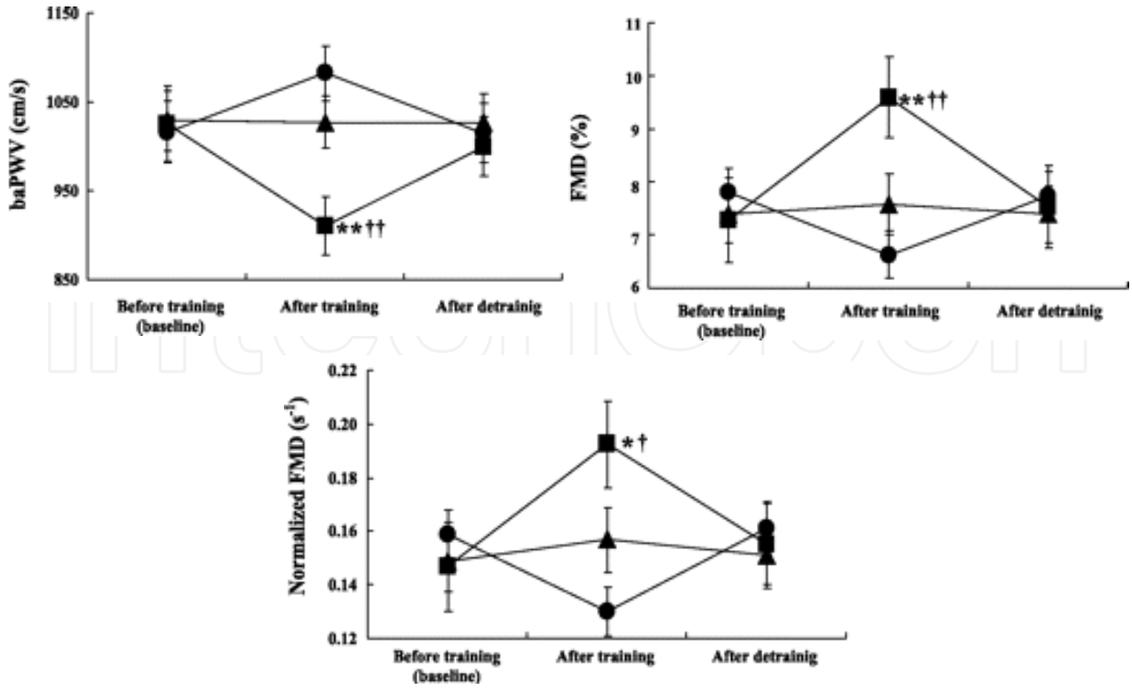

Fig. 6. Changes in brachial-ankle pulse wave velocity (baPWV), percent flow-mediated dilation (%FMD), and normalized FMD in groups that ran before resistance training (RT) (BRT;●), ran after RT (ART;■), or remained sedentary (SED;▲). Values are means ± SE. *P < 0.05; **P < 0.01 vs. baseline. †P < 0.05; ††P < 0.01 vs. BRT group (Quotation from Okamoto et al. 2007).

6.2 Resistance exercise and arterial stiffness

Physical activity could increase bone strength by increasing muscle mass (Bennell et al, 2000). Physical activity reduces skeletal fragility and a predisposition to falling through a combination of increased BMD and improved coordination, balance, reaction time and muscle function (Liu-Ambrose et al, 2004). Resistance training is a critical component in exercise prescription programmes for healthy adults. Resistance training is widely recommended to prevent sarcopenia and osteoporosis (Pollock et al, 2000). Resistance exercise at high intensity [one repetition maximum (1RM), 80%] has generally been regarded as optimal for gaining muscular size and strength (McDonagh, & Davies, 1984). However, high intensity resistance training has been associated with the stiffening of large arteries in young and middle-aged adults (Miyachi et al. 2004, Fig. 7). In contrast, Cortez-Cooper et al (2008) reported that 13 weeks of moderate-intensity resistance training two or three times per week does not reduce central arterial compliance in middle-aged and older adults. In addition, Yoshizawa et al (2009) demonstrated that 12 weeks of moderate-intensity resistance training did not affect arterial stiffness in middle-aged women. Moreover, low-intensity resistance training with short inter-set rest periods reduces arterial stiffness and improves vascular endothelial function (Okamoto et al, 2011). These conflicting result might be due to differences in the intensity of resistance training. Therefore, resistance training might need to be carefully prescribed based on individual pre-existing conditions and the anticipated outcome of the exercise program. Moderate and low intensity resistance training is recommended from the general viewpoints of health promotion and safety.

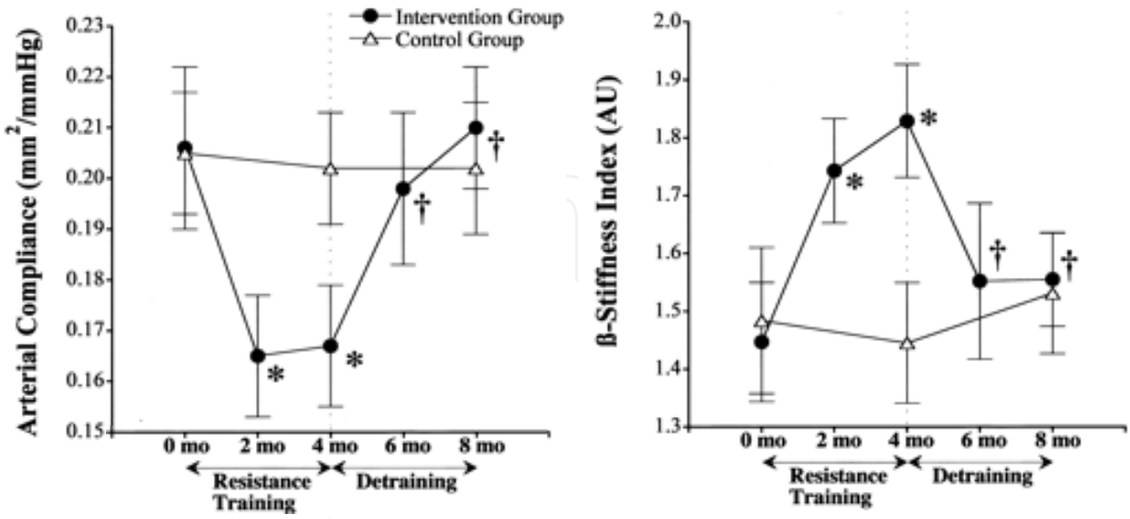

Fig. 7. Changes in carotid arterial compliance (top) and β-stiffness index (bottom) in the intervention group (black circles) and control group (white triangles). Values are mean±SEM. *P<0.05 vs baseline; †P<0.05 vs resistance training period (2- and 4-month values) (Quotation from Miyachi et al. 2004).

6.3 Other types of exercise and arterial stiffness

Physical activity stimulates increases in bone diameter throughout life and diminishes the risk of fractures by mechanically counteracting the rates of bone thinning and bone porosity. Exercise can be associated with an increase in muscle contraction and thus with more strain applied to bone, which is important for bone mass stimulation. Whole body vibration has been investigated from the viewpoints of sport, rehabilitation and treatment for osteoporosis. Whole-body vibration is a new training modality that increases muscle strength and mass to the same extent as resistance training at moderate intensity, which can be of clinical importance in individuals who cannot perform high-intensity and prolonged traditional exercise. Whole body vibration acutely decreases arterial stiffness (Otsuki et al. 2008, Fig. 8). Moreover, whole-body vibration prevents increases in leg arterial stiffness and attenuates increases in systemic arterial stiffness (Figueroa et al, 2011). Thus, whole body vibration is beneficial not only to the skeletal system and musculature but also to the cardiovascular system.

Whole body vibration is feasible not only in healthy humans but also in vulnerable populations such as those with osteogenesis imperfecta (Semler et al, 2007). Whole body vibration reflexes to the lumbar spine can be induced by upright standing on a vibrating platform. The application of vibrations increased bone formation and the metabolism in skeletal muscles and skin (Bleeker et al, 2005; Kerschau-Schindl et al, 2001). As whole body vibration -induced oscillation is propagated at least to the lumbar spine (Rubin et al, 2003), it is reasonable to consider that whole body vibration mechanically stimulates abdominal and leg arteries. Therefore, whole body vibration may reduce arterial tone and decrease arterial stiffness via mechanical stimuli to arteries.

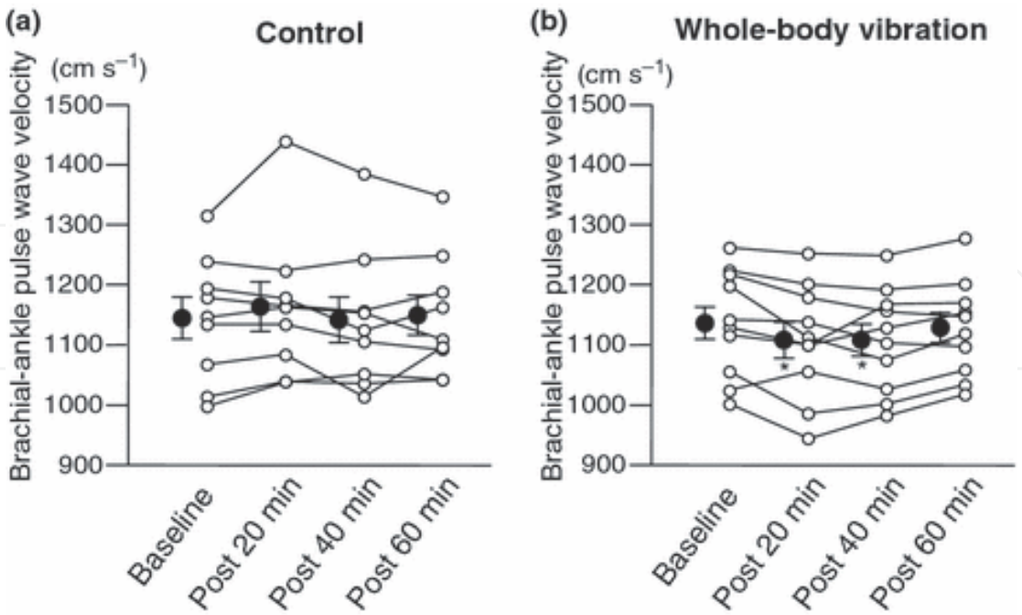

Fig. 8. Brachial-ankle pulse wave velocity (baPWV), an index of arterial stiffness, before and 20, 40 and 60 min after control (a) and whole-body vibration (WBV, b) sessions. Open circles are individual values and closed circles are mean ± SE. *$P < 0.05$ vs. baseline (Quotation from Otsuki et al. 2008).

7. Summary

Based on these results, we encourage the clinical prescription of specific exercise programs to impede the progression of osteoporosis and/or atherosclerosis and to confer health benefits that will assure a better long-term quality of life and decrease the public health burden.

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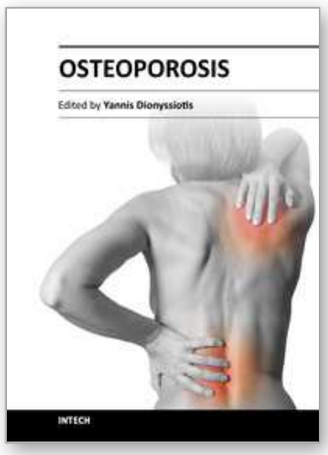

Osteoporosis

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Osteoporosis is a public health issue worldwide. During the last few years, progress has been made concerning the knowledge of the pathophysiological mechanism of the disease. Sophisticated technologies have added important information in bone mineral density measurements and, additionally, geometrical and mechanical properties of bone. New bone indices have been developed from biochemical and hormonal measurements in order to investigate bone metabolism. Although it is clear that drugs are an essential element of the therapy, beyond medication there are other interventions in the management of the disease. Prevention of osteoporosis starts in young ages and continues during aging in order to prevent fractures associated with impaired quality of life, physical decline, mortality, and high cost for the health system. A number of different specialties are holding the scientific knowledge in osteoporosis. For this reason, we have collected papers from scientific departments all over the world for this book. The book includes up-to-date information about basics of bones, epidemiological data, diagnosis and assessment of osteoporosis, secondary osteoporosis, pediatric issues, prevention and treatment strategies, and research papers from osteoporotic fields.

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