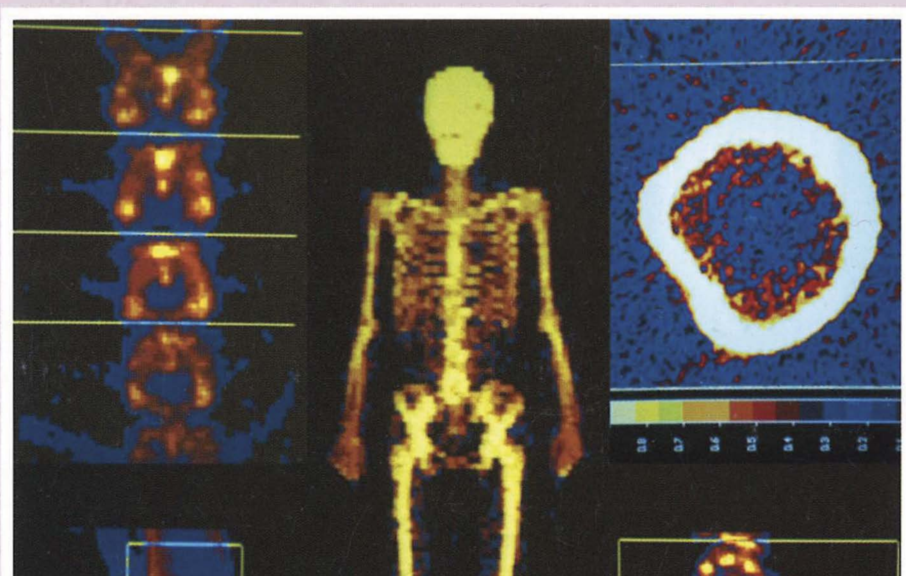
STUDIES IN SPORT, PHYSICAL EDUCATION AND HEALTH

49

Ari Heinonen

Exercise as an Osteogenic Stimulus



UNIVERSITY OF JYVÄSKYLÄ

JYVÄSKYLÄ 1997

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Esitetään Jyväskylän yliopiston liikuntatieteellisen tiedekunnan suostumuksella
julkisesti tarkastettavaksi yliopiston vanhassa juhlasalissa (S212)
maanantaina kesäkuun 9. päivänä 1997 kello 12.

Academic dissertation to be publicly discussed, by permission of
the Faculty of Sport and Health Sciences of the University of Jyväskylä,
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UNIVERSITY OF JYVÄSKYLÄ

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Kaarina Nieminen
Publishing Unit, University Library of Jyväskylä

URN:ISBN:978-951-39-7985-0
ISBN 978-951-39-7985-0 (PDF)
ISSN 0356-1070

ISBN 951-39-0014-2
ISSN 0356-1070

Jyväskylä University Printing House, Jyväskylä
and ER-Paino Ky, Lievestuore 1997

To my family

ABSTRACT

Heinonen, Ari
Exercise as an osteogenic stimulus
Jyväskylä: University of Jyväskylä, 1997
(Studies in Sport, Physical Education and Health,
ISSN 0356-1070;49)
ISBN 95139-0014-2
Tiivistelmä
Diss.
The objective of the present study was to search for an effective exercise mode for strengthening the bones of young and pre- and perimenopausal healthy women in terms of bone mineral density (BMD), bone mineral content (BMC) and selected mechanical characteristics. Altogether 444 healthy women were involved in six experiments comprising two cross-sectional studies, two controlled trials and two randomized controlled trials. The subjects were female athletes and sedentary or physically active premenopausal young and perimenopausal middle-aged women. Information on living habits and health status was obtained with detailed questionnaires. BMD and BMC and bone dimensions were measured by dual energy X-ray absorptiometry. Maximum isometric strength, muscular and cardiorespiratory performance, and dynamic balance were assessed with standard methods. The training programs lasted 12-18 months and consisted of strength training, calisthenics, endurance training, and high-impact training. In the cross-sectional studies the squash players and weightlifters had significantly higher (7-19%) weight-adjusted BMD values than sedentary referents at all the measured sites except the femoral neck of the weight lifters. Unilateral training showed nonsignificant BMD and BMC changes. For the BMD of the femoral neck, the linear trend in the endurance group was significantly different ($p=0.043$) from that of the control group, the trend indicating a maintenace of the prestudy BMD level. The 18-month high-impact training resulted in significant increases in BMD at the loaded sites. These increases amounted to 1.4 - 3.7% in the training group in contrast to changes of 0-1.8% in the control group. The present results indicate that the important components of osteogenic exercise stimulus in premenopausal women are high strain rates and high peak forces in versatile movements. Furthermore, when the repetitive loading magnitude is low, the number of loading cycles is likely to increase in significance for improved bone characteristics.

Key Words: bone dimensions, bone mineral, bone mineral density, endurance training, exercise, high-impact training, loading characteristics, osteoporosis, strength training.

LIST OF ORIGINAL STUDIES

I Heinonen A, Oja P, Kannus P, Sievänen H, Mänttäri A, Vuori I. Bone mineral density in female athletes of different sports. Bone Miner 1993; 23: 1-14.

II Heinonen A, Oja P, Kannus P, Sievänen H, Haapasalo H, Mänttäri A, Vuori I. Bone mineral density in female athletes representing sports with different loading characteristics of the skeleton. Bone 1995;17:197-203.

III Vuori I, Heinonen A, Sievänen H, Kannus P, Pasanen M., Oja P. Effects of unilateral strength training and detraining on bone mineral density and content in young women. A study of mechanical loading and deloading on human bones. Calcif Tissue Int 1994; 55:59-67.

IV Heinonen A, Sievänen H, Kannus P, Oja P, Vuori I. Effects of unilateral strength training and detraining on bone mineral mass and mechanical characteristics of upper limb bones in young women. J Bone Miner Res 1996; 11: 490-501.

V Heinonen A, Oja P, Sievänen H, Pasanen M, Vuori I. Effect of two training regimens on bone mineral density in healthy perimenopausal women: A randomized controlled trial. Submitted.

VI Heinonen A, Kannus P, Sievänen H, Oja P, Pasanen M, Rinne M, Uusi-Rasi K, Vuori I. Randomised controlled trial of high-impact exercise and selected risk factors for osteoporotic fractures. Lancet 1996; 348: 1343-1347.

ABBREVATIONS

ANCOVA	analysis of covariance
ANOVA	one-way analysis of variance
BMC	bone mineral content
BMD	bone mineral density
CI	confidence interval
Control group	term used in original intervention studies
CSMI	cross-sectional moment of inertia
CV	coefficient of variation
CWT	cortical wall thickness
DXA	dual energy X-ray absorptiometry
GLM	general linear model
HR	heart rate
MES	minimal effective strain
Reference group	term used in the original cross-sectional studies
REML	restricted maximum likelihood
RM	maximum weight that can be used for designated number of repetitions
$\dot{V}O_2max$	maximal oxygen uptake
ΣBMC	sum of the five leg sites measured for BMC

ACKNOWLEDGEMENTS

This study was carried out as a part of the larger research program on physical activity and osteoporosis at the UKK Institute for Health Promotion Research during the years 1990-1997.

I am grateful to Professor Ilkka Vuori, M.D., Director of the UKK Institute for Health Promotion Research, for giving me the opportunity to work in constructive and stimulating circumstances and for providing me with the best facilities for scientific work in the field of bone studies.

I express my warmest thanks to the supervisors of my work, docent Pekka Oja, Ph.D., Scientific Director of the UKK Institute, associate professor Jukka Viitasalo,. Ph.D., from the Research Institute for Olympic Sports, and Professor Paavo Komi, Ph.D., from the Department of Biology of Physical Activity, University of Jyväskylä, for their encouragement and support of my work. Dr Oja on whom I have made the most demands, guided me through the scientific field of exercise and spurred me on in my studies over the course of this work. Dr Viitasalo, suggested to me to do thesis, also provided his expertise and offered practical and essential advice during the study. Professor Komi tutored me from the time I began my master's thesis. He introduced research in biomechanics to me and has supported me throughout my studies, especially, in the final stages during the completion of the thesis. I am also grateful to him for his inspiring discussions in related seminars.

I am very much obliged to docent Harri Sievänen, Ph.D., and docent Pekka Kannus M.D., for stimulating discussions and valuable criticism during the completion of the thesis. They advised me often during the writing process. Dr Kannus also offered his critical advice and comments, especially with the respect to the original papers. To Dr Sievänen, I owe special thanks for supporting, helping and advising me during these past few years. He also offered his generous advice with respect to the DXA measurements and the interpretation of the results. These colleagues were always willing to help me with any problems.

I express my warm thanks to my reviewers, Professor Kalervo Väänänen, M.D., and docent Harri Suominen, Ph.D., for their constructive criticism and valuable discussions of the manuscript.

I thank my other co-authors Matti Pasanen, M.Sc., Heidi Haapasalo, M.D., Marjo Rinne, M.Sc., Kirsti Uusi-Rasi, M.Sc., and Ari Mänttäri, M.Sc. To Matti Pasanen I owe special thanks for his advice and assistance in the analysis of statistical data. Marjo Rinne helped with and arranged for, the exercise programs. Kirsti Uusi-Rasi is acknowledged for her contribution as a nutritionist.

I also thank Ms Virpi Koskue for her skillful DXA measurements, Ms Taru Malminen for her help with the volunteer recruitment, and Ms Kirsti Malmivuo for her arrangement of the study schedules.

My warm thanks also go to Ms Riitta Simukka for her skillful technical assistance and help with the figures and software and to Ms Tuula Äyräväinen gave the finishing touches to the layout of this thesis. I owe my warmest thanks to Birgitta Järvinen also for her excellent help in the library.

I thank all the colleagues and the staff of the UKK Institute for their help and comradeship throughout this work.

The English language of the thesis was revised by Georgianna Oja, E.L.S.

Finally, I owe my warmest and fondest thanks to my wife Anne, and my children Eetu, Emmi and Antti, for their everlasting support and patience during the busy years of this study. This thesis is dedicated to them.

The study was supported by grants from the Ministry of Education, Finland.

Tampere, April 1997 Ari Heinonen

CONTENTS

1 INTRODUCTION

Osteoporotic fractures in the elderly are a world-wide epidemic and the predicted aging of populations will accentuate the burden of these fractures on health care systems. The prevailing view is that the major determinant of fracture risk is bone mineral density (BMD) (Cummings et al. 1993, Cummings et al. 1995, Kleerekoper 1995). BMD accounts for 80% - 90% of the variance in the strength of the proximal femur (Lotz and Hayes 1990, Courtney et al. 1994). The risk of hip fracture is approximately doubled for every standard deviation reduction in BMD (Hayes et al. 1996). Thus measures to maximize peak bone mass and maintain bone mass or decrease bone loss would reduce the fracture risk of elderly people. Epidemiological, clinical and experimental exercise studies, in turn, indicate that physical activity is effective in improving and maintaining bone mass and strength and thus in helping to prevent osteoporotic fractures (Johnston and Slemenda 1993, Mosekilde 1995, Kannus et al. 1996). However, the type, intensity, frequency, and duration of exercise that provide maximum anabolic stimulus in bone are still largely unknown (Gutin and Kasper 1992).

The basic form and development of bones of the skeleton are genetically determined, but their final mass and architecture are governed by an adaptive mechanism sensitive to the mechanical environment. Over 100 years ago, Wolff (1892) suggested that bone will accommodate the habitual stress that is imposed upon it. With Wolff's observation in mind, Frost (1987) proposed his "mechanostat theory" to explain the adaptations of bone architecture and mass to its typical mechanical environment. The mechanostat theory maintains that bone adapts through different biological processes within strain ranges or thresholds for bone modeling drift and remodeling. This theory supports the basic biological explanation of the importance of exercise for bone (Mosekilde 1995). In addition, four primary strain variables have been shown to be associated with the regulation of bone mass, namely, strain magnitude, strain cycles, strain rate and strain distribution (Lanyon 1987, 1996). These variables can be included in various sports and exercise modalities. Thus it may be possible to study the effects of exercise on skeleton using cross-sectional models for different athlete groups to determine the type of exercise which best enhances bone mass. Using the results of cross-sectional studies, intervention studies can then be designed to provide further evidence of the effects of diverse exercise types.

2 REVIEW OF THE LITERATURE

2.1 Bone properties

Owing to the inorganic salts impregnated in its matrix, bone differs from other connective tissue by its rigidity and hardness. Bone is both a structural and a metabolic tissue. It serves the following three functions: it supports the body against gravity and acts as a rigid lever system for muscular action; it protects the soft tissues of vital organs and bone marrow; and it acts metabolically as a reserve of ions, especially calcium, for the entire organism.

Bone has two basic architectural structures and is formed of cortical and trabecular bone. Cortical bone is dense solid mass with only microscopic spaces and channels. It covers the external part of the bones. Trabecular bone consists of a lattice of rods, plates and arches. In the long bones, the diaphysis is primarily compact in structure, whereas the epiphysis and metaphysis are mainly filled with trabecular bone. Cortical and trabecular bone have the same matrix composition and structure. Cortical bone comprises 80% and trabecular bone 20% of the skeletal mass. Trabecular bone is metabolically more active than cortical bone (Jee 1988, Baron 1993, Buckwalter et al. 1995), and, as a structure, it is much less stiff and also weaker than cortical bone (Currey 1984).

Adult bone, whether cortical or trabecular, is lamellated. The parallel orientation of collagen fibers alternates from layer to layer and therefore resembles multiple layers of plywood. A circular ring of lamellae can be arranged concentrically around a longitudinal channel centered on a blood vessel, osteon or Haversian system. Each Haversian system is bound by its cement line across which canaliculi pass. The thin tubular channels, canaliculi, connect small lacunae. Entrapped bone cells, or osteocytes, lying in lacunae and within canaliculi communicate through gap junctions. The cortical osteons are cylindrical structures, whereas the trabecular osteons, or packets, are shaped like shallow crescents. Lamellar bone is formed much more slowly than woven bone, in which the collagen fibers are oriented almost randomly (Jee 1988, Baron 1993, Currey 1984).

Bone tissue consists of 76% inorganic salts and 24% organic matrix. The matrix is composed primarily of proteins, glycoproteins, and polysaccharides. Ninety percent of the organic matrix is formed by type I collagen fibers, usually oriented in preferential directions, and noncollagenous proteins (Baron 1993). The amorphous ground substance, which is composed of glycoproteins and proteoclycans, is a noncollagenous cementing substance in which collagen fibers and crystals are embedded. The inorganic components are mainly spindle- or plate-shaped crystals of hydroxyapatite and amorphous calcium phosphate (Jee 1988, Baron 1993, Currey 1984).

This special organization of organic and inorganic materials, as well as the cylindrical form and trabecular network of the bone, results in a combination of strength and lightness. These qualities provide maximum mechanical support with minimal mass (Currey 1984, Kimmel 1993, Mosekilde 1993). The cylindrical bone is mechanically more efficient in bending than solid bone is, and the ends of the trabecular network of long bones is associated with the linear principal stress acting upon a bone. In addition it absorbs impact loads applied across synovial joints. Thus the configuration of bone is designed to provide strength in direct response to weight-bearing stress (Currey 1984, Oxnad 1993).

2.1.1 Bone turnover

Three biological mechanisms are involved in bone turnover at tissue level. Each of these mechanisms has a specific purpose - growth determining the bone size, modeling determining the shape and remodeling maintaining the functional competence of bone. These mechanisms can affect bone mass and respond to mechanical usage in specific ways (Frost 1987, 1988).

Growth can be defined as a genetically programmed enlargement of the entire skeleton, and it is driven by circulating systemic agents and local factors. During growth the activation of muscles and weight-bearing exercise form a mechanical environment that induces the cellular activity to achieve and maintain the normal architecture, shape and size of the skeleton. Growth itself requires modeling to accommodate changes and dimensions while also maintaining relative proportions in specific bones. In humans the growth of bone stops around 16-18 years of age. Growth cannot remove bone but can only add to it (Jee 1988, Frost 1987, 1991b, Parfitt 1994). Consequently, around the age of 20 years "peak bone mass" and density is achieved as a result of growth and modeling (Matkovic et al. 1994, Haapasalo et al. 1996). In healthy persons the suggested main determinants of peak bone mass are race, sex, heredity, hormonal status, nutrition and physical activity (Ott 1991). During growth, skeleton is especially sensitive to mechanical stimuli (Loitz and Zernicke 1992, Biewener and Bertram 1993, Forwood and Burr 1993, Kannus et al. 1995), which may have important consequences on bone mass later in life.

The modeling is defined as the simultaneous removal and formation of bone at different sites by the two mediator mechanisms called resorption and formation drifts. Osteoblasts (bone forming-cells) in formation drifts add new bone, and osteoclasts (bone-resorbing cells) remove bone in resorption drifts over broad surface regions during the modeling process (Frost 1987, 1990a, 1991a, 1991b). Frost (1990a) recognizes two kinds of modeling. Micromodeling organizes cells and collagen during their formation to determine the kind of tissue being formed. Macromodeling controls the gross shapes, sizes, strengths and anatomy of joints, bones, tendons and other organs. For trabeculae these drift patterns are called minimodeling (Frost 1990a). When growth stops, so usually does macromodeling; nevertheless, unlike macromodeling, micromodeling can continue throughout life (Frost 1990b, Kimmel 1993). Modeling increases bone strength by improving geometric properties and adding mass (Kimmel 1993). Macromodeling is thought to add new bone at the periosteum (which lines the external surface of bone) and endosteum (which lines marrow cavity), while micromodeling thickens and rearranges the individual trabeculae (Lanyon et al. 1982, Frost 1991a, Kimmel 1993).

Remodeling is defined as the removal of old bone and the formation of new bone at the same site at different times. Remodeling replaces aged bone and possibly also repairs microcracks (Turner 1991). It occurs at scattered locations on bone surfaces and turns bone into a biologically coupled activation-resorption-formation sequence (Jee 1988, Dalsky 1990, Frost 1990b, 1992, Baron 1993). In the bone replacement process lamellar bone is turned over in small packets named basic multicellular units (Jee 1988, Parfitt 1984, Frost 1990b, 1992). Normally, 80% or more of free bone surface is quiescent with respect to remodeling (Parfitt 1984). In a normal adult person, activation and resorption last one month and formation another three months; thus the time scale for one complete remodeling cycle, called sigma, is about four months (Jee 1988, Frost 1989). Mineralization is completed in another three to four months (Jee 1988). Basic multicellular units act throughout life on periosteal, Haversian, cortical-endosteal and trabecular surfaces (Frost 1988, 1991b, 1992). Bone remodeling can increase bone mass, especially along cortical-endosteal and trabecular surfaces, if resorption cavities are overfilled with new bone, or it can decrease bone mass by underfilling resorption cavities (Turner 1991). Bone remodeling is a complex process that is regulated by the balance that occurs between mechanically prompted physiological signals and signals due to systemic nonmechanical factors (polypeptide, steroid, and thyroid hormones) as well as local factors (growth factors and prostaglandins) (Lanyon 1987, 1990, 1996, Canalis 1993).

2.1.2 Biomechanical properties

Strength and stiffness are two important mechanical properties of bone (Currey 1984). The strength of the structure can be defined as the load at the yield or failure points, or as the ultimate load, depending upon the circumstances (Martin and Burr 1989, Einhorn 1992, Turner and Burr 1993). Strength is an intrinsic property of bone and is independent of its size. Therefore, in the life sciences bone strength is often reported in units of force and in engineering studies in terms of stress or as intrinsic strength (Turner and Burr 1993).

When a load in a known direction is placed on a structure, the deformation of that structure can be measured and plotted on a load-deformation curve, and the strength and stiffness can be determined (Nordin and Frankel 1980). The stiffness or rigidity of the structure is determined as the slope of the load-deformation curve. For normal loading (tension or compression), the stiffness is known as the modulus of elasticity, or Young's modulus, and it is equivalent to the slope of the linear part (elastic region) of the curve (Martin and Burr 1989, Einhorn 1992). The physiological significance of this property relates to the fact that forces applied to bone at any point along this line will only deform the bone temporarily, and, after the load is removed, the bone returns to its original shape (Einhorn 1992). In addition, the midshaft of a long bone has been effectively designed by nature so that it has the greatest stiffness in the direction of its long axis and its greatest impact loading resistance occurs in the transverse direction. This phenomenon suggests that, in general, bone tissue can be optimized for either stiffness or impact resistance (Cowin 1995).

The mechanical properties of bone structure depend upon both the properties of its material and its geometry. The concepts of stress and strain are fundamental to bone biomechanics. These concepts define the properties of material without geometric effects (Martin and Burr 1989, Einhorn 1992, Turner and Burr 1993). Stress is typically defined as force per unit area (the unit of stress is the Pascal=Pa), and it can be classified as compressive, tensile, or shear. Thus stress can be estimated for the cross-section and cross-sectional moment of inertia (CSMI) of long bone and calculated using the following formula:

$$S = \frac{F}{A} + \frac{Mc}{CSMI} \quad \textbf{(eq. 1)},$$

where S is stress, F is axial load, A is cross-section of bone, M is bending moment and c is the distance from the cross-sectional center of mass.

Strain describes the deformation of a material without regard to its structural geometry. Axial strain can be calculated using Hooke's law:

$$\in = \frac{S}{E} \quad \textbf{(eq. 2)},$$

where $\in$ is axial strain, S is stress and E is Young's modulus in the axial direction (van Buskirk 1989). Strain is dimensionless and it is a fraction or a percentage.

Bone strength must be adequate for the mechanical competence required, but bones must also allow for effective locomotion with minimal weight. Thereby, perhaps the most obvious features of long bones are that they are thick-walled hollow tubes, expanded at the ends, and have cancellous rather than compact bone at the expanded ends (Currey 1984). The assumption that the elements of the skeleton are built from a minimum of material is logic and seductive. A minimum of material means that the stresses have to be reduced and they are applied by the force over a cross-sectional surface (Nordin and Frankel 1980, Kummer 1993). There is no doubt that a hollow cylinder is the least mass solution for greatest strength during pure bending and also during torsional loading. The mechanical efficiency of cylinders depends on the CSMI (Figure 1) of the bone, for which the moment or ratio of the column diameter to wall thickness is critical (Currey 1984, Oxnad 1993). The implication is that, to minimize the mass for a fixed CSMI, the whole cross-sectional area should be as far as possible from the neutral axis in order to maximize the ratio of the column diameter to wall thickness. The larger the CSMI, the less the area and therefore the less the mass necessary to maintain a given bending strength. In addition, the material in a structure farthest from a neutral bending axis experiences the most deformation during bending (Currey 1984, Kimmel 1993, Turner and Burr 1993). In other words, geometric properties of a bone refer to the configuration of its mineralized tissue, both the amount and distribution of which are important (Kimmel 1993).

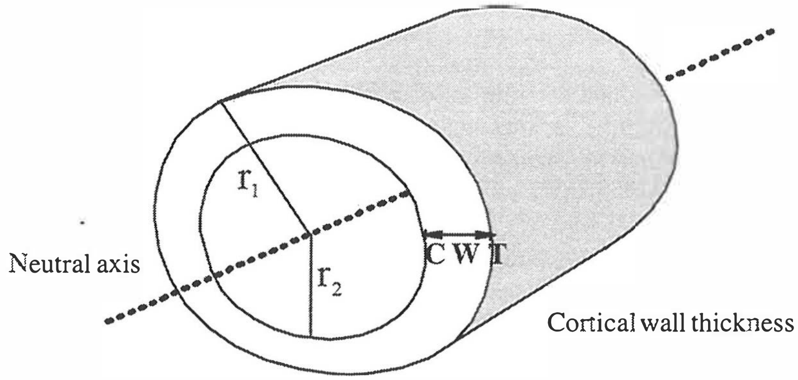

FIGURE 1 Definition of cross-sectional moment of inertia (CSMI) for a circular hollow tube, where r_1 is the outer radius and r_2 is the inner radius and CWT is the cortical wall thickness. CSMI is a measure of the distribution of material around a neutral axis.

The distribution of bone mass and bone geometry are connected to bone strength and stiffness. The CSMI is a geometric property of a structure that describes its resistance to bending. The strength of a bone in resisting static bending then has to be proportional to the following formula (Currey 1984):

$$\frac{CSMI}{c} \quad \textbf{(eq. 3)},$$

Thereby, to have major impact on skeletal strength homeostasis, the CSMI and the neutral bending axis interact at the periostium (Kimmel 1993, Turner and Burr 1993). The principle of the CSMI has been applied clinically by noting that femoral neck CSMI is inversely related to the likelihood of hip fracture (Beck et al. 1992). During exercise-induced bone loading, bone formation accelerates mainly at the periosteal surface on the bone shaft (Raab et al. 1991, Raab-Cullen et al. 1994a, Forwood and Turner 1995, Hillam and Skerry 1995). Thus periosteal formation drifts are accelerated by loading because the rate of osteoblast recruitment is increased. Consequently, the skeleton is not only optimally strengthened by an increase in bone mass, but also by the placement of the new bone at a position that has a maximum positive effect on the CSMI (Kimmel 1993, Hillam and Skerry 1995, van der Wiel et al. 1995). In other words, a small increase in new bone at the periosteal surface increases the CSMI considerably because the CSMI is proportional to the fourth power of the radius.

2.2 Mechanical adaptation of bone

Physical loading is an important determinant of bone mass, architecture, and structural strength. The skeleton's ability to adapt to load and moment-induced mechanical loading was recognized over a century ago, and it is now referred to as Wolff's Law (Wolff 1892). According to the law, the function of the cells responsible for mechanically adaptive modeling and remodeling is presumably to ensure that the variables which they control, such as mass, architecture, and material properties, are appropriate in relation to the applied load. Thus a cascade of events occurs within osteocytes and osteoblasts in response to changes in bone strain, and these events reflect an adaptation to the imposed loading environment in response to factors in the strain environment (Lanyon 1987, Martin and Burr 1989, Drinkwater et al. 1995, Smith and Gilligan 1996).

Bone adapts to changes in the effective stresses by adjusting its characteristics in a direction that tends to keep the internal strain within a physiologically reasonable range (Figure 2). If mechanical loading or disuse causes the strain level to shift outside the "customary mechanical range", the bone takes on a state of overloading or underloading that leads to bone adaptation and an imbalance between bone formation and resorption. The adaptation process can be described as a negative feedback control system (Frost 1983, 1987, Currey 1984, Hart and Davy 1989, Schulteis 1991, Turner 1991) that incorporates Frost's (1987, 1988, 1990a, 1990b, 1992) main "mechanostat" postulations and Lanyon's (1987, 1990) "error signal" concept. According to this approach bone characteristics are controlled by the threshold levels (physiological window) of the mechanical strain above or below which the adaptation begins in a nonlinear manner (Frost 1988, 1992, 1993, Turner 1991). In addition, the capability of bone to respond to mechanical loading is probably determined by a genetically controlled set point which has been further modified by past site-specific loading and several biochemical factors related to age or disease (and its treatment). The biochemical agents can influence bone mass independently or they can influence bone structure by changing the set point of the mechanical feedback system (Frost 1987, 1993, Turner 1991).

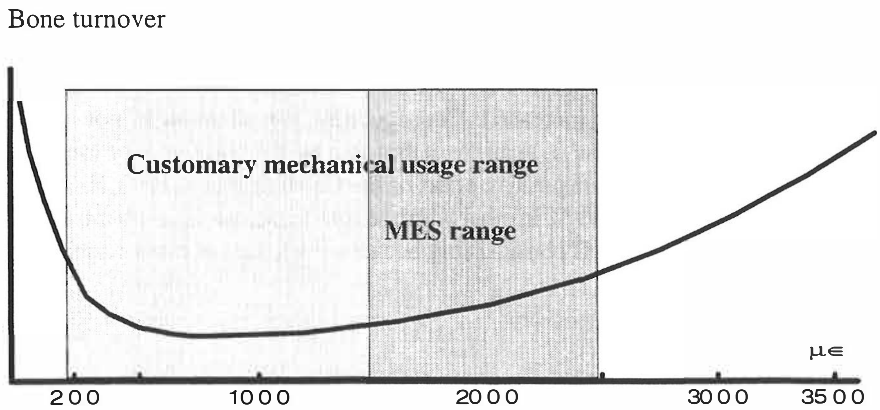

FIGURE 2 Bone adaptation according to the threshold levels of mechanical strain. MES refers to minimal effective strain range.

The response of bone to mechanical loads is immediate and is specific to the bone under load, and involves both cellular and tissue reactions. Skeletal adaptations to mechanical usage would depend on frequent loading cycles and strain "quality". These properties can be determined as the concept of "loading history" (the strain variations a bone has experienced in the past) (Frost 1994). Although skeletal adaptation depends on the loading history, only a single period of loading is capable of converting a quiescent periosteum to one which is actively forming new bone (Turner et al. 1992, Forwood and Turner 1995, Lanyon 1996). Within five minutes of loading the activity of the enzyme glucose 6-phosphate dehydrogenase increases within osteocytes and osteoblasts and the increase is related to the magnitude of the local strain. This process is followed within 24 hours by increased RNA production. In addition, the first few minutes of dynamic loading are accompanied by the release of prostacyclin and prostaglandin E_2 (Lanyon 1987, 1992, 1996, Smith and Gilligan 1996). Both prostaglandin and prostacyclin are produced within the osteoblast layer and can also act directly on growth factors (Lanyon 1996, Smith and Gilligan 1996). With a single period of strain change the orientation of proteoglycan molecules increased within the cortical bone, the osteogenic stimulus lasting for at least 24 hours (Lanyon 1987, 1992). Furthermore, Raab-Cullen et al. (1994b) have shown, in their rat model, that external loading three or four days a week is as effective as daily loading for increasing periosteal bone formation.

Altogether, the strain environment of bones is the product of the loads applied to them and the variables controlled by their cell populations. It seems likely that strain is the most convenient parameter for these cells to use for feedback (Lanyon and Rubin 1984, Martin and Burr 1989, Lanyon 1996). Based on theoretical considerations and animal models, the primary mechanical variables associated with the regulation of bone mass are strain magnitude, strain cycles, strain rate and, also, the distribution of the strain within the skeletal structure (Lanyon 1987, 1996).

2.2.1 Strain magnitude

It has been shown in the animal model that bone formation increases markedly when bone is subjected to progressively larger magnitudes of strain (Rubin and Lanyon 1984a, Lanyon 1987). Frost has proposed the "mechanostat" theory in which he describes a feedback control system in which minimum effective strain (MES) is necessary for bone maintenance (Frost 1987,1988, 1990a, 1992). Bone structure is maintained if the customary mechanical strain remains between 200 and 2500 $\mu\epsilon$ (Lanyon 1987, Frost 1990a, 1990b, 1992, Cowin et al. 1991, Turner 1991). If loading-induced local strain exceeds the MES (range 1500-2500 $\mu\epsilon$) bone enters a state of overuse, the result being an adaptation response and the inducement of modeling (Frost 1990a, 1990b, Cowin et al. 1991, Turner 1991).

When a normally used bone is suddenly subjected to total disuse its peak strains should fall and stay below about 100-200 $\mu\epsilon$ (Frost 1992). Immobilization stimulates bone resorption and depresses formation, the result being decreased volume-related bone mass and deteriorated material and architectural properties (Minaire 1989). The bone loss is the most rapid during the first few weeks of immobilization, whereafter the rate is slower. The steady state is reached when the bone formation and resorption become balanced, most likely within six months after the injury (Young et al. 1986, Minaire 1989, Sievänen et al. 1994a, 1996a). The extent and rate of bone mass recovery during remobilization have remained a controversial issue (Mazess and Whedon 1983, Jaworski and Uhthoff 1986, Minaire 1989, LeBlanc and Schneider 1991). It seems certain that the time needed for recovery is clearly longer than the time needed to reduce the bone mass, and the recovery seems to be incomplete (Andersson and Nilsson 1979, Kannus et al. 1992, Sievänen et al. 1994a, 1996a). Moreover, bone mineral mass has been shown to decrease after the cessation (Dalsky et al. 1988) or decrease of training (Lane et al. 1990) and this finding is consistent with the adaptation hypothesis.

2.2.2 Strain cycles

The number of loading cycles is also a factor determining the adaptive response of skeleton to loading. Although this factor is clearly less important than the strain magnitude (Rubin and Lanyon 1984a, Lanyon 1987, Whalen and Carter 1988), a minimum number of loading cycles is still required for a response (Rubin and Lanyon 1984a). With in their avian model Rubin and Lanyon (1984a) showed that the osteogenic response to loading (2000 $\mu\epsilon$) became saturated after 36 consecutive loading cycles lasting only a total of 72 s per day. Further loading cycles produced no additional osteogenic response and only four loading cycles per day were sufficient to prevent resorption. Thus, only a few loading cycles (<50) are needed at each distribution, and the duration of each stimulus needs only to be short (Lanyon 1996). On the other hand, in their theoretical model, Carter et al. (1987) and Whalen and Carter (1988) have suggested that the importance of the number of loading cycles probably increases in significance when the strain magnitude is low. This possibility is consistent with the findings that the data recorded during normal activities of animals over a 24-hour period show relatively few peak strain events (Fritton et al. 1996).

From the theoretical point of view, Carter et al. (1987) have developed a mathematical model that relates bone mineral mass to the daily stress histories of proximal femur and calcaneus (Whalen and Carter 1988). In their model, the first approximation was that the most important parameters of the loading history to be considered are the magnitudes of the cyclic stresses and the number of applied loading cycles. In their model (Carter et al. 1987) constant daily stimulus $S*$ can be expressed as

$$S* \propto \sum_{day} n_1 \left(\sigma_i / \sigma_{ult}\right)^m \quad \textbf{(eq. 4)}$$

where σ_i is the single effective stress parameter, σ_{ult} is the effective stress for failure, n_i represents loading cycles per day and m is a constant. The value of m is a weighting factor for the relative dependence of the stimulus on stress ratio and loading cycles. If $m = 1$, the importance of the stress ratio and the number of cycles are of the same order. The importance of high stress magnitude increases when the value of m increases (Carter et al. 1987). According to the study of Carter et al (1981) m can obtain values from 2 to 6. For example, if the stress magnitude is doubled and $m = 6$, the number of loading cycles should increase 64 times to produce a similar effect.

2.2.3 Strain distribution

It has been suggested that different strain distributions can produce different dose-response relationships between peak strain magnitude and change in the cross-sectional area. Rubin and Lanyon (1984b, 1985, 1987) found that loading avian ulna at only 1000 $\mu\epsilon$ in an unusual direction could stimulate new bone formation. Lanyon (1984, 1987, 1996) suggested that the strain required to elicit an adaptive response may be lower if the manner of loading differs from the usual pattern of loading. In addition, Biewener and Bertram (1993) suggested that adaptive modeling of bone may be more sensitive to a strain distribution that differs markedly from normal or to a pattern of functional strain rather than to increased strain magnitude *per se*.

2.2.4 Strain rate

In the animal sudies, it has been suggested that the rate at which bone is subjected to strain is an important factor in the adaptive response (O'Connor et al. 1982, Lanyon 1987, Turner et al. 1995). Turner et al. (1995) and Weinbaum et al. (1994) proposed that mechanical loads are coupled to the bone cells by stress-generated fluid flow within the bone tissue, which depends on the rate of change of bone strain. If the bone responded only to strain magnitude or to alterations in strain distribution, it should be possible to cause bone to model or remodel using static loads. In addition, the mechanism responsible for perceiving and responding to such small biophysical signals, the maximum deformations being of the order of <0.3%, must be extremely sensitive (Rubin and McLeod 1996). Consequently, the rate at which the strain is developed has to be an important factor in the adaptive response (Martin and Burr 1989). Strain rate, on the other hand, is proportional to dynamic load magnitude. Therefore, peak strain magnitude may be as equally osteogenic as strain rate.

It has also been suggested that bone formation response is strongly dependent on the frequency of strain. In this respect, most effective functionally induced strain occurs in the range of 15 to 30 Hz, a bandwidth that is typically associated with gait (Rubin and McLeod 1994, 1996). The osteoregulatory relevance of these high-frequency, low-magnitude strain energies has been evaluated at the tissue and cell level (Rubin and McLeod 1996). Furthermore, the mechanical signals become more osteogenic if frequency increases over 10 to 60 Hz (Rubin and McLeod 1996). There is, on the contrary, an association between strain rate and high frequency. For example, if frequency increases, strain is developed and released at a more rapid rate.

2.2.5 Summary of the osteogenic mechanical stimulus

The concept of uniform optimal strain magnitude in relation to a feedback system as derived from theoretical and animal models has been proposed to control the functional adaptation of bone (Lanyon and Rubin 1984, Frost 1987). Strain rate has been suggested to have an important role in the creation of the adaptive response, and it is proportional to the dynamic load magnitude (O'Connor et al. 1982). In addition, strain distribution is an important factor. It has been suggested that skeletal remodeling is related to "error signal", the difference between local strain caused by habitual and specific loading (Lanyon 1987). Moreover, low-magnitude, frequency-specific (15-30 Hz) strain is critical (Rubin and McLeod 1994, 1996). Consequently, all the strain-related variables, even strain cycles, are integrated into dynamic loading conditions. Recent studies suggest that cyclic mechanical forces cause a flow of interstitial fluid through the canalicular network and also deformations in the extracellular matrix (Weinbaum et al. 1994, Klein-Nulend et al. 1995, Turner et al. 1995). Weinbaum et al. (1994) and Turner et al. (1995) have suggested that bone cells respond to stress-generated fluid flow within the bone matrix, and fluid flow increases when strain gradients are increased across the tissue and when strain rate increases. However, the exact characteristics of the stimulus of mechanically induced bone formation is not completely understood, but, according to current knowledge, effective exercise programs should involve high strain or high strain rates and unusual strain distributions. In other words, in practical terms, effective exercise regimens should consist of high mechanical force or a high rate of force application and also versatile movements.

2.3 Other factors modifying bone adaptation

A concept of a feedback control system for bone structure that describes the interaction between mechanical and other factors such as nutrition, age, and hormonal stimuli, which can modify the adaptation process, has been proposed by Frost (1983, 1987). Moreover, bone mass is a complex trait that is determined by several interacting genetic, metabolic and environmental factors (Brandi et al. 1994, Bronner 1994). It has been demonstrated that genetic influences account for 60-80% of the interindividual variation of bone mass (Pocock et al. 1987, Slemenda et al 1991, Seeman et al. 1996).

Calcium. Nutrient intake, body composition and physical activity contribute to bone mass (Rice et al. 1993, Song et al. 1994, Houtkooper et al. 1995, Nichols et al. 1995, Nieves et al. 1995, Young et al 1995). Although the exact nature of the association between calcium intake and BMD and changes in BMD remain unclear (Houtkooper et al. 1995, Nieves et al 1995), adequate calcium intake in childhood, adolescence and also, for women during adulthood is considered essential to attain and maintain optimal bone mineral mass and size (Dawson-Huges 1990, Johnston et al. 1992, Bronner 1994, Parfitt 1994, Nieves et al. 1995, Specker 1996). On the other hand, there seems to be no association between the intake of calcium and BMD (Riggs et al. 1987, Angus et al. 1988, Wickham et al. 1989, van Berestijn et al. 1990, Uusi-Rasi et al. 1995).

Age. Throughout growth, but particularly at or before puberty, the ability of bone to adapt to mechanical loading is much greater than after maturity (Parfitt 1994). Especially trabecular bone is apparently sensitive to changing hormone concentrations at puberty (Slemenda et al. 1994). In a cross-sectional study with tennis and squash players Kannus et al. (1995b) showed that the benefit of mechanical loading with respect to the BMD of the playing arm is about two times greater if girls start playing at or before menarche rather than after it. This findings may be due to the fact that the adolescent growth spurt is the only time in life when bone is added in substantial amounts to both the inside and the outside of the cortises (Parfitt 1994). On the other hand, the bone mass and density of the elderly depend on both the peak bone mass attained during skeletal maturation and the rate of involutional bone loss thereafter (Eisman et al. 1993, Jonhston and Slemenda 1993, Bonjour et al. 1994).

Hormones. Although osteoporosis is most common among postmenopausal women, it also occurs in persons of any age whose bone mass has fallen below a critical level. The endocrine profile of young female athletes is very similar to that of postmenopausal women in that both groups have low levels of estrogen (Snow-Harter 1994, Snow 1996). Low vertebral and peripheral BMD has been reported for amenorrheic athletes in several studies. Many studies have found menstrual irregularity, particularly amenorrhea, to be associated with low lumbar spine BMD (Drinkwater et al. 1984, Marcus et al. 1985, Prior et al. 1990, Myburgh et al. 1993), but other peripheral bone sites may also be affected (Drinkwater et al. 1990). However, it has been suggested that high mechanical loading can at least partially override the negative influence of low hormone levels in athletes (Robinson et al. 1995).

For women at menopause, estrogen deprivation has the most important influence on bone mass. Decreased efficiency of intestinal and renal calcium handling increases the level of calcium intake necessary to maintain neutral calcium balance (Dalsky 1990, Marcus 1996). As a consequence bone becomes more sensitive to parathyroid hormone, which is the primary regulator of the extracellular fluid calcium concentration. Vitamin D_3, calcitonin and gonadal hormone also control calcium regulation (Bouvier 1989, Russell 1990, Marcus 1996). In addition, inadequate calcium presumably increases PTH secretion, which subsequently restores and maintains blood calcium levels at the expense of the skeleton through resorption (Parfitt 1987, Heaney 1996, Marcus 1996).

A steep decrease in estrogen levels occurs during the six-month period around menopause, and at about the same time serum levels of testosterone, androstenedione and sex hormone-binding globulin also slightly decrease (Slemenda et al. 1987, Rannevik et al. 1995). On the other hand, optimal peak bone mass seems to be related to appropriately timed androgen secretion (Vanderschueren and Bouillon 1995). Furthermore, serum levels of androgen hormones seem related to the bone mass in pre-, peri-, and postmenopausal women (Heiss et al. 1995, Vanderschueren and Bouillon 1995).

During the last five years, growth hormone and insulin-like growth factor I have received much attention as possible anabolic agents for treating of osteoporosis and other age-related phenomena, for example, loss of muscle mass (Johansson et al. 1993). Both growth hormone and insulin-like growth factor I exert anabolic effects on bone. It has been shown *in vitro* that insulin-like growth factor I is synthesized by bone-derived cells and this process is influenced by growth hormone, estrogens, para thyroid hormone, vitamin D_3 and other agents known to affect bone metabolism. It has also been suggested that growth hormone may, at least in part, act via an increased synthesis of insulin-like growth factor I in osteoblasts (Baylink et al. 1993, Johansson et al. 1993, Schmid 1993, Rosen et al. 1994).

Weight and body composition. Weight is known to be positively correletated with BMD (Bauer et al. 1993, Edelstein et al. 1993, Felson et al. 1993, Suominen 1994). Thus, the association between body composition and bone density may be determined at least in part by skeletal responses to mechanical forces induced by greater body weight and a weight-related beneficial effect of higher estrogen concentrations (Slemenda 1995). In their study of twins Young et al. (1995) showed that lean mass was the major independent determinant of bone mass at the hip, both pre- and postmenarche. Nichols et al. (1995) also found that regional lean tissue mass appears to be a better predictor of BMD than regional fat mass. On the other hand, it has been shown that the total body fat mass is the most significant predictor of total body BMD in pre- and postmenopausal women (Reid et al.

1992). Consequently, the effect of fat and lean tissue mass varies according to the level of physical activity and age. In addition, muscle mass has been shown to be significantly positively related to bone density in older men and women (Doyle et al. 1970, Hughes et al 1995). The weight of muscle reflects the forces exerted on bone to which it is attached, and muscle weight is an important determinant of bone mass (Doyle et al. 1970). Furthermore, muscle strength has been reported to predict between 15% and 20% of the variance in bone mineral mass of the hip, spine, and radius (Pocock et al. 1989, Snow-Harter et al. 1990, Eickhoff et al. 1993).

2.4 Exercise as an osteogenic stimulus: the experimental and clinical evidence

Physical activity constitutes a major mechanical loading factor for bone. The important role that physical activity plays in regulating bone modeling and remodeling is commonly accepted. However, the type, intensity, frequency, and duration of exercise that best enhance bone mineral accumulation are still largely unknown. The extent to which a bone can alter its form due to exercise and the extent to which growing and mature bones have similar adaptive capacities also remain unclear (Biewener and Bertram 1993).

Bone mass and density depend on both the peak bone mass and the rate of involutional bone loss during the adult years and later in the life (Johnston and Slemenda 1993, Matkovic et al. 1994). Peak bone mass is determined by the interaction of genetic endowment and mechanical stress, as modified by nutritional and endocrine influences (Smith 1994). It has been shown that exercise can be used to prevent osteoporosis; it can increase bone mass (Snow-Harter and Marcus 1991, Suominen 1993, Välimäki et al. 1994, Smith 1994, Mosekilde 1995, Kannus et al. 1996), affect bone architecture (Beck et al. 1992, Bouxsein et al. 1993), decrease age-related bone loss (Mosekilde 1995, Kannus et al. 1996) and reduce the risk of falls (Fiatarone et al. 1990, Smith 1994, Tinetti et al. 1994, Province et al. 1995, Myers et al. 1996).

Growing and mature skeletons respond differently to mechanical stimuli at different stages of growth and aging (Biewener and Bertram 1993, Kannus et al. 1995, Young et al. 1995). Exercise can be used to increase peak bone mass in childhood and adolescence as a prophylactic measure for osteoporosis. It seems to have the greatest influence on skeleton during growth and maturation (Haapasalo et al. 1994, Kannus et al. 1995). With an animal model, it has been shown that exercise accelerates the development of the skeleton and thus increases the mechanical competence of the bone (Søgaard et al. 1994). In addition, the response of skeleton to mechanical loading is site-specific at different ages (Jones et al. 1977, Pirnay et al. 1977, Huddleston et al. 1980, Jacobsen et al. 1984, Haapasalo et al. 1994, Kannus et al. 1994) and decreased functional loading is associated with bone loss (Krolner and Toft 1983, Dalsky et al. 1988, Nishimura et al. 1994). Therefore normal loading activity at each location is an important functional determinant of bone mass (Lanyon 1996). Furthermore, exercise may be even more important for bone geometry in conjunction with maintaining bone mass and preventing age-related bone loss (Beck et al. 1992, Bouxsein et al. 1993, Ferretti et al. 1993, Mosekilde et al. 1994).

In human exercise studies the changes in bone mass are small, and local rather than generalized, and the attainable changes take place slowly (Lanyon 1996). During the past decade, many exercise training studies have used training programs designed, primarily, to increase cardiorespiratory fitness rather than local bone loading (Marcus et al. 1992, Bassett 1995, Lanyon 1996). Different exercise modalities and sports load the skeleton at different sites and in different ways, and thus the training response may vary. Strength training, for instance, consisting of high loads and few repetitions, may induce strain levels above the MES (shown to be between 1500 - 2500 $\mu\epsilon$). On the other hand, the rate of force application or the multidirectional movements rather than the magnitude of force as such may be important in some sports, for example, in gymnastics (Nichols et al. 1994, Kirchner et al. 1995, Robinson et al. 1995, Taaffe et al. 1995) and dance (Grimston et al. 1993, Alekel et al. 1995), and thus initiate bone adaptation.

It is obvious that different training regimens produce different loading characteristics of the skeleton, and therefore a review of the results of experimental and clinical studies on the primary mechanical loading variables associated with the changes in the regulation of bone mineral mass is in order.

2.4.1 High-magnitude loading

An analysis of human studies supports the hypothesis that high peak forces of loading (or high strain magnitude) may have a greater effect on bone mass than large numbers of loading cycles (Whalen and Carter 1988). Nilsson and Westlin (1971) were among the first to observe that the density of the distal femur in athletes was significantly greater than that of nonathletes. The highest values were recorded for weightlifters. Several other cross-sectional studies have reported higher bone mineral mass in weightlifters than in sedentary controls and athletes in other sports (Granhed et al. 1987, Block et al. 1989, Heinrich et al. 1990, Virvidakis et al. 1990, Conroy et al. 1993). The BMD of the lumbar spine, femoral neck, and distal and proximal radius has been found to be up to 10% higher in female weightlifters than the controls (Davee et al. 1990, Heinrich et al. 1990). Young and middle-aged male weightlifters also have greater femoral and spinal bone mineral mass (Nilsson and Westlin 1971, Granhed et al. 1987, Block et al. 1989, Colletti et al. 1989, Conroy et al. 1993, Karlsson et al. 1993), and elderly weightlifters have greater calcaneus mineral mass than nonathletes (Suominen et al. 1989, Suominen and Rahkila 1991). In addition, Karlsson et al. (1995) showed that male weightlifters had an indication of higher bone formation than sedentary controls when measured by biochemical markers (osteocalcin).

As anabolic strereoids are used among weightlifters, the possible role of steroids in bone metabolism should be considered. One study has addressed this question. Fiore et al. (1991) examined the effects of powerlifting on midradius and distal radius and bone metabolism in a group of athletes who were taking androgens. They found that anabolic steroids did not provide any further stimulus for osteoblast activity and bone formation.

Despite the evidently positive influence reported for weight training on bone mineral mass in cross-sectional studies (Nilsson and Westlin 1971, Granhed et al 1987, Heinrich et al. 1990, Virvidakis et al. 1990, Xia Qu 1992, Conroy et al. 1993, Karlsson et al. 1993), prospective weight-training studies have demonstrated only moderate (0.8% to 3.8% on the average) effects on regional bone mineral mass (Gleeson et al. 1990, Peterson et al. 1991, Pruitt et al. 1992, Snow-Harter et al. 1992, Menkes et al. 1993, Nelsson et al. 1994, Ryan et al. 1994, Friedlander et al. 1995, Lohman et al. 1995). Men appear to respond better than women to an increase in regional BMD during shorter periods of training (Menkes et al. 1993, Ryan et al. 1994). Furthermore, premenopausal and postmenopausal women may respond differently to training. For postmenopausal women, Pruitt et al. (1992) observed a significant difference in the change in BMD of the lumbar spine between a strength training group and a control group (+1.6% versus -3.6% on the average). For premenopausal women aged 30-40 years, Gleeson et al. (1990) reported a significant, but smaller difference in the change in lumbar BMD (+0.8 % versus -0.5% on the average). The study of Lohman et al. (1995) also showed a 2% average increase in BMD after 18 months of strength training. For young premenopausal women (20-35 years), Snow-Harter et al. (1992) and Friedlander et al. (1995) reported a significant difference in the regional increase in BMD (1~2%) between a strength-training group and a control group. On the other hand, the study of Pruitt et al. (1995) showed that in older women strength training did not significantly increase regional BMD in comparison with that of a control group.

Strength training seems to increase site-specific bone mineral mass in women, although the skeletal response to loading is characteristic for different age phases (Forwood and Burr 1993). On the other hand, nonweight-bearing sports that incorporate forceful muscular contractions, such as swimming, confer no beneficial effects on the bone mass of young women (Taaffe et al. 1995).

Moreover, van der Wiel et al. (1995) showed that a short duration of exercise with additional mechanical loading (strain magnitude) leads to the most pronounced effects on bone mineral mass and mechanical variables in rats. Hillam and Skerry (1995) also found that six short daily periods of mechanical loading *in vivo* inhibit modeling-related bone resorption and stimulate bone formation in growing rats. Altogether, the heavy loading of bone causes an elevated bone formation response, and increased mechanical loads stimulate modeling, with an increase in periosteal bone formation (Raab et al 1990,1991, Raab-Cullen et al. 1994a). Similarly, weight training may stimulate bone formation through the direct action of muscle contractions on bone or through the increased effect of axial compressive loading (Chilibeck et al. 1995).

2.4.2 Repetitive loading

It seems likely that the functional adaptation of bones depends also on loading history (Carter et al. 1981, 1987), being mediated in some fashion by the repetitive loading (or cyclic strain) developed in the bone associated with its use (Lanyon 1984, Rubin and Lanyon 1984a, 1984b). Although it has been shown that only a few loading cycles with high strain magnitude may be required to produce an adaptive response in a bone (Rubin and Lanyon 1984a), the importance of the number of loading cycles probably increases when the strain magnitude is low (Whalen and Carter 1988).

The number of skeletal loading cycles, such as steps per day, may become high during daily living. In their 20-year follow-up study Cooper et al. (1995) showed that the most important factor for peak bone mass was physical activity and growth. Physical activity was determined by the daily walking distance and participation in sports. Higher bone mineral mass has been observed in runners than in sedentary persons. In the studies by Lane et al. (1986), Marcus et al. (1985) and Wolman et al. (1991), runners had a higher bone mineral mass in the lumbar spine and femur than controls. On the other hand, Heinrich et al. (1990), Buchanan et al. (1988) and Bilanin et al. (1989) did not find significant differences between young runners and controls. In addition, Michel et al. (1989) found that men over 60 years of age and women who had done more than 217 minutes of aerobic weight-bearing exercise a week had higher bone mineral mass than less active subjects. Suominen and Rahkila (1991) observed similar results. They found that 70- to 81-year-old speed-trained (sprinters, jumpers) men who had trained 50-1300 km during the study year had significantly higher BMD than did those who trained less than 50 km. Ballard et al. (1990) also found a relationship between high physical activity ($\geq$ 8.5 METS) and the bone mineral mass of distal radius. With regard to the importance of weight-bearing (i.e., ground reaction force of the skeleton), previous studies on rowing (Wolman et al. 1991) and swimming (Orwoll et al. 1989, Risser et al. 1990, Taaffe et al 1995), typical nonweight-bearing exercises, suggest that gravity plays an important role in the process of bone mineralization.

Endurance training, particularly running and also fast walking, produce repetitive weight-bearing impact with the ground and therefore is likely to stress the calcaneus, tibia, patella, femur and also lumbar spine. Margulies et al. (1986) reported an 11% gain in the bone mineral mass of the left distal tibia among 240 military recruits after a rigorous daily, 14-week training program. The bone mineral mass of the right tibia showed a 5% increase.

Studies on the effects of walking on skeleton have revealed conflicting results. Uusi-Rasi et al. (1994) found no differences between premenopausal letter or newspaper carriers walking 6 km a day and sedentary office workers of the same age walking 1.5 km a day. However, Krall and Dawsonhuges (1994) found that postmenopausal women who habitually walk more than 7.5 miles (12 km) a week, or about 1 mile (1.6 km) each day, had a higher mean bone mineral mass for the whole body and leg regions than women who walked shorter distances. Cavanaugh and Cann (1988) showed that brisk walking does not prevent bone loss in postmenopausal women, and White et al. (1984) found the same results for walking and dancing. On the other hand, several authors have reported that calisthenics and walking combined can either attenuate axial skeleton bone mineral mass loss or even increase bone mineral mass in postmenopausal women (Smith et al. 1984, 1989, Chow et al. 1987, Simkin et al. 1987, Dalsky 1988, Hatori et al. 1993, Krall and Dawsonhughes 1994, Kohrt et al. 1995, Prince et al. 1995). Moreover, Kohrt et al. (1995) showed that weight-bearing exercise positively affects femoral neck in older women and that exercise and estrogen therapy have additive effects on BMD of the lumbar spine and Ward's triangle. Prince et al. (1995) found that postmenopausal women who took calcium supplements and exercised had less bone loss at the femoral neck site when compared with subjects on calcium supplementation alone, whereas exercise alone had no effect on femoral neck during the two-year study. Similar results were reported by Nelson et al. (1991). They showed that a one-year walking program plus high dietary calcium increased BMD by 2.0% at femoral neck, but neither exercise nor calcium alone had an effect on femoral neck, lumbar spine or distal radius in postmenopausal women.

Although most of the data available suggest that the effect of aerobic training, mainly as walking, on human bone is beneficial, there seems to be an intensity threshold. Hatori et al. (1993) showed that the bone mineral mass of the lumbar spine increased with very fast walking (7.2 km/h) performed at intensities exceeding the anaerobic threshold. In contrast, slower walking (6.2 km/h) at intensities below the anaerobic threshold was not successful in increasing the mineral mass of lumbar bone. In addition, Martin and Notelowitz (1993) found that walking speeds of less than 6.4 km/h did not increase lumbar bone mineral mass. Likewise, findings by Dalsky et al. (1988) and Chow et al. (1987) support the concept that high-intensity weight-bearing exercise (70-90% of $\dot{V}O_2max$) increases or maintains bone mineral mass in postmenopausal women.

Animal studies have also shown that aerobic exercise such as running stimulates bone formation and increases bone mass and strength (Saville and Whyte 1969, Raab et al. 1991) In a recent study Peng et al. (1994) showed that running exercise was able to prevent the loss of bone strength induced by estrogen deficiency in rats. Nordsletten et al. (1994), however, found no positive effect of high-intensity training on the development of osteopenia in rats. In addition, Wheeler et al. (1995) had rats running with three different intensities. Their results indicate that bone adapts to its loading by increasing mineral mass and by increasing cortical bone area and mechanical properties, but they did not find any dose response.

2.4.3 High-impact loading

Using an animal model, O'Connor et al. (1982) found a strong correlation between a positive remodeling response and both the strain rate and the strain magnitude. They suggested that the strain rate had the most important influence on the magnitude of new bone deposition. Previous cross-sectional studies support the concept that training producing strain at a high rate and high peak forces in diverse movements is the most effective in enhancing bone formation in young women (Risser et al. 1990, Slemenda and Johnston 1993, Fehling et al. 1995, Friedlander et al. 1995, Kirchner et al. 1995, Robinson et al. 1995, Taaffe et al. 1995). Robinson et al. (1995) investigated bone mineral mass in two groups of competitive young female athletes with different skeletal loading patterns: gymnasts and runners. The gymnasts exhibited higher bone mineral mass in the femoral neck and lumbar spine (6-12 %) than did runners and controls. Taaffe et al. (1995) found similar results; young female gymnasts had greater bone mineral mass at both appendicular and axial sites than swimmers and controls. Fehling et al. (1995) and Kirchner et al. (1995) also showed that, when height and weight were controlled, the impact loading group (gymnasts and volleyball players) had higher bone mineral mass than swimmers and controls. Judged from these studies high-impact weight-bearing training is beneficial for bone accretion.

Recent longitudinal studies using an exercise regimen in which a rapidly rising force profile (jumping) (Grove and Londeree 1992, Bassey and Ramsdale 1994, 1995), have shown an increase in trochanteric (Bassey and Ramsdale 1994) bone mineral mass in premenopausal women or the maintenance of lumbar bone mineral mass in early postmenopausal women (Grove & Londeree 1992). Nielsen et al. (1992) found that five months of gymnast's training had a systemic effect on bone in elderly women. Furthermore, Nichols et al. (1994) examined the effect of a 27-week gymnastic training program on bone mineral mass in young female gymnasts. They found that the gymnasts had higher bone mineral mass in the lumbar spine than the controls, and it increased after the training.

Moreover, Umemura et al. (1995) investigated the effects of jump training on bone hypertrophy in rat in comparison with the effects of running training. They found that for bone hypertrophy jump training, which had a high strain rate and magnitude, was a more effective training mode than running.

Altogether, all these findings indicate that high-impact exercise (i.e., high strain rate) is effective in improving and maintaining bone mineral mass and preventing age-related bone loss. According to recent literature (Lanyon 1992, 1996, Rubin and McLeod 1996), high-impact exercise such as jumping may be an appropriate type of training with which to influence osteogenic response, as it would place a variety of forces on bone.

2.5.4 Summary

Cross-sectional studies of active and sedentary populations have shown a positive correlation between activity level and bone mineral mass (Snow-Harter and Marcus 1991, Suominen 1993, Chilibeck et al. 1995). Several cross-sectional findings in athletic groups have shown that athletes, especially those who are strength trained or high-impact trained, have greater bone mineral mass than nonathletes. These differences amount to 10% or more. An apparent positive effect of activity on bone is more marked in cross-sectional studies than in prospective ones (Drinkwater et al. 1995). The explanation may be a selection bias or differences in the duration, frequency and intensity of the training programs. Few longitudinal studies have been reported (Lohman et al. 1995), and, due to a lack of randomization into exercise and control groups and poor subject compliance, definite conclusions cannot be drawn. In addition, little attention has been given to understanding the type, intensity, frequency and duration of exercise. Moreover, bone has sometimes been measured at nonloaded sites in both cross-sectional and longitudinal studies. There is a definite need for additional well-designed cross-sectional and longitudinal studies to determine qualitatitive and quantitative adaptation responses of bones to various training modes with different loading characteristics.

3 PURPOSE OF THE STUDY

The objective of the present study was to search for an effective exercise mode with which to influence BMD and bone mineral content (BMC) and the estimated mechanical characteristics of young and pre- and perimenopausal healthy women. More specifically, the aims were:

1) To identify, using a cross-sectional study design (I, II), the characteristics of osteogenic exercise stimulus and to determine its possible site-specificity by comparing the bone mineral density of athletes representing sports that produce different types of loading on the bones

2) To determine the specific effects of different types of exercise training on BMD (III, IV, V, VI), BMC (III, IV), and estimated mechanical characteristics of bones (IV) at different skeletal sites in controlled intervention studies
and

3) To describe the characteristics of effective osteogenic exercise stimulus on the basis of the results of the aforementioned studies (I, II, III, IV,V, VI).

4 MATERIAL AND METHODS

4.1 Subjects and design

Altogether 444 healthy women were involved in the present studies. The subjects were female athletes, and sedentary or physically active premenopausal young and perimenopausal women. The athlete group included nationally or internationally ranked Finnish squash players, weightlifters, aerobic dancers, orienteerers, speed skaters, cross-country skiers and cyclists. The training history of the athletes ranged from 3 to 13 years of sport-specific training (I, II). In the exercise intervention trials, the subjects volunteered to be in the training or in the control group (III, IV) or were randomly selected from volunteers to the training or to the control group (V, VI).

None of the subjects had any disease or used medication that might have affected bone or had any diseases that might have limited the training or testing. The number of weekly exercise sessions (e.g., walking, jogging, swimming or aerobic) of the nonathletes ranged from two to five per week.

Selected characteristics of the subjects are presented in Table 1. The number of subjects in the beginning of the intervention studies, the number of drop outs, and the design, training and duration of the study are presented in Table 2. Detailed information on the study designs and the training programs are given in the original reports.

TABLE 1 Characteristics of the subjects in the different studies (I-IV), means (standard deviations).

	N	Age	Height	Weight	BMI*
I, II					
Squash players	18	25.0 (3.9)	166 (6)	62 (6)	22.4 (2.3)
Weight lifters	18	24.6 (3.9)	165 (7)	67 (11)	24.3 (3.3)
Aerobic dancers	27	28.3 (3.7)	166 (5)	57 (4)	20.7 (1.1)
Orienteerers	30	23.3 (3.1)	169 (5)	59 (5)	20.8 (1.5)
Speed skaters	14	21.4 (8.6)	168 (6)	63 (7)	25.9 (3.3)
Cross-country skiers	28	21.3 (3.2)	169 (6)	62 (9)	21.6 (2.2)
Cyclists	29	24.0 (5.7)	166 (5)	62 (8)	22.4 (2.4)
Physical active referents	25	22.6 (2.8)	167 (7)	61 (8)	22.0 (2.9)
Sedentary referents	25	23.8 (4.7)	166 (5)	59 (6)	21.5 (2.1)
III					
Training group	12	21.0 (2.5)	167 (5)	58 (6)	20.8 (2.4)
Control group	12	22.0 (3.0)	167 (8)	61 (11)	22.1 (3.3)
IV					
Training group	13	23.8 (5.0)	166 (7)	64 (13)	23.2 (4.4)
Control group	19	25.7 (5.2)	165 (4)	62 (7)	22.3 (2.4)
V					
Calisthenics group	26	53.1 (0.9)	161 (6)	69 (10)	26.6 (3.8)
Endurance group	23	52.9 (0.9)	163 (5)	70 (11)	26.2 (3.7)
Control group	27	53.1 (0.8)	161 (5)	64 (8)	24.9 (3.0)
VI					
Training group	49	39 (3)	164 (6)	62 (7)	23.2 (2.6)
Control group	49	39 (3)	165 (5)	62 (7)	22.9 (2.3)

N = number of subjects included in the statistical analysis

TABLE 2 Study design, number of drop-outs, training and determination of fitness and duration in the original studies.

	Study	Study design	Drop-outs	Training/ determination of fitness	Duration
I, II	Squash players, Weightlifters, Orienteerers, Speed skaters, Cross-country skiers, Cyclists, Physical active referents, Sedentary referents	Cross-sectional study The athletes represent sports with different skeletal loading characteristics		Training history, cardiorespiratory fitness test, maximal isometric strength tests	
III	Control group	Controlled exercise trial	3		Training: 12 months
	Training group		5	Unilateral leg-press strength training, 5 x 10 x 80 % of 1RM, 3.9 times/week	Detraining: 3 month
IV	Control group	Controlled exercise trial	1		Training: 12 months
	Training group		5	Unilateral elbow flex/ext strength training with dumbbells, 5 x 10 x 80 % of 1RM, 2.8 times/week	Detraining: 8 months
V	Control group	Randomized controlled exercise trial	11		18 months
	Calisthenics group		9	Calisthenics training for large muscle groups, Endurance training at 55-57 % (HR) of VO_2max, 3.1 times/week, 50 min	
	Endurance group		8		
VI	Control group	Randomized controlled exercise trial	4		18 months
	Training group		10	Progressive high-impact exercise, 2.5 times/week, 60 min	

RM = maximum weight that can be used for the designated number of repetitions; HR = heart rate; VO_2max = maximal oxygen uptake
flex/ext = elbow flexion and extension

4.2 Measurements

4.2.1 Questionnaires, cardiorespiratory fitness and maximal isometric strength tests

The measurements and the variables reported in the original studies are listed in Table 3. The day-to-day precision of the measurements, expressed as the coefficient of variation (CV%), are also shown in Table 3.

Information on living habits and health status such as training history (I, II) or physical activity (III, IV, V, VI), injuries, medication, known diseases, diet, menstrual status, possible vitamin or mineral suplementation and the consumption of alcohol and cigarettes was obtained with detailed questionnaires (Table 3).

Directly (Oja et al. 1991a) or indirectly (Oja et al. 1991b) assessed maximal oxygen uptake ($\dot{V}O_2max$) was used as the measure of cardiorespiratory fitness. In the direct assessments a progressive step protocol was used either on a bicycle ergometer or a treadmill depending on the cardiorespiratory requirements of each sport. The test was continued to the voluntary maximum (Table 3).

The maximal isometric strength of the trunk extensors and flexors, forearm flexors and extensors, and leg extensors was measured with a strain gauge dynamometer (Heinonen et al. 1994). The leg extensor power or lower limb explosive performance capacity was evaluated using a vertical counter-movement jump test, first without extra weight and then with an additional weight of 10% of body mass (Sillanpää et al. 1995). The dynamic balance of the subjects was tested by a figure-8 running test (Tegner et al. 1986) (Table 3).

Detailed information on the sampling procedures, the participation rates, exclusion criteria, the training history and physical activity of the subjects, and the measurement protocols is given in the original reports.

4.2.2 Bone measurements

Bone mineral characteristics. Bone mineral mass, as determined by dual energy X-ray absorptiometry (DXA), is the most easily measurable determinant of bone strength in humans, and it has recently appeared to be the most effective measure for assessing BMC and areal BMD (Sievänen 1996b). BMD seems to be a more appropriate parameter than both BMC and the average bone width (i.e., area) within a given projection in that it provides two-dimensional macroscopic information on bone geometry (Sievänen et al. 1994b, 1996b).

In the original studies, BMD, BMC, bone width, and estimated cortical wall thickness (CWT) was measured at several skeletal sites (Table 2). The BMC values measured at five lower-limb sites were summed up (ΣBMC) in one study (III). The change in ΣBMC was considered to indicate the total osteogenic effectiveness of the training on the lower limb (III).

TABLE 3 Variables measured in the original studies and the methods used.

Variables	Studies	Methods/references	CV %
Anthropometry			
Height	I-VI		
Weight	I-VI		
Body mass index	I-VI		
Body fat, %	III-VI	Four skinfolds, Durnin et al. (1974)	
	I-II	BIA 106, RJL System INC.	
Cardiorespiratory fitness			
$\dot{V}O_2$ max	I, II,	Medikro 202E (Oja et al. 1991a)	
"	V	Sensor Medics 2900Z "	
"	VI	Walking test (Oja et al.1991b)	
Isometric strength		Isometric dynamometry	
Trunk extension/flexion	I, II, V, VI	Digitest, Heinonen et al. (1994)	5.1 - 5.9
Leg press	I-III,V, VI	Tamtron, " "	5.4
Elbow flexion	I-II, IV-VI	Digitest, " "	9.7
Elbow extension	IV	Digitest	
Grip strength	IV	Standard grip strength meter	
Vertical jump		Contact platform, Digitest	
Without extra weight	VI	Sillanpää et al. (1995)	3.4
With additional weight of 10%	VI		
Dynamic balance			
Running in figure of 8	VI	Digitest, Tegner et al. (1986)	
Questionnaires (living habits, health status, training history, menstrual status)	I-VI		
Calcium intake	I, III	Questionnaire	
	II, IV, V	Seven-day calcium intake diary	
	VI	Three-day dietary record	
Bone measurements,		DXA, Norland XR-26	
Bone mineral density (BMD, g/cm^2)			
Lumbar spine	I-III, V, VI	Sievänen et al. (1992)	1.7
Femoral neck	I-III, V, VI	" "	1.3
Distal femur	I-III, VI	" "	1.2
Patella	I-III, VI	" "	1.0
Proximal tibia	I-III, VI	" "	0.7
Calcaneus	I-VI	" "	1.3
Proximal humerus	IV	Sievänen et al. (1993)	0.8
Humeral shaft	IV	" "	0.5
Radial shaft	IV	" "	0.7
Ulnar shaft	IV	" "	1.3
Distal radius	I-III, V, VI	Sievänen et al. (1993)	0.7
Distal forearm	V	" "	0.7

(continued)

TABLE 3 continued

Variables	Studies	Methods/references	CV %
Bone mineral content (BMC, g)			
ΣBMC	III		0.6
Lumbar spine	III	Sievänen et al. (1992)	1.3
Proximal humerus	IV	" "	1
Humeral shaft	IV	Sievänen et al. (1993)	0.5
Radial shaft	IV	" "	0.5
Ulnar shaft	IV	" "	1.1
Distal forearm	IV	Sievänen et al. (1993)	0.8
Bone width			
Proximal humerus	IV	Sievänen et al. (1996b)	0.9
Humeral shaft	IV	" "	0.3
Radial shaft	IV	" "	1.0
Ulnar shaft	IV	" "	1.0
Cortical wall thickness (CWT, mm)			
Humeral shaft	IV	Sievänen et al. (1996b)	0.7
Radial shaft	IV	" "	1.2
Ulnar shaft	IV	" "	2.1
Cross-sectional moment of inertia (CSMI, mm^4)			
Humeral shaft	IV	Sievänen et al. (1996b)	1.0
Radial shaft	IV	" "	3.1
Ulnar shaft	IV	" "	3.5
Section moduli (Z)			
Radial shaft	IV	Sievänen et al. (1996)	2.1
Ulnar shaft	IV	" "	2.6
Strain index	IV		

CV % = Coefficient of variation (standard deviation/mean) x 100 %; $\dot{V}O_2max$ = maximal oxygen uptake; ΣBMC = sum of the BMC of the five measured leg sites.

Biomechanical analysis. Bone mineral mass accounts for most (about 80%) of overall bone strength (Dalen et al. 1976, Hansson et al. 1980), the remaining qualitative share being determined by bone geometry, internal architecture, geometric properties and the material quality of the bone (Carter and Hayes 1976, Currey 1984, Goldstein 1987, Cowin 1989, Einhorn 1992). The DXA parameters contain some additional information on the skeletal structure and bone mass distribution. Recently, various extensions to BMD and BMC parameters have been developed to describe geometric characteristics of bone (Martin and Burr 1984, Beck et al. 1990, Bouxsein et al. 1993, Faulkner et al. 1993, Hsu et al. 1993, Myers et al. 1993, Sievänen et al. 1994b, 1996b, Yoshikawa et al. 1994). Thus CSMI can be determined using single photon absortiometry (SPA) or DXA data (Martin and Burr 1984, Beck et al. 1992, Yoshikawa et al. 1994). Furthermore, it is also possible to estimate an index for bone bending strength using DXA by dividing CSMI by half of the bone width (eq. 3) at the given site (Sievänen et al. 1996b).

Consequently, a biomechanical analysis was made for the radius and ulna in one original report (IV). Detailed information about the biomechanical analysis is also given in the original report (IV).

4.3 Statistical methods

The means and standard deviations (SD) had been given as descriptive statistics.

In studies I and II, the subject characteristics and performance variables of the athlete groups and reference groups were compared with the one-way analysis of variance (ANOVA). When the ANOVA indicated a significant difference ($p<0.05$), Tukey's studentized range method was used as the post-hoc test. For estimating the differences in BMD between the athlete groups and the sedentary reference group, an analysis of covariance (ANCOVA) was used. Weight, known to correlate positively with BMD (Bauer et al. 1993, Edelstein and Barret-Conner 1993, Felson et al. 1993), was used as a covariate.

In studies III and IV, ANCOVA was used to determine the effects of exercise intervention on cardiorespiratory fitness (V), isometric strength (III, IV, V) and bone measurement (III, IV). General linear models (GLM), with restricted maximum likelihood (REML) estimation, were used to determine the effects of exercise intervention on BMD, muscular performance and cardiorespiratory fitness in studies V and VI and dynamic balance in study VI. This type of analysis made it possible to incorporate the incomplete data into the models at the time points at which some values were missing for the variables. In study V, the difference was evaluated in two ways: 1) as the simple post-training difference and 2) as a linear trend obtained from a regression analysis of the measured or estimated individual data.

The training effect in both the ANCOVA and GLM analysis was determined as a group difference (training group versus control group) for the post-training BMD, BMC, muscular performance, dynamic balance and cardiorespiratory fitness, the difference being adjusted by the baseline values (III - VI). In addition, the differences were adjusted for estrogen status (BMD only) in study V.

5 RESULTS

5.1 Bone mineral density in female athletes

All the athlete groups except the weightlifters had a higher ($p<0.01$) $\dot{V}O_2max$ than the sedentary and physically active referents. As expected, the endurance athletes had the highest $\dot{V}O_2max$ values. The athletes also had higher isometric strength than the referents. The relative muscle strength (N/kg) was highest in the aerobic dancers, weightlifters and squash players.

The squash players (7-19%) and weightlifters (7-19%) had significantly higher weight-adjusted BMD values for all the measured sites (lumbar spine, femoral neck, distal femur, patella, proximal tibia, calcaneus and distal radius) than the sedentary referents did, with the exception of the BMD of the femoral neck in the weightlifters. The aerobic dancers, orienteerers, speed skaters, and cross-country skiers had a significantly higher BMD at the loaded sites than the sedentary referents did. These differences were less than 10%, except for that of the calcaneus of the aerobic dancers (14%). Thus the observed differences in the BMD values between the groups suggest a site-specific effect for loading. Furthermore, the cyclists' and physically active referents' BMD values did not differ from those of the sedentary referents at any site.

Figure 3 shows the weight-adjusted BMD differences at the distal femur, proximal tibia and calcaneus (the loaded sites in most of the studied sports) between the athlete groups representing different types of loading and sedentary referents.

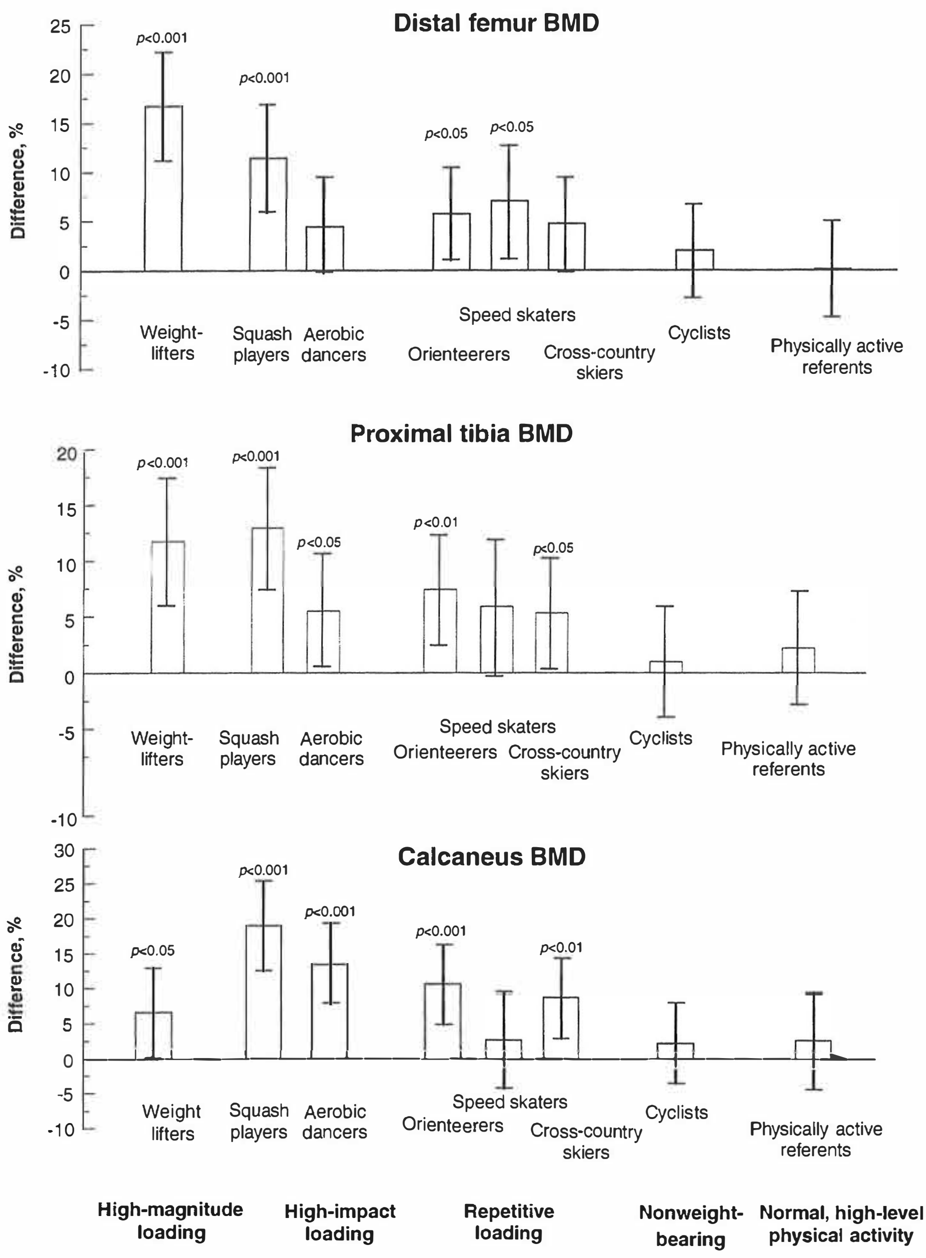

FIGURE 3 Relative difference of the weight-adjusted bone mineral density (BMD) at the loaded lower-limb sites of the female athlete groups and the physically active reference group from that of the sedentary reference group (I-II). The grouping of the athletes was based on the specific bone loading characteristics of the respective sports. The bars indicate the 95 % confidence interval.

5.2 Changes in bone mineral density and content in different types of exercise intervention

Unilateral 12-month strength training of the left lower limb (III) significantly increased (24% in the left trained limb) muscular strength in the training group as compared with that of the control group (5%). The pattern of the muscular strength changes (IV) was similar after the 12 months of upper-limb unilateral strength training with dumbbells. For the trained left limb, the significant mean increase in isometric elbow flexion was 14% as compared with that of the control group (1%), and the extension strength increase (21%) was also significant (control group 4%). Consequently, 12 months of unilateral high-intensity strength training for lower-limb (III) and upper-limb (IV) bones was effective in increasing muscular strength.

The mean BMD changes in the trained limb were from 1.1% (femoral neck) to 2.2% (proximal tibia) in the training group and from -0.6% to 1.5% in the control group. The mean BMC changes were from 0.1% (distal forearm) to 2.3% (proximal humerus) in the training group and from 0.2% to 2.5 % in the control group. No significant intergroup differences were observed in the BMC and BMD of the lower- and upper-limb bones. For the left patella, there was a significant ($p = 0.02$) intergroup difference, whereby the BMD increased an average of 1.6% in the training group and decreased 0.6% in the control group (III). As an example, the ΣBMC (III) is shown in Figure 4 for the lower limb.

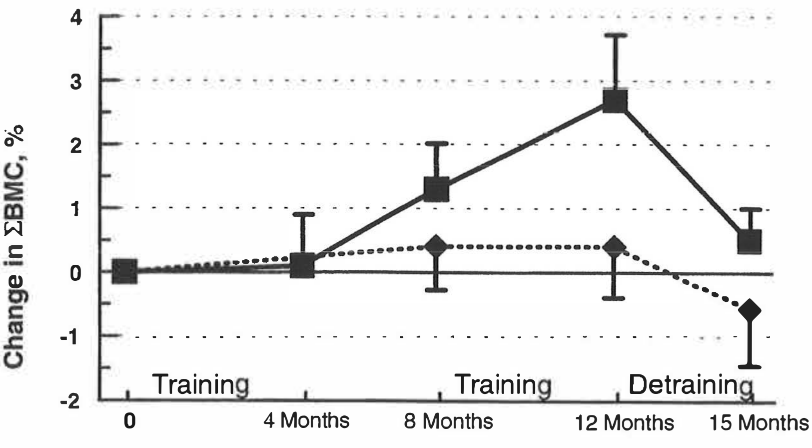

FIGURE 4 Ghange in the sum of the bone mineral content (Σ BMC) of the five measured sites (mean, standard error) in the left trained leg during 12 months of unilateral training and three months of detraining by healthy young women (III). The solid line represents the training group and the broken line the control group.

Three months after the training period (III), the mean strength was virtually unchanged in the training group, while muscular strength had increased by 3% in the control group. The BMD values of the trained lower limb returned almost to the baseline level in the training group, except for that of the femoral neck and calcaneus. In addition, the ΣBMC decreased steeply (Figure 4). During the detraining period of eight months in the upper-limb training study (IV), the mean strength of the trained limb decreased about 7% in elbow flexion and 8% in elbow extension. The corresponding changes in the control group were -5% and 1%, respectively. Conversely, there were slight increases in the BMC values, especially for the proximal humerus, but there were no significant intergroup differences at any of the measured sites.

Whereas the strength training increased the isometric muscular strength, the maximal strength was not significantly affected by the 18-month calisthenics or endurance training of previously sedentary perimenopausal women (V) or by the high-impact training of premenopausal women (VI). However, high-impact training significantly improved vertical jump (without extra weight 4% and with additional weight 20%) in the training group as compared with that of the control group (0% and 15%) (VI). In addition, the effects of endurance training and impact training favored the endurance group (15%) (V) and the high-impact trainees (4%) (VI), the effect being significant as compared with that of the control group.

Study V was aimed at evaluating the effects of 18-month calisthenics and endurance training regimens on BMD in a group of perimenopausal women. For the BMD of the femoral neck BMD, the linear trend in the endurance group was significantly different (p=0.043) from that of the control group, the trend indicating a maintanence of the prestudy BMD level. In the callisthenics group, the training effect was not significant. For the BMD of the lumbar spine, calcaneus and distal radius, there were no significant training effects in either the endurance or the callisthenics group except for the distal radius, for which the linear trend (p=0.006) and post-training difference (p=0.007) were significantly lower in the endurance group than in the control group. These sites showed a clear negative trend as compared with corresponding control data. The time courses of the change in the BMD of the femoral neck are presented in Figure 5 for the training groups and the control group.

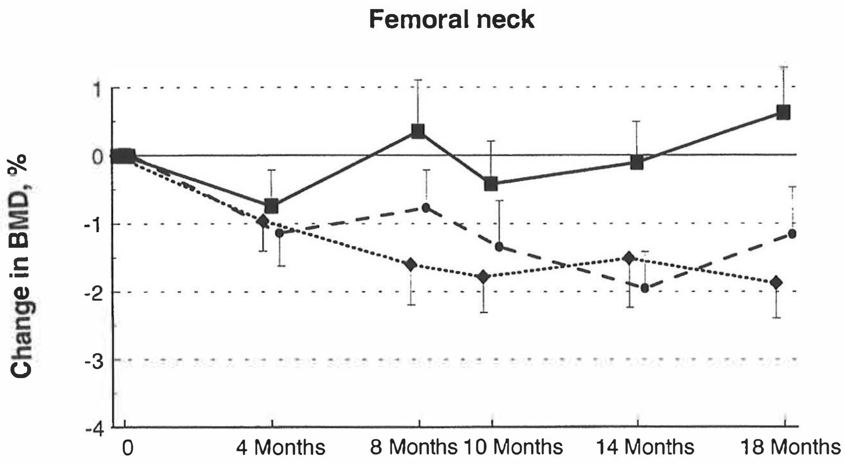

FIGURE 5 Time course of the change in the bone mineral density (BMD) of the lumbar spine of the healthy perimenopausal women (V) who completed the study (mean± standard error). The solid line represents the endurance group, the dotted lines the callisthenics group, and the broken linc thc control group.

Finally, study VI was designed to determine whether 18-month high-impact training would beneficially modify axial and lower limb BMD. In general, at the loaded sites of the skeleton, the BMD increases in the trainees were consistently larger than those in the controls. Across the entire study period, the percentage change in BMD among the subjects who completed the study (39 subjects in the training group and 45 subjects in the control group) are presented in Figure 6. The estimated post-training difference between the groups was statistically significant in favor of the impact trainees at the lumbar spine ($p=0.009$), femoral neck ($p=0.012$), distal femur ($p<0.001$), patella ($p=0.004$), proximal tibia ($p<0.001$) and calcaneus ($p<0.001$).

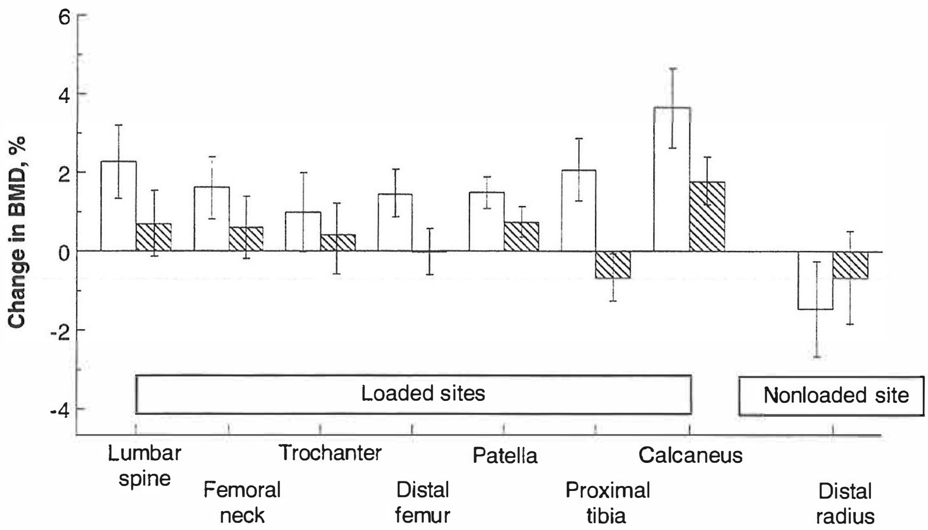

FIGURE 6 Change in bone mineral density (BMD) at the loaded and nonloaded sites in healthy premenopausal women after 18-month high-impact training (VI). The bars indicate the 95% confidence intervals. The open bars belong to the training group and the shaded bars to the control group.

5.3 Changes in the estimated mechanical characteristics after strength training

In study IV, there were no significant intergroup changes in the upper-limb bones over time for any of the biomechanical variables. Thus the bone width, CWT and CSMI remained unchanged after the strength training. The mean estimated strain induced by the strength training remained within the customary mechanical strain range, being from 1900 to 2200$\mu\epsilon$ during flexion and extension training of the forearm bones. The training caused only a 15% increase in strain with respect to the baseline level. Figure 7 shows the 95% confidence intervals for the estimated strain during the course of the training.

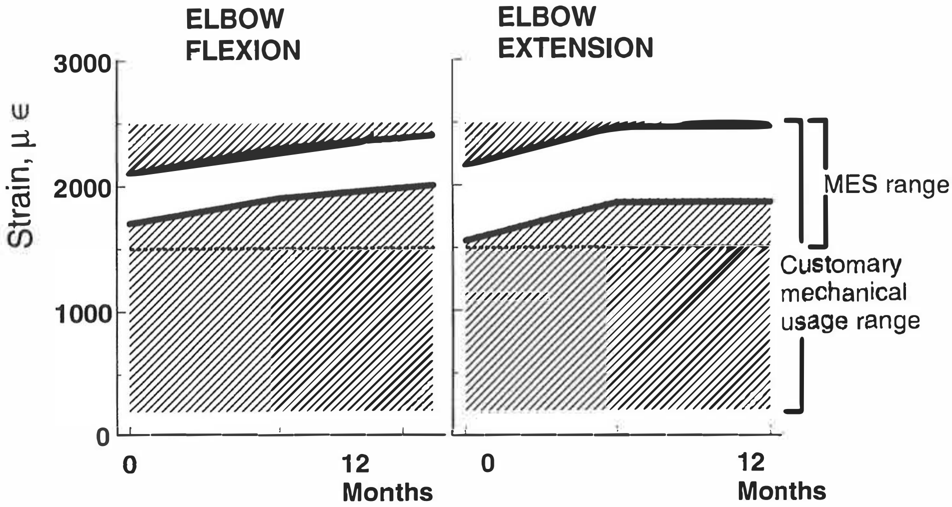

FIGURE 7 Estimated strain in the forearm shaft of healthy young women during 12 months of training (IV). The white area represents the 95 % confidence intervals of the estimated strain in the loaded forearm during the training period. (MES=minimal effective strain)

6 DISCUSSION

Although this study focused on the role of exercise in bone adaptation, it is inappropriate to model bone mass regulation in terms of a single regulator. The capability of bone to respond to mechanical loading is probably determined by a genetically controlled set point that is further modified by site-specific loading history and several metabolic and nutritional factors such as hormones and calcium (Frost 1987, 1993, Turner 1991). Furthermore, some authors have reported that adequate calcium in childhood and adolescence is essential for the attainment of optimal bone mineral mass and size (Bronner 1994). Menstrual disturbances have negative effects on bone mineral mass accumulation (Drinkwater et al. 1990, Prior et al. 1990). In the present studies, only three athletes were amenorrheic (II) and the mean calcium intake in all the groups met the recommended daily intake of 800 mg for adult females. With respect to adult women (such as women in the present studies) oral contraceptive use is of concern although it seems that oral contraceptives do not affect bone mineral mass in adults (Mazess and Barden 1991, Melton et al. 1993). Consequently, the main confounding factors which modify bone adaptation were controlled in studies I-VI, and thus it seemed warranted to analyze physical loading as the main osteogenic stimulus.

In general, the findings of the present studies indicate that exercise regimens designed to increase or maintain bone mass in women should involve high-impact loading or high magnitude loading and unusual loading distributions. The main finding of the cross-sectional studies (I, II) was that athletes whose sport causes high-magnitude or high-impact loading or both (i.e., weightlifting and squash playing) had the highest weight-adjusted BMD values at all the measured sites. In addition, the athletes engaged in sports with repetitive weight-bearing impact loading (aerobic dancers, orienteerers, speed skaters, and cross-country skiers) had a higher BMD at the loaded lower-limb sites than the nonathletic passive referents. Strength-training intervention, despite the clear training effect on muscular strength (high-magnitude loading) did not significantly increase BMD, BMC or the estimated mechanical characteristics of the bone at any measured site except the patella. However, endurance training (repetitive loading) at relatively high intensity maintained the BMD of the femoral neck of healthy perimenopausal women. Furthermore, high-impact training (high-impact loading) effectively loaded the lumbar spine and lower limbs of premenopausal women and caused BMD to increase.

The cross-sectional studies (I, II) focused on comparing the BMD of athletes representing sports that produce different types of loading on the skeleton by determining whether differences in high-magnitude loading, impact loading (accelerating or decelerating movements), repetitive weight-bearing impact, repetitive pliant movements, or nonweight-bearing activity produced by different sports would be reflected in the BMD of the athletes. Consequently, it seems reasonable to examine the effects of strength training, endurance training, calisthenics and high-impact training intervention according to the results obtained for the athlete groups. In addition, it is appropriate to evaluate the results according to the loading characteristics (i.e., high-magnitude, high-impact and repetitive loading associated with bone mineral mass).

6.1 High-magnitude loading

The results (I) showed that weight training (i.e., high peak forces and high-magnitude loading) seemed to be more effective in increasing bone mass than endurance training (i.e., repetitive weight-bearing impact and pliant movements). During competitive weight lifting, high peak forces stressed the skeleton and imposed high magnitudes of strain on bones. The data demonstrated significant BMD differences at all the measured sites of the weightlifters, as compared with the sedentary referents (Figure 3). Most of the differences were more than 10%. The lack of a difference in the calcaneus and femoral neck may be explained by a lack of high-magnitude loading at these sites. In their biomechanical analysis Andersson et al. (1996) found that, while the magitudes of peak stress or strain on femoral neck were of the same order of magitude for weight-lifting, walking, jogging and rope jumping, the magnitude of peak stress or strain rates were significantly lower in weightlifting than in other exercises. These findings support the assumption that the response of BMD to training is site specific.

The BMD values of the intensively training female weightlifters were more than 10% higher than those of comparable referents in the present study (I) and also in other investigations (Davee et al. 1990, Heinrich et al. 1990). Similar observations have been made for male weightlifters (Nilsson and Westlin 1971, Granhed et al. 1987, Block et al. 1989, Colletti et al. 1989, Conroy et al. 1993, Karlsson et al. 1993). However, the present strength-training studies (IV, V) with adults showed only a moderate 0.1-2.3% mean change in the mineral mass of regional bone. This finding is consistent with the mean changes of 0.8-3.8% in other similar studies (Gleeson et al. 1990, Peterson et al. 1991, Pruitt et al. 1992, 1995, Snow-Harter et al. 1992, Menkes et al. 1993, Nelson et al. 1994, Ryan et al. 1994, Friedlander et al. 1995, Lohman et al. 1995).

Granhed et al. (1987) calculated the load on the lumbar spine in elite male powerlifters during an extremely heavy lift. During competitive weightlifting, the compressive stress on the lumbar spine (L_3) ranged from 18.4 to 36.2 kN, values which are 18-36 times body weight. According to Hooke's law (eq. 2), the axial strain range in the lumbar spine (L_3) of powerlifters was from about 500 to 4800 $\mu\epsilon$, provided that Young's module is between 3.8 GPa (Jensen and Mosekilde 1990) and 17 GPa (Carter et al. 1981). Thus this simple estimation shows that the strain on L_3 in powerlifters definitely exceeds the customary mechanical strain range (200- 2500 $\mu\epsilon$), which is typically observed for long bones during normal everyday loading, and the minimal effective strain level was shown to be 1500-2500 $\mu\epsilon$.

In study IV, the mean estimated strain in the forearm bones fell within the customary mechanical strain range and the loading-induced increase in strain was only 15% (Figure 7). Similarly, using data from study III, Sievänen et al. (1995) showed that the mean estimated axial strain on femoral shaft (E = 17 G Pa) during a leg press was between 1000 and 2000 $\mu\epsilon$). To initiate a positive adaptive response, mechanical strain must exceed the MES (Frost 1987, 1988,1990a, 1990b, 1992, Turner 1991). If it is assumed that the baseline strain represents strain typical of what the bone has been adapted to and the large width of the MES range is taken into consideration, the observed negligible response to loading in studies III and IV seems plausible. In other words, when one takes into account the wide "lazy zone" of the customary mechanical usage range within which mechanical strain induces practically no bone formation, the moderate effects of training found for bone mass in this study as compared with the BMD of the lumbar spine of intensively trained weightlifters are not surprising.

On the other hand, Sievänen et al. (1996a) showed that, during 46 weeks of intense unilateral strength training in the form of the leg press, the average strain index for the left patella increased about 47% above the baseline. This finding may indicate that, if the baseline strain index represents typical deformation induced by loading, the lazy zone would be wide. This possibility congrues with the observation that BMD decreases after the cessation (Dalsky et al. 1988) or decrease of training (Lane et al. 1990). The observations of study III also agree with these findings. The BMD seemed to decline in most bones where the greatest decline of loading occurred (distal femur and proximal tibia). These BMD values approached the baseline level three months after the cessation of training. The observations made during the training (III, IV) are consistent with the nonlinear nature of the skeletal responsiveness to specific loading environments (Lanyon 1987, Frost 1988, 1992, 1993, Biewener 1991, Turner 1991) and the time constraints of the remodeling process of the bone (Jee 1988, Frost 1989).

Altogether, the high mechanical loading that stresses the skeleton and the high strain magnitude in strength training are the most probable reasons for the high BMD values of weightlifters. This assumption congrues with the findings of Granhed et al. (1987) that, when powerlifters execute an extremely heavy lift, the compressive forces on L_3 are two or three times higher than what has been found as the maximum ultimate strength of experimentally tested vertebrae (Hansson et al. 1980). The weightlifters had a longer (on the average four years) sport-specific training history and a higher training intensity and volume than the subjects in the present training studies. These differences probably explain the differences in the results of cross-sectional studies on weightlifters and training studies with previously sedentary women who trained at moderate intensity for one to two years.

6.2 Repetitive loading

With an animal model, Rubin and Lanyon (1987) showed that increasing loading repetition does not bring any additional increase in bone mineral mass. However, the results of studies I and II showed that orienteerers, speed skaters and cross-country skiers had significantly higher BMD values at the loaded sites than the sedentary referents did (Figure 3). These results are in accordance with those of Lane et al. (1986), Marcus et al. (1985) and Wolman et al. (1991), which indicate that runners had a higher bone mineral mass in their lumbar spine and femur than controls. Running produces repetitive weight-bearing impact with the ground and therefore is likely to stress the calcaneus, tibia, patella and femur. For example, the reaction forces acting on the lower limb in running can be two to five times body weight (Subotnick 1985) and those on the vertebrae can be 1.75 greater than body weight (Capozzo 1983). Thus it seems possible that the effects of running on lower limb bones and vertebrae are caused by the great number of loading cycles that cause moderate impact loading. This possibility is supported by the present findings from cross-country skiers (I, II), whose sport is weight-bearing exercise, but much of the work consists of smooth movements in which impact does not play any significant role.

In study VI multiexercise endurance training at a relatively high intensity (72% of the $\dot{V}O_2max$) prevented age-related bone loss and maintained the BMD of the clinically important femoral neck of healthy perimenopausal women. Similar results were found for postmenopausal women by Hatori et al. (1993), Martin and Notelovitz (1993), Dalsky et al. (1988) and Chow et al. (1987), whose findings also support the concept that high-intensity endurance exercise (70-90% of the $\dot{V}O_2max$) increases or maintains BMD in postmenopausal women. Unfortunately, femoral neck BMD was not measured in these studies, and it remains unclear whether there was a training effect on this clinically relevant site.

The positive effect on the BMD (VI) of the femoral neck in the endurance group can be explained by the fact that fast walking and jogging, which were the main components of the training, produced ground reaction forces, which can be 1.2 - 1.5 times body weight during walking (Grove and Londeree 1992) and two to five times body weight during running (Subotnick 1985). The forces acting across the hip joint during walking are up to 4.8 times higher than the forces produced by body weight only (Bergman et al. 1993). Thus, during fast walking or jogging, the lower limbs are loaded by impacts, whose magnitude and rate of force application can be much higher than in slow customary activities and, in addition, whose effect may be enhanced by repetitive loading cycles.

Using the mathematical model (eq. 4.) of Carter et al. (1987) one can evaluate theoretically the influence of repetitive weight-bearing loading on lower-limb bones. During walking at a speed of 1.4 m/s the largest principal strain is about 400 $\mu\epsilon$ in the tibia (Lanyon et al. 1975), a value, which falls within the customary mechanical strain range. Applying these values in the equation and giving the values 4 and 6 to m, the number of loading cycles (steps) should be approximately 2900 - 26 000 in walking (1.4 m/s) in order for the bone structure to be maintained. A larger deformation occurs while the subject is running at a speed of 2.2 m/s, producing principal strain of about 800 $\mu\epsilon$ (Lanyon et al. 1975) (i.e., about one-third the MES level). Thus, in this case, the number of loading cycles should be approximately 5400 to 66000 (eq. 4) for the bone to be in a state of overuse and result in an adaptation response.

When walking 30 minutes at a speed of 1.4 m/s (5.0 km/h) and with a step length of 0.6 m, a person's total number of steps is about 4200. According to the aforementioned estimations, this kind of walking seems to be enough to maintain bone mineral mass. During 30 minutes of running at a speed of 2.2 m/s (7.9 km/h), about 5700 steps are taken, and this rate may be enough to result in an osteogenic stimulus. These estimations congrue with the findings in study V, which suggested that endurance exercise may maintain BMD in the femoral neck of perimenopausal women.

The preceding calculations are based on simple assumptions and do not take into account the strain distribution that may play an important role in bone adaptation to mechanical loading. Furthermore, bone tissue is nonhomogenic and anisotrophic, which introducces a largc variation into Young's modulus and also into the cross-sectional area. In addition, according to other theoretical models and some experimental results (Mikic and Carter 1995), the cycles with higher strain magnitudes are commonly weighted much more heavily than cycles of lower magnitude.

In general, it seems that the number of loading cycles is clearly less important than the strain magnitude (Rubin and Lanyon 1984a, Lanyon 1987, Whalen and Carter 1988). However, the importance of the number of loading cycles probably increases in significance when the strain magnitude is low. Burr et al. (1996) showed that strain is maintained below 2000 $\mu\epsilon$ even under conditions of strenuous activity. Thc principal, compressive and shear strain was greatest for uphill and downhill zigzag running in their study. Hence unusual loading, for example, in fast walking and uphill or downhill walking, may also be an important factor for the adaptive response of the skeleton.

6.3 Uncustomary loading

Lanyon et al. (1982) have suggested that the strain magnitude alone is not the most important determinant of bone adaptive response. Rubin and Lanyon (1984a, 1985, 1987) found that loading avian ulna at only 1000 $\mu\epsilon$ in an unusual direction could stimulate new bone formation. Lanyon (1984, 1987) suggested that the strain required to elicit an adaptive response may be lower if the loading pattern differs from what the bone is accustomed to. Biewener and Bertram (1993) also suggested that adaptive modeling of bone may be more sensitive to such a strain distribution, which differs markedly from normal or to a pattern of functional strain rather than to increased strain magnitude *per se*. The observed difference in the BMD of the femoral neck in both squash players and weightlifters, compared with controls, suggests that their sports have different strain distribution characteristics in this region (I, II). The squash players had a 19% higher BMD in the calcaneus than the sedentary referents did, whereas the weightlifters' BMD at this site differed from that of the referents by only 7%. On the contrary, the difference in the patella BMD was 7% for the squash players and 18% for the weightlifters. These findings also suggest the importance of site-specific functional strain and a different strain distribution for the patella and calcaneus (Lanyon 1987, Frost 1990a).

In study IV, elbow flexion and extension training apparently loaded forearm bones in a normal direction (i.e., in a direction to which the bones were already accustomed). This finding implies that a bone adapts to a range of strain environments and that adaptive responses would be more easily generated by a variety of different loading conditions (Martin and Burr 1989). The findings of study III supported this suggestion; despite high-intensity (80% of 1 RM) unilateral leg-press training for 12 months, only slight (< 2%) increases in the BMD of the lower extremities of young women were observed. The main reason for the small effect was probably the unidirectional characteristics of the loading. In study III and in study IV the training probably did not produce sufficient mismatch between the strain pattern produced by the loading and the customary strain pattern needed for bone adaptation in weight-bearing and nonweight-bearing bones.

6.4 High-impact loading

Study II showed that squash players, whose training caused high accelerating and decelerating movements (i.e., impact loading), had the highest weight-adjusted BMD values at all the measured sites, as compared with those of the regularly exercising controls. Furthermore, aerobic dancers, who also experienced high impact loading during training, had significantly higher BMD values in the loaded sites than the sedentary referents did. These findings agree with those of earlier cross-sectional studies indicating that training producing strain with a high rate and peak force in diverse movements is associated with the greatest differences in BMD between athletic and sedentary young women (Risser et al. 1990, Slemenda and Johnston 1993, Fehling et al. 1995, Friedlander et al. 1995, Kirchner et al. 1995, Robinson et al. 1995, Taaffe et al. 1995).

In study VI, in which an exercise regimen with a rapidly rising force profile (jumping) was applied for 18 months, showed significant BMD increases (1.4 - 3.7%) at the loaded sites (lumbar spine, femoral neck, distal femur, patella, proximal tibia and calcaneus) in premenopausal women. The training consisted of aerobic jumping and step exercises, in which the magnitude of the ground reaction forces was gradually increased by increasing the height of the foam fences and the number of step-benches. It was concluded that the high-impact exercises that load bones with a rapidly rising force profile in versatile movements improved skeletal integrity significantly. Bassey and Ramsdale (1994, 1995), and Grove and Londeree (1992) also used an impact training regimen and have shown an increase or maintenance of bone mineral mass in premenopausal and postmenopausal women.

The bone tissue modeling/remodeling response is sensitive only to dynamic strain. Therefore rather than the strain magnitude *per se* the total number of strain events, the number of events per unit of time, or the strain rates involved in the loading regimen may be critical characteristics of the mechanical environment the bone tissue is attuned to (Rubin and McLeod 1996). Animal models have shown that a positive remodeling response strongly correlates with the strain rate, and also with the strain magnitude (O'Connor et al. 1982). Studies II and VI support this concept by showing that squash playing, aerobic dance and jump training, involving high-impact loading and thus producing high stress and effective strain at a high rate of force development on bones, is related to high BMD values.

In terms of the rate of force application, the leg-press training of study III and the elbow flexion and extension strength training with dumbbells of study IV probably produced too low a strain rate, because the subjects used high loads (80% of 1 RM) and were apparently unable to use maximum power (speed) in the training movements. In these studies the mean estimated strain magnitudes on femoral shaft (Sievänen et al. 1995) (III) and on forearm bones (IV) remained within the range of ordinary mechanical strain, and the loading induced change in the strain level was relatively small at the target bones. The training-induced strain rates should have been higher or the strain distribution more irregular to initiate bone formation to a greater extent .

During fast walking the loading direction and the rate on the lower-limb skeleton are altered by the short heel strike and high ground reaction forces (Grove and Londeree 1992, Subotnick 1985) and hip reaction forces (Bergman et al. 1993) as compared with ordinary walking. The strain in bone tissue has been shown to be proportional to the speed of walking (Rubin and Lanyon 1982). Consequently, fast walking, uphill walking and slow jogging, as used in study V, were likely to produce higher strain rates and a different distribution of strain as compared with customary walking during normal daily routines. In contrast, the BMD changes in the callisthenics group (V) did not differ from the values of the control group, probably because the training movements were slow and smooth and resulted in an insufficient magnitude of loading stimulus, as suggested also by the unchanged muscular strength. Consequently, the calisthenics program, as used in study V, did not meet the bone formation criteria of high strain rate and uncustomary strain distribution.

It has recently been shown that bone adaptation is also dependent on loading frequency (Rubin and Mcleod 1994, 1996). On the other hand, high frequency is related to high strain rate, and thus it is possible to estimate maximal frequencies produced by the high impact training. In the jumping exercise, for instance, the average force rise times ranged from 13 to 40 ms (Heinonen et al. unpublished pilot study). If a sinusoidal form is assumed for the force production, the maximum frequency (f) of the jumping exercise can be estimated as follows:

$$f = \frac{1}{2\pi T} \quad \textbf{(eq. 5.)},$$

where T is the force rise time. Given these average force rise times, the average maximum frequency in the jumping exercise was between 0.4 and 12 Hz. Actually, there is probably a more rapidly rising part in the force curve than in a simplified sinusoidal model, which indicates a frequency content higher than 12 Hz. This frequency would probably fall in the high-frequency band, which has been shown to initiate substantial new bone formation even at low strain magnitudes (Rubin and McLeod 1994). In other words, the higher the strain rate, the wider the strain frequency spectrum. If frequency-specific strain is substantiated by experimental evidence, it could be a safe and feasible way with which to apply exercise in the prevention of osteoporosis. Altogether, high-impact exercise (high accelerating and decelerating movements) such as jumping, aerobic dance and squash playing seems to be an effective type of training with which to induce osteogenic response in bone.

6.5 Biomechanical environment

Despite a clear training effect on muscular strength in study IV, the training did not cause an increase in BMC or BMD, or in the estimated mechanical characteristics (width, CWT and CSMI). It is known that the mechanical competence of bone may improve as geometric changes occur without essential changes in bone mass taking place (Kimmel 1993). Apparently bone mass is the best measurable determinant of bone strength in humans, but it must be noted that, despite its major contribution to bone strength, it is not the only determinant of structural strength (Mosekilde 1993). The other factors are the geometric properties and the material quality of the bone (Carter and Hayes 1976, Currey 1984, Cowin 1989, Einhorn 1992). It may be possible that training could result in an improvement in bone strength due to changes in bone geometry and material quality without a notable increase in BMD or BMC (Carter and Hayes 1977). For bending, the CSMI of a structure is more important for the resisting of loads than is its mass or density (Kimmel 1993), and substantial changes in CSMI may occur without corresponding changes in bone mass (Turner

1991). Thus, for study IV, it is conceivable that, even if only small changes in BMC or BMD were obtained, in agreement with several previous longitudinal strength training trials (Gleeson et al. 1990, Pruitt et al. 1992, Snow-Harter et al. 1992, Menkes et al. 1993, Ryan et al. 1994), the forearm bones might have improved their mechanical competence through geometric changes. In general, bones resist loading best when their structure and geometry are adapted to the direction of customary loading (Einhorn 1992). It may be that in study IV the elbow flexion and extension training with dumbbells was too "customary" in terms of the loading history of the studied bones.

The obvious interplay of bones and muscles in the appropriate handling of external load should also be taken into consideration. In other words, the role of the entire biomechanical environment should be recognized. Currey (1984) has argued that bones tend, if possible, to be loaded in compression and not in bending. On the other hand, muscles not only provide the necessary moment equilibrium in all joints, but also compensate and reduce the bending stress of bones while increasing the axial compressive load (Currey 1984, Munih et al. 1992). In study IV, for instance, the estimated strain remained within the ordinary strain range probably because the brachioradial muscle compensated and reduced the bending stress in the forearm bones during elbow flexion, while the radius and ulna supported each other during elbow extension. If so, the skeletal loading caused by rapidly increased loading conditions may be reduced by strengthening the muscles and improving the interplay between all the biomechanical components (muscles, tendons, ligaments, bones) of the movements.

The magnitude of the force and the rate of force application affecting human skeleton are mainly determined by the movement conditions (velocity of the segments, number of repetitions, muscular activity) and the boundary conditions (anthropometric factors, fitness level, surface, weather, and type of shoes) (Lees 1981, Nigg 1985, Ricard and Veatch 1994). Thus any change in movement conditions affects the kinematics and kinetics of the movement and probably also the mechanical stress affecting the bone. A change in the boundary conditions may have an additional effect on the stress of the musculoskeletal system (Lees 1981, Nigg 1985). Therefore, in contrast to absolute peak stress, the differences in the movement and boundary conditions of different sports and exercises may well induce different strain distributions and different strain rate characteristics for bones.

The rate of force application or the changing movement factors, rather than the magnitude of force as such, may be more important as osteogenic stimuli in some sports, for example in squash, gymnastics (Nichols et al. 1994, Fehling et al. 1995, Kirchner et al. 1995, Taaffe et al.1995) and dance (Grimston et al. 1993, Michaud et al. 1993), than in other sports (e.g., weightlifting). The relationship between force and acceleration or deceleration implies that sports involving highly accelerating and decelerating movements (i.e., impact loading) produce high stress and thus effective strain on bones. The data of studies I-VI support these concepts. Similar results have been reported for basketball (Risser et al. 1990) and volleyball players (Risser et al. 1990, Kirchner et al. 1995) and gymnasts (Fehling et al. 1995, Kirchner et al. 1995, 1996, Robinson et al. 1995, Taaffe et al. 1995), whose sports involve comparable loading on the lower extremities. In addition, the playing arm of tennis and squash players, which is mostly loaded by impact during the stroke in conjunction with frequent, rapid and multidirectional movements, has clearly higher BMD and BMC values than its nonplaying counterpart (Haapasalo et al. 1994, Kannus et al. 1994).

7 GENERAL CONCLUSIONS

The cross-sectional comparison of the BMD of athletes representing sports that produce different types of loading on bones showed that weight-bearing exercises are associated with increased BMD and that the response of BMD to training is site-specific. These results suggest that sports that produce high-impact loading (high strain rates) in versatile movements such as in squash and high-magnitude loading such as in weight training include an effective osteogenic loading stimulus. The results also showed that squash players and weightlifters have clearly higher BMD values at the loaded sites than sedentary referents do. Furthermore, in sports including repetitive loading, the athletes had higher BMD values at the loaded lower-limb sites.

The findings of the exercise intervention studies were consistent with the cross-sectional observations, both showing that high-impact exercise that loads bones with a rapidly rising force profile in versatile movements improves skeletal integrity in premenopausal women. In addition, endurance training with repetitive lower extremity loading results in the maintenance of BMD in the clinically important femoral neck of perimenopausal women.

On the other hand, progressive, monotonous high-intensity strength training (high-magnitude loading) does not seem to be an effective stimulus with which to increase BMD, BMC or the estimated bone mechanical characteristics of young women, even if the training is clearly effective in increasing muscular strength. This findings implies that the interaction of bones and muscles plays an important and relatively unrecognized role in the development of bone strength and suggests that the entire biomechanical environment should be carefully considered when the osteogenic efficiency of physical loading is evaluated.

Thus, the present results indicate that the important components of osteogenic exercise stimulus in premenopausal women are high strain rates and high peak forces in versatile movements. In addition, the importance of the number of loading cycles probably increases in significance if the repetitive loading magnitude is low at the loaded sites.

8 TIIVISTELMÄ

Tämän tutkimuksen tavoitteena oli poikkileikkaus- ja kokeellisin liikuntainterventiotutkimuksin tunnistaa ja määrittää harjoitusmuotoja, jotka lisäävät nuorten ja vaihdevuosi-ikää lähestyvien naisten luun tiheyttä (BMD), luun mineraalimäärää (BMC) ja eräitä luun mekaanisia ominaisuuksia. Kaikkiaan 444 tervettä naista osallistui kuuteen tutkimukseen, joista kaksi oli poikkileikkaustutkimusta, kaksi kontrolloitua ja kaksi kontrolloitua satunnaistettua tutkimusta. Koehenkilöt olivat luustoa eri tavoin kuormittavan lajin aktiiviurheilijoita sekä fyysisesti aktiivisia tai vähän liikkuvia nuoria ja vaihdevuosi-ikää lähestyviä naisia. Elämäntavat ja terveyden tila selvitettiin kyselylomakkeella. BMD, BMC ja luun mittasuhteet mitattiin kaksienergisellä röntgenabsorptiolla (DXA). Isometrinen lihasvoima, hengitys- ja verenkiertoelimistön kunto ja dynaaminen tasapaino mitattiin tavanomaisin menetelmin. Harjoitusohjelmien pituudet olivat 12-18 kk ja sisälsivät voimaharjoittelua, voimistelua, kestävyysharjoittelua ja isku-tärähdys-tyyppistä hyppely-, aerobic- tai stepharjoittelua. Poikkileikkaustutkimuksissa squashpelaajien ja painonnostajien BMD-arvot olivat tilastollisesti merkitsevästi (6-19%) korkeammat lähes kaikissa mitatuissa luustopisteissä kuin vähän liikkuvilla verrokkihenkilöillä. Toispuoleinen harjoittelu ei vaikuttanut merkitsevästi BMD- ja BMC-arvoihin. Kestävyysharjoittelijoiden reisiluun kaulan BMD:n lineaarinen kasvutrendi 18 kk:n harjoittelun jälkeen oli merkitsevästi suurempi kuin kontrollien osoittaen, että kestävyysharjoittelu ylläpiti tämän kliinisesti tärkeän luualueen BMD:tä. Kahdeksantoista kuukauden isku-tärähdys-tyyppinen harjoittelu lisäsi kuormitettujen luiden BMD:tä 1.4 - 3.7%. Muutokset vertailuryhmässä olivat vastaavana aikana merkitsevästi pienemmät (0-1.8%). Tulokset viittaavat siihen, että osteogeenisen liikuntaärsykkeen tärkeimpiä komponentteja ovat vaihtelevien liikkeiden aiheuttamat luun nopeat muodon muutokset ja korkeat voimahuiput. Myös alhainen kuormitustaso saattaa parantaa luuston ominaispiirteitä, mikäli kuormitussyklien lukumäärä on suuri.

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ORIGINAL PAPERS

I

Bone mineral density in female athletes of different sports

by

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Bone and Mineral 1993; 23, 1-14

https://doi.org/10.1016/S0169-6009(08)80086-4

ELSEVIER SCIENTIFIC PUBLISHERS IRELAND

Bone and Mineral 23 (1993) 1–14

BONE AND MINERAL

Bone mineral density of female athletes in different sports

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(Received 16 October 1992; revision received 14 May 1993; accepted 14 May 1993)

Abstract

Anthropometry, training history, cardiorespiratory and muscular performance capacity, and bone mineral density (BMD) were studied in female orienteers ($n = 30$), cross-country skiers ($n = 28$), cyclists ($n = 29$), weight lifters ($n = 18$) and in a reference group ($n = 25$). BMD was measured at lumbar spine, femoral neck, distal femur, patella, proximal tibia, calcaneus and distal radius by dual energy X-ray absorptiometry. The weight lifters had significantly higher weight adjusted BMD ($P < 0.001$) than the referents at all sites (9–26%) except in femoral neck and calcaneus. Of the endurance athletes, the orienteers were the only group which had significantly higher BMD ($P < 0.05$) than referents, only at distal femur (5%) and proximal tibia (5%). BMD did not differ significantly at any skeletal site between subjects with different calcium intake. Weight training seems to provide more effective osteogenic stimulus than endurance training. The differences in BMD at different sites between the groups were consistent with specificity of the stimulus to the training of the studied sports.

Key words: Bone mineral density; Female athletes; Physical fitness; Training history

1. Introduction

Previous studies provide evidence that bone mineral density (BMD) is significantly higher in athletes than in age-matched healthy non-athletic subjects [1–9]. In comparisons between sports, it has been shown that male and female athletes using weight training have higher BMD values than gender-matched athletes in other sports [1,3,4].

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SSDI 0169-6009(93)00610-F

Exercise may exert a very local effect on the highly stressed parts of the skeleton (e.g., on the playing arm of tennis players) [10–12]. Similarly, spinal BMD is higher in rowers, whose sport requires intense lower back exertion than in dancers and runners [13]. Different sports may load the skeleton at various sites in different ways. Running produces impact loading on the lower limbs, weight lifting creates extreme torques in the lumbar spine and wrist, whereas cycling produces varying muscle tension in smooth movements without weight-bearing. Thus, it is to be expected that the training response of different skeletal sites varies according to the sport-specific loading. However, exact data are sparse.

The purpose of this study was to determine whether there are site-specific differences in the BMD of female athletes involved in long-term diverse sporting disciplines and to assess whether these differences are related to the musculoskeletal requirements specific to each sport.

2. Material and methods

2.1. Subjects

A total of 105 Finnish competitive female athletes were recruited to participate in the study. The group included 30 orienteers, 29 cyclists, 18 weight lifters and 28 cross-country skiers. Twenty-five moderately active female physiotherapy students served as the reference group. None of them was or had been a serious competitive athlete. Descriptive group characteristics of the subjects are presented in Table 1. None of the subjects had any diseases or had ever used medication that may have affected the bone. All of the measurements of the athletes and referents were taken within an 8-month period during the training season.

2.2. Training history

Information on living habits and health status was obtained with detailed questionnaires. The training history was documented in detail with a training recall diary covering the previous 5 years. The reference group reported their physical activity over the previous 3 years.

2.3. Calcium intake

Calcium intake was estimated from the approximate quantity of milk (a 0.2-l glass of milk contains about 200 mg calcium) [14] and cheese (slice of cheese contains about 100 mg calcium) consumed daily. The assessment of the calcium intake was based on questionnaire.

2.4. Menstruating status

The assessment of the menstruating status of the subjects was based on data from a prospective diary and the monitoring of morning body temperature during 6 months at the time of the study. This assessment was used to determine how many amenorrheic subjects belonged to each group. The subjects were classified into amenorrheic and normally menstruating and oral contraceptives users. The amenorrheic subjects had, at most, 1 menstruating cycle during the 6 months. Normal menstruating cycle consisted of normal ovulation (temperature rise 0.3–0.5°C) and duration of 23–35 days.

Table 1
Characteristics of the athlete groups and reference group (mean and S.D.)

	Referents $n = 25$	Orienteers $n = 30$	Cross-country skiers $n = 28$	Cyclists $n = 29$	Weight lifters $n = 18$	P value (F)
Age (years)	22.6 (2.8)	23.3 (3.1)	21.3 (3.2)	24.0 (5.7)	24.6 (4.6)	0.049
Height (cm)	167 (7)	169 (5)	169 (6)	166 (5)	165 (7)	0.102
Weight (kg)	61.2 (8.3)	59.3 (4.6)^{e}	61.6 (8.9)	61.8 (7.7)	66.7 (11.1)^{b}	0.057
BMI* (kg/m^2)	22.0 (2.9)^{e}	20.8 (1.5)^{e}	21.6 (2.2)^{e}	22.4 (2.4)	24.3 (3.3)^{a,b,c}	0.000
Body fat** (%)	25.1 (5.4)	21.6 (3.5)^{d,e}	22.5 (4.2)	25.3 (5.0)^{b}	25.7 (5.5)^{b}	0.004
Sport-specific training (years)		12.9 (3.1)	10.9 (3.5)	6.0 (3.1)	3.6 (1.1) $n = 15$	

*BMI, Body mass index.
**Body fat was measured by a bioimpedance analyzer (BIA 106, RJL Systems Inc., Michigan, USA).
Superscripts indicate a significant ($P < 0.05$) mean difference between groups as follows:
[a]Significantly different from reference.
[b]Significantly different from orienteers.
[c]Significantly different from cross-country skiers.
[d]Significantly different from cyclists.
[e]Significantly different from weight lifters.

2.5. Cardiorespiratory fitness tests

The cardiorespiratory fitness testing method was selected to match the cardiorespiratory requirements of each sports. The cyclists, weight lifters and referents performed their maximal exercise test on a bicycle ergometer (Siemens-Elema RE 820, Rodby Elektronik AB, Enhörna, Sweden). Orienteers and cross-country skiers were tested on a treadmill (Telineyhtymä, Kotka, Finland). A progressive 3-min step protocol (20–30 W/step) was used in the bicycle ergometer test. The treadmill protocol consisted of 3-min progressive uphill running (initial speed 6.3 km/h and inclination 1%) for the orienteers and uphill ski-pole walking (initial speed 6.0 km/h and inclination 2.3%) for the skiers. The grade and speed were increased every third minute according to the theoretical oxygen consumption increase of 5 ml/kg per min.

The test was continued to voluntary maximum. An electrocardiogram was recorded and monitored (recorder: Mingocard 4, Siemens-Elema, Sweden; monitor: Cardiac Monitor 573, Kone Oy, Finland) throughout the test. Expired air was analyzed continuously throughout the test for oxygen consumption ($\dot{V}O_2$) and related measures with a Medikro 202E automatic metabolic analyzer (Medikro, Kuopio, Finland). The following variables were derived as the measures of maximal performance capacity: test time, maximal oxygen consumption ($\dot{V}O_2max$), maximal heart rate (HRmax), maximal ventilation ($\dot{V}$Emax), and maximal respiratory quotient (RQ).

2.6. Maximal isometric strength test

Maximal voluntary contraction (MVC) was measured after 3 practice contractions. Three maximal efforts were recorded, and the mean of the 2 best values was used as the test score.

The MVC of the trunk extensors and flexors was measured by a strain gauge dynamometer (measurement range, 0–2.5 kN; Juhantalo Ky, Digitest, Muurame, Finland). The subjects were tested in a standing position with the pelvis and knees stabilized.

The MVC of the leg extensors was measured with a leg press dynamometer. The subjects sat on the dynamometer chair in an upright position with their knees and ankles at a 90° flexion angle. They then pressed maximally against strain gauges (measurement range, 0–25 kN; Tamtron, Tampere, Finland) located under their feet. The signal representing the peak force was amplified and recorded by a voltmeter.

The MVC of the dominant forearm flexors was measured with an arm flexion-extension dynamometer. The subjects stood straight with elbows flexed 90° and supported. A strain gauge (measurement range, 0–2.5 kN; Digitest, Muurame, Finland) was fixed to the hand grip, and the signal was amplified and recorded with a voltmeter from which the peak force reading was available.

The day-to-day precision of the strength measurements expressed as the coefficient of variation, ranged from 5.4% (leg extension) to 9.7% (forearm flexion). The reproducibility of the strength measurements was determined by testing 15 sedentary middle-aged women 3 times within 2 weeks.

2.7. Bone densitometry

Bone mineral density (BMD) was measured at the following seven sites: the lumbar spine (L2–L4), and the femoral neck, distal femur, patella, proximal tibia, calcaneus and distal radius of the dominant extremity (Fig. 1). A Norland XR-26 dual energy X-ray absorptiometric scanner (Norland Inc, Forth Atkinson, WI, USA) was used. The in vivo day-to-day precision of the BMD expressed as the coefficient of variation, ranged from 0.7% (proximal tibia) to 1.9% (distal radius). The method has been described in detail elsewhere [15]. During the 8 months of the study, no machine drift was observed.

2.8. Statistical methods

The mean and standard deviations were calculated for subject characteristics, performance variables and BMD. The subject characteristics and performance variables of the groups were compared with the one-way analysis of variance (ANOVA). When the ANOVA indicated a significant difference ($P < 0.05$), Tukey's Studentized range method was used as the post-hoc test. For estimating the BMD differences between the athlete groups and the reference group, analysis of covariance was used (ANCOVA). Weight, known to have positive correlation to BMD [4,16], was used as a covariate. Preliminary calculation suggested that, to achieve a statistical power of 80% in detecting a clinically important (our estimation as 5%) difference in BMD between the groups significant at the 5% level, approximately 30 subjects per group were needed for the study.

3. Results

3.1. Training history

The orienteers reported the greatest number of years of sport-specific training, followed by the cross-country skiers, cyclists and weight lifters (Table 1). The mean

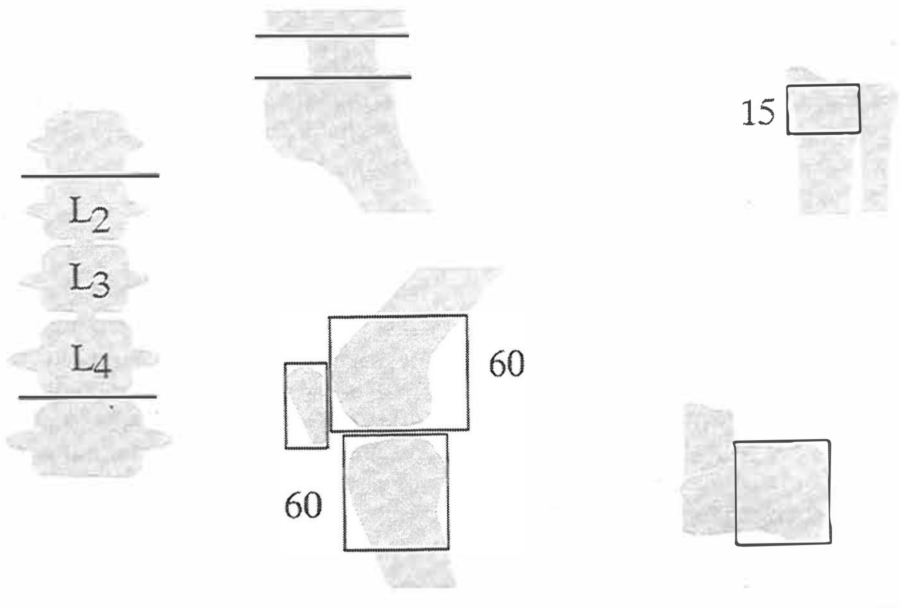

Fig. 1. Anatomic sites of the BMD measurements for lumbar spine, femoral neck, distal femur, patella, proximal tibia, calcaneus and distal radius. The dimensions given are in millimetres.

exercise frequency of the orienteers, cyclists and cross-country skiers during the last inquiry year was statistically significantly higher ($P < 0.01$) than that of the weight lifters and the referents (Table 2). The endurance athletes reported a higher mean number of training hours for the last 5 years than the weight lifters and referents. During the last year of inquiry the mean of the training hours of the reference group was less ($P < 0.01$) than those of the athlete groups, but there were no significant differences between the athlete groups (Table 2).

3.2. Calcium intake

The estimated mean calcium intake from milk and cheese was as follows: 56 athletes (15 orienteers, 17 cyclists, 8 weight lifters and 16 cross-country skiers) and 7 referents consumed more than 800 mg of calcium/day. Fourteen athletes (3 orienteers, 7 cyclists, 2 weight lifters and 2 cross-country skiers), and 4 referents consumed less than 500 mg of calcium/day. Thirty-five athletes (11 orienteers, 5 cyclists, 7 weight lifters and 10 cross-country skiers) and 14 referents consumed 500–800 mg of calcium/day. Since Finnish food provides plenty of calcium from other sources as well [17] the actual calcium intake of our subjects per day was likely to be more than this estimated intake. There were no significant differences in BMD at any skeletal site between the subjects with different calcium intake.

3.3. Menstruating status

The prospective menstrual diaries and the measurements of morning body temperature showed that 3 athletes were amenorrheic (1 cross-country skier, 1 weight lifter and 1 cyclist). The amenorrheic athletes' BMD values did not differ from their group BMDs. Thirty-six athletes (7 cross-country skiers, 14 orienteers, 7 weight lifters and 8 cyclists) and 19 referents used oral contraceptives.

3.4. Cardiorespiratory fitness

The mean absolute and relative $\dot{V}O_2$max (in l/min and ml/kg per min) of the orienteers, cyclists and cross-country skiers was significantly higher ($P < 0.01$) than that of the reference group and the weight lifters (Table 3). Furthermore, the orienteers and cross-country skiers had a higher ($P < 0.01$) $\dot{V}O_2$max than the cyclists (Table 3).

3.5. Maximal isometric strength

Table 4 gives the maximal absolute and relative (strength/weight, N/kg muscle strength for all groups. The strength of the leg extensors was greatest in the weight lifters. The strength of the leg extensors of the orienteers and cyclists was also greater ($P < 0.01$) than that of the reference group. The cross-country skiers had greater leg extensor and forearm flexor strength ($P < 0.05$) than the reference group. The forearm flexor strength of the weight lifters was greater ($P < 0.01$) than that of the orienteers, cyclists and referents and the weight lifters had greater ($P < 0.05$) trunk extensor strength than the cyclists.

3.6. Bone mineral density

In general, the weight lifters were the only athlete group that showed a

Table 2
Training history of the athlete groups and reference group in the last inquiry year (mean and S.D.)

Training	Referents	Orienteers	Cross-country skiers	Cyclists	Weight lifters	P value (F)
Total amount (h)	202 (135)[b,c,d,e] n = 25	446 (70)[a] n = 28	574 (60)[a] n = 25	556 (338)[a] n = 28	429 (129)[a] n = 14	0.000
Training sessions/week	4.8 (2.9)[b,c,d] n = 25	7.6 (1.2)[a,e] n = 30	7.8 (1.6)[a,e] n = 28	7.2 (3.2)[a,e] n = 29	5.3 (1.2)[b,c,d] n = 17	0.000
Sport-specific training		3466 (924) km n = 11	5274 (761) km n = 16	8566 (4431) km n = 28	713 (524) tons n = 12	

Superscripts indicate a significant ($P < 0.05$) mean difference between groups as follows:
[a]Significantly different from reference.
[b]Significantly different from orienteers.
[c]Significantly different from cross-country skiers.
[d]Significantly different from cyclists.
[e]Significantly different from weight lifters.

Table 3
Cardiorespiratory fitness of the athlete groups and reference group (mean and S.D.)

Cardiorespiratory variable	Referents $n = 25$	Orienteers $n = 30$	Cross-country skiers $n = 27$	Cyclists $n = 28$	Weight lifters $n = 18$	P value (F)
$\dot{V}O_2$ max, relative (ml/kg per min)	43.3 (6.5)[b,c,d]	58.3 (4.4)[a,d,e]	59.8 (4.2)[a,d,e]	53.7 (5.6)[a,b,c,e]	40.1 (4.7)[b,c,d]	0.000
$\dot{V}O_2$ max, absolute (l/min)	2.74 (0.37)[b,c,d]	3.46 (0.35)[a,e]	3.65 (0.39)[a,d,e]	3.30 (0.38)[a,c,e]	2.66 (0.31)[b,c,d]	0.000
HRmax (beats/min)	191 (5)	192 (7)	191 (8)	192 (7)	187 (9)	0.233
$\dot{V}E$ max (l/min)	111 (15)[c,d]	122 (16)	126 (18)[a,e]	124 (16)[a,e]	110 (10)[c,d]	0.001
RQ max	1.13 (0.06)[b,c]	1.09 (0.04)[a]	1.08 (0.05)[a]	1.10 (0.07)	1.12 (0.04)	0.006
LA max (mmol/l)	8.60 (1.47)	7.78 (1.52)	8.65 (2.02)	8.44 (1.22) $n = 27$	8.38 (1.26)	

$\dot{V}O_2$ max, maximal oxygen uptake; HRmax, maximal heart rate; $\dot{V}E$ max, maximal minute ventilation; RQ max, respiratory quotient: LA max, maximal lactate.
Superscripts indicate a significant ($P < 0.05$) mean difference between groups as follows:
[a]Significantly different from reference.
[b]Significantly different from orienteers.
[c]Significantly different from cross-country skiers.
[d]Significantly different from cyclists.
[e]Significantly different from weight lifters.

Table 4
Maximal isometric strength of the athlete groups and reference group (mean and S.D.)

Strength variable	Referents n = 25	Orienteers n = 30	Cross-country skiers n = 28	Cyclists n = 29	Weight lifters n = 18	P value (F)
Trunk extensors						
kg	67.1 (10.2)[c]	67.4 (7.6)[c]	72.0 (9.9)	66.6 (8.0)[c]	79.3 (11.0)[a,b,d]	0.000
N/kg	11.0 (1.3)	11.4 (1.2)	11.8 (1.4)	10.8 (1.1)[e]	12.1 (1.9)[d]	0.009
Trunk flexors						
kg	45.7 (10.4)[e]	47.3 (7.6)[c]	51.0 (7.9)	46.6 (9.5)[c]	57.8 (13.0)[a,b,d]	0.000
N/kg	7.5 (1.5)	8.0 (1.3)	8.4 (1.5)	7.6 (1.4)	8.7 (1.4)	0.021
Leg extensors						
kg	130.2 (25.2)[d,e]	146.1 (18.9)[e]	147.5 (20.6)[e]	157.4 (27.6)[a,e]	189.6 (19.5)[a,b,c,d]	0.000
N/kg	21.3 (3.2)[b,c,d,e]	24.7 (3.0)[a,e]	24.1 (2.6)[a,e]	25.6 (3.7)[a,e]	28.9 (3.8)[a,b,c,d]	0.000
Forearm flexors						
kg	18.1 (3.6)[e]	18.9 (3.7)[e]	20.8 (3.8)[e]	19.4 (3.1)[e]	24.4 (5.5)[a,b,c,d]	0.000
N/kg	3.0 (0.5)[c,e]	3.2 (0.5)[e]	3.4 (0.4)[a]	3.2 (0.5)[e]	3.7 (0.6)[a,b,d]	0.001

Superscripts indicate a significant ($P < 0.05$) mean difference between groups as follows:
[a]Significantly different from reference.
[b]Significantly different from orienteers.
[c]Significantly different from cross-country skiers.
[d]Significantly different from cyclists.
[e]Significantly different from weight lifters.

Table 5
BMD of the athlete groups and reference group (mean and S.D.)

Site of measurement	BMD (g/cm^2)				
	Referents $n = 25$	Orienteers $n = 30$	Cross-country skiers $n = 28$	Cyclists $n = 29$	Weight lifters $n = 18$
Lumbar spine (L2–L4)	1.071 (0.103)	1.068 (0.096)	1.072 (0.098)	1.067 (0.117)	1.230 (0.132)
Femoral neck	0.983 (0.114)	1.000 (0.106)	1.035 (0.117)	0.963 (0.105)	1.082 (0.156)
Distal femur	1.261 (0.118)	1.320 (0.096)	1.321 (0.125)	1.288 (0.124)	1.505 (0.160)
Patella	1.057 (0.109)	1.091 (0.092)	1.080 (0.109)	1.068 (0.090)	1.284 (0.142)
Proximal tibia	1.104 (0.105)	1.151 (0.072)	1.139 (0.107)	1.094 (0.114)	1.234 (0.139)
Calcaneus	0.671 (0.083)	0.699 (0.050)	0.694 (0.077)	0.654 (0.069)	0.700 (0.095)
Distal radius	0.350 (0.046)	0.352 (0.033)	0.348 (0.101)	0.368 (0.041)	0.453 (0.054)

systematically higher mean weight adjusted BMD than the referents. Absolute BMD values are given in Table 5. Weight was correlated significantly ($P < 0.001$) with BMD at each site (r in the range 0.39–0.51). The weight adjusted BMD differences between athlete groups and reference group are given in Fig. 2.

In the weight lifters, the mean weight adjusted BMD of the lumbar spine, distal

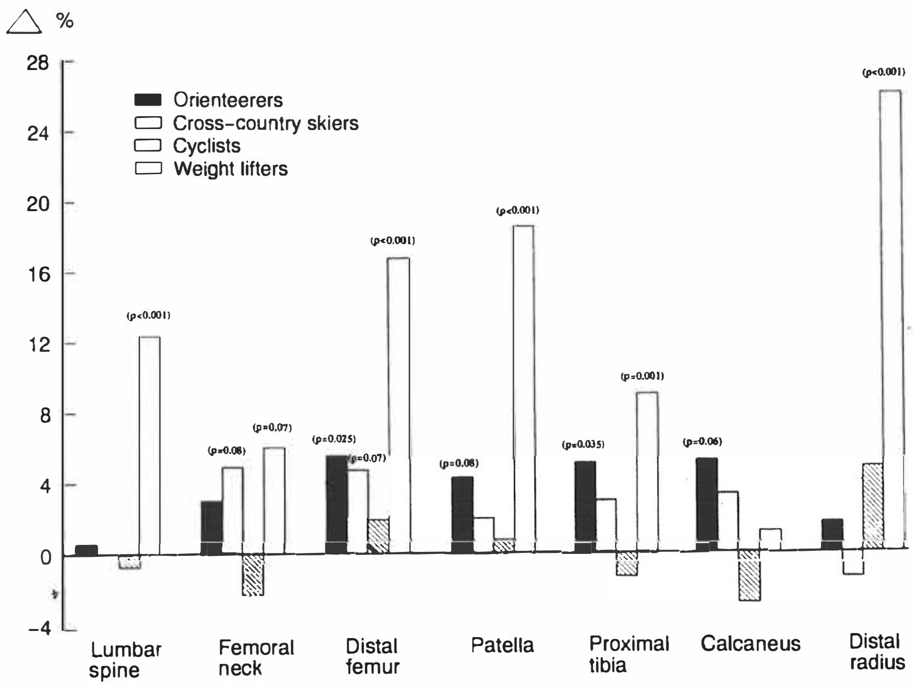

Fig. 2. Relative deviation of the weigth-adjusted BMD of the athletic groups from that of the reference group (%).

femur, patella, proximal tibia and distal radius was higher ($P < 0.001$) than that of the reference group. In addition, in comparison with the reference group, the weight lifters had higher BMDs in the femoral neck but the difference was not significant. Compared with the other athlete groups, the weight lifters had higher BMD in the lumbar spine, distal femur, patella and in the distal radius (Fig. 2).

In the orienteers, the mean weight adjusted BMD of the distal femur and proximal tibia was higher ($P < 0.05$) than that of the reference group. In addition, orienteers' BMDs in the patella and calcaneus was higher than that of the reference group, but the difference was not significant. In cross-country skiers, the BMD in the femoral neck and distal femur was higher than in the referents but the difference was not significant (Fig. 2).

4. Discussion

Our results showed that the weight lifters had a higher BMD at most skeletal sites than the reference group and the other athlete groups. In different sports, exercise loads affecting the skeleton can vary in many ways, such as in their intensity and in the direction of the forces on the skeleton. For example, the reaction forces produced in the lower limb during running can be 2–5 times body weight [18] and those produced in the vertebrae can be a factor of 1.75 higher than body weight [19]. However, during competitive weight lifting, compressive loads on the lumbar spine range from 18.4 to 36.2 kN [8], values which are 18–36 times body weight.

It has been shown that muscle strength and mass are significantly related to BMD in trained athletes [20]. In the present study the weight lifters had the highest maximal isometric strength (from leg extensors 28.9 N/kg to forearm flexors 3.7 N/kg) in all of the measured muscle groups and the highest BMD at most of the measured sites. Orienteering and cross-country skiing primarily load the lower extremities in addition to being weight-bearing activities. The athletes participating in these sports had a consistently, although not significantly, higher BMD and extensor strength in the lower extremities (24.7 N/kg for orienteers and 24.1 N/kg for cross-country skiers) than the reference group (21.3 N/kg). Previous studies on tennis players [10–12] and rowers [13] have shown similar site specificity of training.

Our results are in accordance with those of previous studies that have shown male weight lifters and female body builders to have significantly higher BMD than controls [3,4,8,9]. In addition, weight lifters' BMD in the lumbar spine, femoral neck and radius has been found to be significantly higher than the corresponding values of other athlete groups [1,3,4]. The high mechanical loading that stresses the skeleton in weight lifting is the most probable reason for the high BMD values.

Previous prospective studies on weigth training have shown modest (1–2%) or no increase in BMD after short training period (that is, training about 1 year or less) [21–24]. In this study, weigth lifters had longer (on average 4 years) sport-specific training history, higher training frequency and intensity and used heavier loads than sedentary subjects in these prospective studies. These differences probably explain the differences in the results.

The cyclists' relatively low BMD values in the lumbar spine and lower extremities may be explained by the fact that cycling does not include vertical weight-bearing activity. Our results for cyclists agree well with the results from previous studies on rowing and swimming, typical non-weight-bearing exercises; the study of Wolman et al. [13] on rowers and those of Risser et al. [25] and Orwoll et al. [26] on swimmers suggest that gravity plays an important role in the process of bone mineralization. In our study, the cyclists had the lowest BMD values among the athlete groups except in the distal radius, where their BMD was about 5% higher than that of the other endurance-trained athletes. These findings may be due to the fact that, in the cycling position, the weight of the upper body is supported by the wrists. It has been found that hands generate significant forces during cycling [27].

In the studies by Lane et al. [6], Marcus et al. [28] and Wolman et al. [29], runners had a higher BMD in the lumbar spine and femur than the controls. On the other hand, Heinrich et al. [4] and Bilanin et al. [30] did not find significant differences between runners and controls. Running, particularly in orienteering, produces repetitive weight-bearing impacts with the ground and therefore is likely to stress the calcaneus, tibia, patella and femur. Indeed, the orienteers in the present study had 4.3–5.5% higher weight-adjusted BMD values for these bones than the reference group did, the difference in distal femur and proximal tibia being significant (see Fig. 2).

Cross-country skiing is a weight-bearing exercise, but much of the work consists of pliant movements in which impact does not play any significant role. However, in the weight-bearing bones, especially in the femur (femoral neck and distal femur), cross-country skiers seem to have higher (~ 5%) weight-adjusted BMD values than the reference group (see Fig. 2). This may be due to the new skating style. The relatively low BMD in the distal radius of the cross-country skiers was an unexpected finding because these athletes do much work with their arms and hands.

In this study, the referents were not sedentary. Previous studies have used sedentary subjects as the reference group, and their physical activity has probably been less than in our study [1–9]. Our reference group reported 5 exercise sessions/week on average and 202 training hours during the last year of inquiry. Thus, the referents exercised 30 min × 5 times/week on average. In addition to high leisure-time activity, the curriculum of the physiotherapy education involved a considerable amount of exercise and manipulative therapy practices. The referents' BMD of the lumbar spine (1.071 g/cm^2, S.D. 0.103 g/cm^2) was similar to normative data provided by the manufacturer for Western European young women (mean age, 25 years) (1.08 g/cm^2, S.D. 0.11 g/cm^2). In contrast, the corresponding referents' BMD values at the femoral neck (0.983 g/cm^2, S.D. 0.114 g/cm^2) were higher than those of the manufacturer's (0.93 g/cm^2, S.D. 0.12 g/cm^2). The femoral neck values of the reference group indicate that their lower limb BMD may be higher than that of corresponding young age-matched, sedentary women. Thus, the relatively small differences in BMD between our endurance athletes and our referents may be partly explained by the high activity level of our reference group.

All of the athletes in our study were competitive athletes with a long training history. The orienteers and cross-country skiers had trained systematically over 10 years, the cyclists for 6 years and weight lifters for 4 years, on average. Consequently, the duration of sport-specific training did not explain the weight lifters' higher BMD, at least within the time limits of our study.

Altogether, our results support the hypothesis of Lanyon [31] that short periods of high peak forces are more effective in producing an anabolic effect on bone mineralization than long periods of repetitive loading with lower peak loads. With an animal model, Rubin and Lanyon [32] showed that increasing the number of repetitions of loading does not bring any additional increase in BMD. Lanyon [31] suggests that the osteogenic potential of a loading regimen is maximized if it causes strains of high magnitude and at high rate in a distribution to which the skeleton is unaccustomed. Thus, weight training would be more effective in increasing bone mass than endurance exercise.

In conclusion, the results of this study suggest that weight training provides a better osteogenic stimulus than endurance training. The results are consistent with the hypotheses that weight-bearing exercises increase BMD and that response of BMD to training is site specific.

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II

Bone mineral density in female athletes representing sports with different loading characteristics of the skeleton

by

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Bone 1995; 17:197-203

https://www.sciencedirect.com/science/article/pii/8756328295001513

ELSEVIER

Bone Vol. 17, No. 3
September 1995:197–203

ORIGINAL ARTICLES

Bone Mineral Density in Female Athletes Representing Sports With Different Loading Characteristics of the Skeleton

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To address the hypothesis that osteogenic effect of physical loading increases with increasing strain rates and peak forces, we examined 59 competitive Finnish female athletes (representing three sports with different skeletal loading characteristics), physically active referents (they reported an average of five various types of exercise sessions per week), and sedentary referents (two sessions per week) using dual energy X-ray absorptiometry. The measured anatomic sites were at the lumbar spine, femoral neck, distal femur, patella, proximal tibia, calcaneus, and distal radius. The athlete group consisted of aerobic dancers (N = 27), squash players (N = 18), and speed skaters (N = 14). The squash players had the highest values for weight-adjusted bone mineral density (BMD) at the lumbar spine (13.8% $p < 0.001$ as compared with the sedentary reference group), femoral neck (16.8%, $p < 0.001$), proximal tibia (12.6%, $p < 0.001$) and calcaneus (18.5%, $p < 0.001$). Aerobic dancers and speed skaters also had significantly higher BMD values at the loaded sites than the sedentary reference group, the difference ranging from 5.3% to 13.5%. The physically active referents' BMD values did not differ from those of the sedentary referents at any site. The results support the concept that training, including high strain rates in versatile movements and high peak forces, is more effective in bone formation than training with a large number of low-force repetitions. (*Bone 17:197–203; 1995*)

Key Words: Bone mineral density; Female athletes; Loading characteristics; Peak forces; Peak strain rates; Sports.

Introduction

The important role of physical loading in regulating of bone modeling and remodeling is commonly accepted. However, the type, intensity, frequency, and duration of exercise that best enhance bone mineral accumulation are still largely unknown. Several cross-sectional studies have reported higher bone mineral density (BMD) and bone mineral content (BMC) in athletes than in sedentary controls[1,17,18,32] and a higher BMD in weightlifters than in athletes in other sports.[4,12,17,18,32,52] These studies, along with our previous cross-sectional study on weightlifters and endurance athletes,[17] support the hypothesis of Lanyon[22,23] and Whalen and Carter[54] that high peak forces of loading may have a greater influence on bone mass than a large number of completed loading cycles. Furthermore, Lanyon,[21,22] O'Connor et al.[33] and Rubin and Lanyon[40] have suggested that the high strain rates may be even more osteogenic than the absolute peak forces of the loads. These authors have also suggested that the stimulus required to produce an adaptive response in bone depends on the strain distribution across a skeletal structure.[23,41]

The training involved in squash, aerobic dance, and speed skating characteristically produces versatile impact-type loading (accelerating and decelerating movements) and pliant movements on the skeleton. The training involved in these sports is thus likely to result in high strain rates and versatile distribution of strain in the target bone. Therefore, the purpose of this study was to further address the hypothesis that the osteogenic effect of physical loading increases with increasing peak forces and strain rates by studying the BMD of squash players, aerobic dancers, and speed skaters and their controls.

Material and Methods

Subjects

We previously investigated four groups of nationally or internationally ranked competitive Finnish female athletes.[17] In this study, similar data from 18 squash players, 27 aerobic dancers, and 14 speed skaters were evaluated. The two reference groups consisted of 25 healthy sedentary women who were recruited through a local nursing school (the sedentary reference group, less than 3 exercise sessions per week) and 25 physically active physiotherapy students (physically active reference group, 3 or more exercise sessions per week). None of the sedentary or physically active referents was or had been a serious competitive athlete. None of the subjects had any disease or had ever used medication that might have affected bone tissue. The age, weight, height, and body mass index and other characteristics of the subjects are given in **Table 1.**

Training History, Calcium Intake, and Menstruating Status

The training history, including years of active sports-specific training, training sessions per week, total training hours per year, and the starting age of the sport specific training were documented with a training recall diary covering the previous five

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8756-3282/95/$9.50
SSDI 8756-3282(95)00151-3

Table 1. Characteristics of the athlete groups, the physically active reference group, and the sedentary reference group, means (standard deviations)

	Squash players N = 18	Aerobic dancers N = 27	Speed skaters N = 14	Physically active referents N = 25	Sedentary referents N = 25	p value (F)
Age (years)	25.0 (3.9)	28.3 (3.7)^{c,d,e}	21.4 (8.6)^{b}	22.6 (2.8)^{b}	23.8 (4.7)^{b}	<0.001
Height (kg)	166 (6)	166 (5)	168 (6)	167 (7)	166 (5)	0.940
Weight (cm)	61.7 (6.2)	57.3 (4.2)	63.2 (6.6)	61.2 (8.3)	59.4 (6.1)	0.053
BMI* (kg/m^2)	22.4 (2.3)	20.7 (1.1)	22.4 (1.2)	22.0 (2.9)	21.5 (2.1)	0.042
Body fat** (%)	24.4 (5.1)	24.4 (5.1)^{a,b,c}	25.9 (3.3)^{b}	25.1 (5.4)^{b}	25.9 (4.9)^{b}	0.002
Training history						
Training hours (in the last inquiry year)	382 (246)^{e} N = 15	339 (154)^{e} N = 22	351 (181)^{e} N = 12	202 (135)	45 (52)^{a,b,c} N = 22	<0.001
Training sessions/week	6.4 (3.5)^{e} N = 17	6.2 (2.6)^{e} N = 26	6.0 (2.2)^{e} N = 13	4.8 (2.9)	2.3 (1.5)^{a,b,c} N = 21	<0.001
Sport-specific training (years)	5.5 (2.7)	6.6 (3.7)	9.3 (7.2)			0.061
Starting age of sports (years)	16.7 (4.3)^{c}	21.8 (8.3)^{c}	10.3 (2.6)^{a,b}			<0.001
VO_2 max*** (mL/kg/min)	48.8 (5.1)^{d,e}	51.6 (4.9)^{d,e}	47.8 (5.2)^{e}	43.3 (6.5)^{a,b}	40.4 (4.7)^{a,b,c}	<0.001
Isometric strength						
Trunk extensors (N/kg)	13.2 (1.4)^{d,e}	12.5 (1.4)^{d,e}	12.2 (1.3)	11.0 (1.3)^{a,b}	11.2 (1.6)^{a,b}	<0.001
Trunk flexors (N/kg)	8.7 (2.0)	8.7 (1.6)	9.2 (1.7)^{d,e}	7.5 (1.5)^{c}	7.5 (1.2)^{c}	0.002
Leg extensors (N/kg)	25.0 (3.8)^{d,e}	24.5 (3.0)^{d}	27.5 (3.1)^{d,e}	21.3 (3.2)^{a,b,c}	21.7 (3.2)^{a,c}	<0.001
Forearm flexors (N/kg)	3.1 (0.4)	3.4 (0.7)^{d,e}	3.0 (0.5)	3.0 (0.6)^{b}	2.8 (0.6)^{b}	<0.001

*BMI, body mass index.
**Body fat was measured by a bioimpedance analyzer (BIA 106, RJL System Inc., Michigan, USA).
***VO_2 max, maximal oxygen uptake.
Superscripts indicate a significant ($p < 0.05$) mean difference between groups as follows: [a]significantly different from squash; [b]significantly different from aerobic dancers; [c]significantly different from speed skaters; [d]significantly different from physically active referents; [e]significantly different from sedentary referents.

years. Reference groups reported their physical activity over the last three years. The questionnaire also included questions on injuries, medication, known diseases, diet, possible vitamin and mineral supplementation, and the consumption of alcohol and cigarettes.

Calcium intake was estimated from a seven-day calcium intake diary. The assessment of the menstruating status of the subjects was based on data from a prospective six-month diary of the occurrence and duration of the menses and the monitoring of morning body temperature during six months at the time of the study. This assessment was used to determine how many amenorrheic subjects belonged to each group. The subjects were classified into "amenorrheic," "normally menstruating," and "oral contraceptives users." The amenorrheic subjects had, at most, one menstruating cycle during the previous the six months. A normal menstruating cycle consisted of normal ovulation (temperature rise 0.3°–0.5°) and duration of 23–35 days.

Cardiorespiratory Fitness and Maximal Isometric Strength

Directly assessed maximal oxygen uptake (VO_2 max) was used as the measure of cardiorespiratory fitness. The testing protocol was selected to match the cardiorespiratory requirements of each sport.[17] The squash players, aerobic dancers, speed skaters, and referents performed their maximal exercise test on a bicycle ergometer (Siemens–Elema RE 820, Rodby Elektronik AB, Enhörna, Sweden). A progressive 3 min step protocol (20–30 W/step) was used as the test protocol.

The maximal isometric strength of the trunk extensors and flexors and dominant forearm flexors of all the subjects was measured with a strain gauge dynamometer (Digitest, Muurame, Finland). The maximal strength of the leg extensors was measured with an isometric leg press dynamometer (Tamtron, Tampere, Finland).[16,17] The day-to-day precision of the strength measurement expressed as a coefficient of variation, ranged from 5.4% (leg extension) to 9.7% (forearm flexion).[16]

Bone Densitometry

BMD was measured using dual energy X-ray absorptiometry (XR-26 Norland Inc., Fort Atkinson, WI, USA) at the following seven skeletal sites: lumbar spine (L2–4), femoral neck, distal femur, patella, proximal tibia, calcaneus, and distal radius of the dominant extremity. All scanning and analyses were made by the same operator. The in vivo day-to-day precision of the BMD measurement, expressed as the coefficient of variation, ranged from 0.7% (proximal tibia) to 1.9% (distal radius). The measurement procedures have been described in detail elsewhere.[42] During the whole study period, no significant machine drift was observed.

Statistical Methods

The mean and standard deviations were calculated for the subject characteristics, performance variables, and BMD. The subject characteristics and performance variables of the groups were compared with one-way analysis of variance (ANOVA). When the ANOVA indicated a significant difference ($p < 0.05$), Tukey's studentized range method was used as the post-hoc test. For estimating the BMD differences between the present groups, analysis of covariance (ANCOVA) was used. Weight, known to be positively correlated with BMD,[3,6,8,17] was used as the covariate.

Results

Training History, Calcium Intake, and Menstruating Status

The training history characteristics from last inquiry year of the athletes and referents are given in Table 1. The subjects in the physical active group reported an average of five exercise sessions per week and 200 training hours in the last inquiry year. The corresponding numbers for the sedentary referents were two sessions per week and 45 training hours, respectively. In both groups, the reported physical activity included various types of exercises, such as walking, jogging, swimming, cycling, and aerobics. Compared with the sedentary referents, the athlete groups' mean training hours per year and the mean training sessions per week were clearly higher ($p < 0.01$).

The average calcium intake/day was as follows: squash players consumed 840 (382) mg, aerobic dancers 819 (305) mg, speed skaters 1062 (320) mg, and sedentary referents 764 (290) mg of calcium/day. The seven-day calcium intake diary[49] indicated that Finnish food provides plenty of calcium sources. There were no significant differences in the BMD at any skeletal site between subjects with different calcium intakes.

The prospective menstrual diaries and the measurements of the morning body temperature showed that in the present groups there were no amenorrheic subjects. Twenty-one athletes (8 squash players, 11 aerobic dancers, 2 speed skaters), 19 physically active referents, and 12 sedentary referents used oral contraceptives.

Cardiorespiratory Fitness and Maximal Isometric Strength

The athlete groups had a higher ($p < 0.01$) VO_2 max than the sedentary and physically active referents (Table 1). Table 1 shows the relative muscle strength (strength/weight, *N*/kg) of the athlete groups and the physically active and sedentary reference groups. The strength of the *trunk extensors* of the squash players and aerobic dancers was greater than that of the sedentary referents ($p < 0.01$). The speed skaters had greater ($p < 0.05$) strength of the *trunk flexors* than the sedentary reference group. The strength of the *leg extensors* was greater in the speed skaters than in the sedentary referents ($p < 0.01$). In the squash players, the strength of the *leg extensors* was also higher ($p < 0.05$). The strength of the *forearm flexion* of the aerobic dancers was higher ($p < 0.01$) than that of the sedentary referents (Table 1).

Bone Mineral Density

The squash players had the highest weight-adjusted BMD values at all of the measured sites. The absolute BMD values at the present data are given in **Table 2.** The weight-adjusted BMD differences (mean ± 95% confidence intervals) between the athlete groups, the physically active reference group, and the sedentary reference group are given in **Figure 1.** For comparison, results of the weightlifters, orienteerers, cross-country skiers, and cyclists of the previous study[17] are also shown in Figure 1.

Compared with the sedentary referents, the squash players had significantly higher mean weight-adjusted BMD values at the lumbar spine (13.8%), the femoral neck (16.8%), the distal femur (11.2%), the patella (6.7%), the proximal tibia (12.6%), the calcaneus (18.5%), and the distal radius (11.3%). For the aerobic dancers (vs. the sedentary referents), the mean weight-adjusted BMD was significantly higher at the femoral neck (8.5%), the proximal tibia (5.5%), and the calcaneus (13.6%). On the other hand, the aerobic dancers had a significantly lower BMD in the distal radius (−7.8%) compared with the sedentary reference group (Figure 1).

In the speed skaters, the BMD of the distal femur (7.2%) was significantly higher than that of the sedentary referents. Physically active referents' BMD values did not differ from those of the sedentary referents' at any site (Figure 1).

Discussion

This study determined site-specific BMDs of young competitive female athletes engaged in three sports producing different types of skeletal loading. All of the athletes had trained sport specifically for at least 3 years and 300 h per year. The main finding of the present and our previous[17] studies was that athletes whose training caused strain of high magnitude, high strain rates, or both (i.e., squash players and weightlifters) had the highest weight-adjusted BMD values at all measured sites. In addition, we found that the BMD values of the groups with nonweight-bearing sports (cyclists) or general physical activity only (the physically active referents) did not seem to differ from those of the sedentary referents.

The focus of this cross-sectional study was on determining whether differences in repetitive weight-bearing impacts, repetitive pliant movements, impact loading, accelerating, or decelerating movements produced by different sports would be reflected in the BMD of the athletes. Our previous study[17] showed that weight training (i.e., high peak forces) seemed to be more effective in increasing bone mass than endurance exercise (i.e.,

Table 2. BMD of the athlete groups, the physically active reference group, and sedentary reference group, mean (standard deviations)

Skeletal site	BMD (g/cm^2) Squash players N = 18	Aerobic dancers N = 27	Speed skaters N = 14	Physically active reference N = 25	Sedentary reference N = 25
Lumbar spine (L2–4)	1.216 (0.131)^c	1.092 (0.111)	1.138 (0.129)	1.071 (0.103)	1.059 (0.106)
Femoral neck	1.155 (0.117)^c	1.041 (0.107)^b	1.031 (0.107)	0.983 (0.114)	0.971 (0.128)
Distal femur	1.405 (0.094)^c	1.291 (0.124)	1.357 (0.105)^a	1.261 (0.118)	1.248 (0.125)
Patella	1.127 (0.080)^a	1.063 (0.084)	1.116 (0.115)	1.057 (0.109)	1.045 (0.107)
Proximal tibia	1.220 (0.085)^b	1.120 (0.099)^a	1.151 (0.123)	1.104 (0.105)	1.071 (0.106)
Calcaneus	0.760 (0.081)^c	0.709 (0.062)^c	0.661 (0.070)	0.671 (0.083)	0.631 (0.064)
Distal radius	0.409 (0.055)^b	0.334 (0.040)^b	0.352 (0.032)	0.350 (0.046)	0.368 (0.044)

Superscripts indicate a significant mean difference between sedentary reference group and the given groups as follows: $^a p < 0.05$; $^b p < 0.01$; $^c p < 0.001$.

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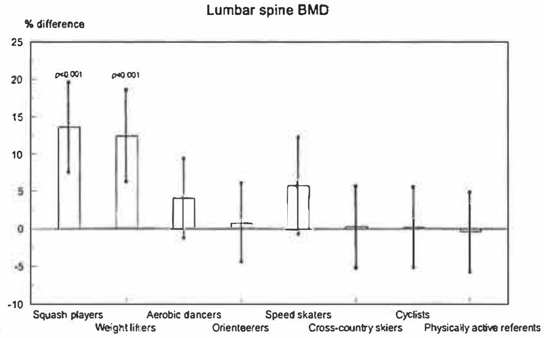

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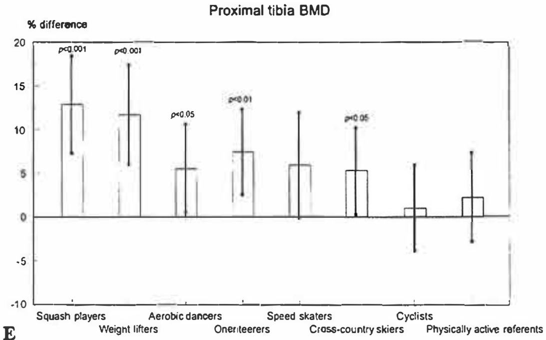

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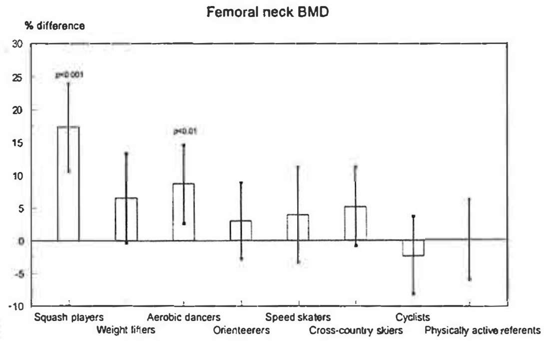

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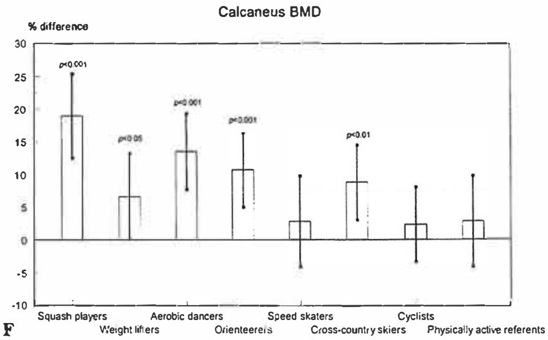

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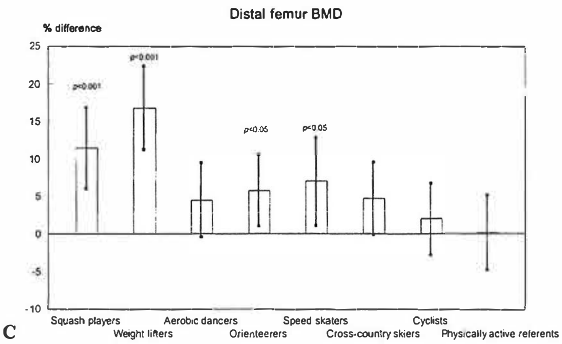

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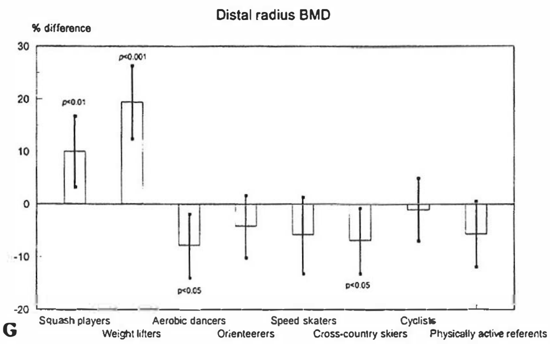

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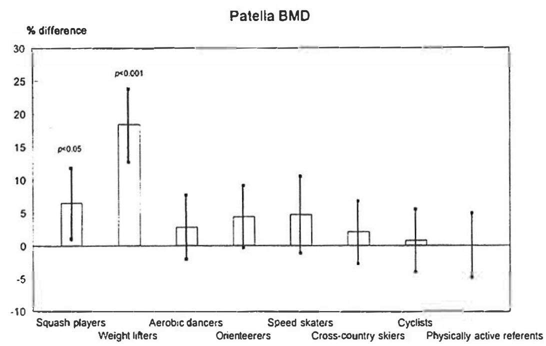

D

Figure 1. Relative difference of the weight-adjusted BMD in the athlete groups, and the physically active reference group from that of the sedentary reference group. The bars indicate the 95% confidence interval. The results of the weightlifters, orienteerers, cross-country skiers, and cyclists of the previous study (Ref. 3) are also shown.

repetitive weight-bearing impacts and pliant movements). With our present results, the previous data demonstrated significant BMD differences at all of the measured sites in squash players and weightlifters, as compared with sedentary referents. These differences were more than 10% (10% change represents about one SD at population and thus indicates a significant reduction in terms of fracture risk[4]) at all skeletal sites except in the patella of the squash players and the calcaneus and femoral neck of the weight lifters (Figure 1). Furthermore, aerobic dancers, orienteerers, speed skaters, and cross-country skiers had significantly higher BMD values than the sedentary referents at the loaded sites, but, with the exception of the calcaneus of the aerobic dancers (13.6%), these differences were less than 10% (Figure 1). In this context it must be noted that bone mass, despite of its major contribution on bone structural strength, is not the only determinant of strength; geometric and qualitative parameters should be taken into consideration.[7,29]

The squash players had 18.5% higher calcaneal BMD than the sedentary referents, whereas the weightlifters' BMD differed from the sedentary referents by only 6.6%. On the contrary, the difference in patella BMD was 6.7% for the squash players and 18.4% for the weightlifters (Figures 1D, F). These results demonstrate that the importance of site—and loading—specifically increased strains on the patella and calcaneus (10) and the differences appear to reflect the effects of impact-type loading on the calcaneus and quadriceps-induced mechanical loading on the nonweight-bearing patella.

Compared with sedentary referents, athletes whose training did not intensively load the upper limbs seem to have lower BMD at the distal radius. This might be due to a "steal phenomenon" or redistribution of bone mineral from nonloaded sites to loaded sites in physically active individuals. Smith et al.[43] reported a decline in bone mineral of the upper limb bones after the first year of aerobic conditioning exercise. The authors suggested that a greater rate of bone loss in the first year might be mineral redistribution from the upper appendicular skeleton in response to the demand of bone formation in the lower extremities and spine.[43] Unfortunately, they did not measure lumbar spine and lower limb bone mineral, and thus it remained unclear whether there was a true redistribution of bone mineral. Our previous studies on tennis and squash players showed that the control persons had slightly greater BMC and BMD in their nondominant arms compared with players, although the differences were not significant at any measured site.[15,19]

In cross-sectional studies on athletes, an inherent problem is the possible self-selection of the subjects. For example, weightlifters may have a genetically stronger body structure and thus a higher BMD.[47] On the other hand, in our previous study[15] we examined both upper extremities of squash players (in whom the playing had loaded the playing arm only), and their side-to-side BMD and BMC difference averaged 11.5%, while in the referents the difference was only 2.7%. Thus, mechanical loading seemed to have resulted in increased BMC and BMD. Consequently, it is likely that the high peak forces in weightlifters,[4,12,52] the intense jumping activity of aerobic dancers,[38,28] the repetitive impact-type activity (running) of orienteerers,[36,46,51] and the repetitive movements of speed skaters[51] and cross-country skiers[9,44] have resulted in an increased BMD at the loaded sites. Concurrent results were recently obtained by Karlsson et al. in weightlifters.[20] They concluded that the observed higher BMD was indeed due to the training program, and not to heredity.

Peak strain magnitude[4,12,17,18,22,23,32,52] is probably only one of the strain-related variables capable of producing osteogenic stimulus.[13,21] It has also been suggested that the rate at which the strain is evolved and how the strain is distributed within the bone structure are important factors in the adaptive response.[24,26] The observed differences in the BMD of the femoral neck in both squash players and weightlifters suggest that these sports have different strain distribution characteristics in this region. The magnitude of the force and the rate of force application affecting human skeleton are mainly determined by the movement conditions (velocity of the segments, number of repetitions, the muscular activity) and the boundary conditions (anthropometric factors, fitness level, surface, weather, and type of shoes).[25,31,37] Thus, any change in the movement conditions affects the kinematics and kinetics of the movement and probably also the mechanical stress affecting the bone. Moreover, a change of boundary conditions may have an additional effect on the stress on the musculoskeletal system.[25,31] Therefore, in contrast to absolute peak stress, the differences in the movement and boundary conditions of different sports may well induce various strain distributions and different strain rate characteristics on bones.

The rate of force application or the changing movement factors rather than the magnitude of force as such may be more important in some sports (e.g., in squash, gymnastics,[30] and dance[13,28]) than in other sports (e.g., weightliting). For example, in tennis (a similar and even slower game than squash), the forces and the influence of the friction of the playing surface are known to produce high torques on the bones of the lower extremities.[31] Furthermore, the relationship between force and acceleration/deceleration ($F = m \times a$) implies that sports involving highly accelerating and decelerating movements (i.e., impact loading) may produce high stresses and thus effective strain on bones. Our present data support these concepts. Risser et al.[38] reported similar results for basketball and volleyball players, whose sports involve comparable loading on the lower extremities. In addition, the playing arm of tennis and squash players, which is mostly loaded by impacts during the stroke in conjunction with frequent, rapid, and multidirectional movements, has clearly highly BMD and BMC values than its nonplaying counterpart.[15,19]

The considerable BMD differences observed between different sports (especially between weightlifters and squash players) can be explained, at least partly, by the large differences in the type, intensity, and duration of the physical activity of these athletes. The apparent overlap in the training modalities between different sports may, however, partly confound this explanation. Nevertheless, despite the evidently positive influence reported for weight training on BMD and BMC in cross-sectional studies,[4,12,17,18,32,52] prospective weight-training studies have shown only a modest or no increase in BMD.[19,27,34,35,39,45,53] Intense weight training has been used in few prospective studies only.[27,53] Menkes et al.[27] reported an increase (2.0–3.8%) in regional BMD in a high-intensity (85% of 1 RM) training group of older men after a rather short training period, 16 weeks. We found a smaller (<2%) increase in BMD in the lower extremities of young women during 12 month unilateral leg-press strength training (80% of 1 RM).[53] We felt that the main reason for the small effect of the training was the monotonous unidirectional characteristic of the loading. In all probability, this type of training produced neither sufficient strain nor a high strain rate in a distribution to which the skeleton was unaccustomed. Two recent studies used an exercise regimen in which a rapidly rising force profile (jumping) was provided.[2,14] However, these studies also showed a modest (2–3%) increase in BMD, perhaps due to the relatively short duration of the training (12 months) and also age (>30 years).

Compared with weight training, the training of squash players probably consists of versatile movements with higher loading impacts. In addition, in our study the squash players had a longer sport-specific training history (Table 1). Our previous study suggested that the accumulation of bone mass due to physical activity seems to be most effective if the activity is started not later than the growth spurt.[15] However, in contrast to the weightlifters and squash players, the endurance athletes, except the cyclists, had started their sport-specific training before their growth spurt but no compatible increase in BMD was observed. Furthermore, the sport-specific training years of the weightlifters and squash players were fewer than those of the endurance athletes. Also, as can be expected in the light of findings in endurance athletes, the active referents' BMDs did not differ from those of the sedentary referents'. One explanation may be that despite quite a high level of general physical activity, active referents' training did not exceed the habitual level of bone loading. Our previous insignificant BMD differences among women representing different occupational activities support this explanation.[48] Altogether, the independent role of type, duration, and starting age of sports in increasing the BMD remains unclear and needs further well-controlled investigations.

In conclusion, the results of this study indicate that athletes engaged in sports producing high strain rates in versatile movements (squash) have clearly higher BMD values than sedentary referents at potentially loaded sites. In addition, high peak stresses as produced by weight training have a clear positive effect on BMD.[17] These findings support the concept, derived from animal studies,[21–23,33,40,41,54] that high strain rates and high peak stresses are more effective in enhancing bone formation than a large number of low-force repetitions. These cross-sectional observations among athletes may provide a useful basis for developing exercise regimens that would prevent osteoporosis in nonathletic women.

Acknowledgments: The authors thank Virpi Nieminen for her expert DXA measurements and Kirsti Uusi-Rasi, M.Sc., for her assessment of calcium intake. Financial support was obtained from the Juho Vainio Foundation and The Ministry of Education in Finland.

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Date Received: February 23, 1995
Date Revised: April 18, 1995
Date Accepted: April 19, 1995

III

Effects of unilateral strength training and detraining on bone mineral density and content in young women. A study of mechanical loading and deloading on human bones

by

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Calcified Tissue International 1994; 55: 59-67

https://doi.org/10.1007/BF00310170

IV

Effects of unilateral strength trained detraining on bone mineral mass and mechanical characteristics of upper limb bones in young women

by

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Journal of Bone and Mineral Research 1996; 11: 490-501.

https://doi.org/10.1002/jbmr.5650110410

V

Effect of two training regimens on bone mineral density in healthy perimenopausal women: A randomized controlled trial

by

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Manuscript

https://asbmr.onlinelibrary.wiley.com/doi/pdf/10.1359/jbmr.1998.13.3.483

VI

Randomised controlled trial of high-impact exercise and selected risk factors for osteoporotic fractures

by

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The Lancet 1996; 348: 1343-1347

https://www.thelancet.com/pdfs/journals/lancet/PIIS0140673696042146.pdf

THE LANCET

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Reprinted from THE LANCET Saturday 16 November 1996
Vol. 348 No. 9038 Pages 1343–1347

THE LANCET 42 BEDFORD SQUARE LONDON WC1B 3SL UK

Randomised controlled trial of effect of high-impact exercise on selected risk factors for osteoporotic fractures

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Summary

Background Osteoporotic fractures among the elderly are common, and without preventive measures the burden of these fractures on health-care systems will increase further. The purpose of this randomised controlled study was to evaluate, in premenopausal women, the effects of high-impact loading on several determinants of osteoporotic fractures.

Methods 98 healthy, sedentary female volunteers aged 35–45 years were randomly assigned to either a training (n=49) or a control group (n=49). Progressive high-impact exercises were done three times per week for 18 months. We measured bone mineral density (BMD) in specific axial and lower-limb sites, by dual-energy X-ray absorptiometry, at baseline and after 12 and 18 months. Maximum isometric strength, muscular and cardiovascular performance, and dynamic balance were also assessed.

Findings BMD at the femoral neck, a weightbearing site, increased significantly more in the training group (mean 1·6% [95% CI 0·8–2·4]) than in the control group (0·6% [−0·2 to 1·4], p=0·006). By contrast, at non-weightbearing sites, such as the distal radius, there was no significant difference between the training and control groups (−1·5% [−2·7 to −0·3] *vs* −0·7% [−1·9 to −0·5], p=0·60). In the training group there was a significant improvement in vertical jump and predicted oxygen consumption per min at maximum exercise compared with controls.

Interpretation High-impact exercises that load bones with a rapidly rising force profile in versatile movements improve skeletal integrity, muscular performance, and dynamic balance in premenopausal women. If done on a regular basis, this type of exercise may help decrease the risk of osteoporotic fractures in later life. Long-term studies are required to show whether these 18-month results can be translated into long-term benefit.

Lancet 1996; **348:** 1343–47
See Commentary page 1326

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Introduction

Osteoporotic fractures in the elderly are a worldwide epidemic, and the predicted ageing of populations will accentuate the burden of these fractures on health-care systems.[1] Balance, falling, the falling direction and mechanism, orientation of the faller, protective neuromuscular reflexes, local shock-absorbing capacity, and bone strength are factors associated with the risk of bone fractures due to falls.[2-5] The propensity to fall is also associated with muscle strength and power of the lower limbs.[6,7]

In conjunction with the risk factors for falling, bone mineral density (BMD) is one of the most important determinants of fracture risk. BMD accounts for 80–90% of the variance in the strength of the proximal femur.[8] The risk of hip fracture is approximately doubled for every 1 SD reduction in BMD.[9] Epidemiological, clinical, and experimental exercise studies, in turn, indicate that physical activity is crucial in improving and maintaining bone mass and strength, thus helping to prevent osteoporotic fractures.[10] Improved physical fitness is associated with better muscle strength, reaction time, balance, and coordination—all of which help to prevent falls and fall-induced fractures.[7,11,12]

Prevention of osteoporosis has targeted young and premenopausal women[13] who are likely to be willing to participate in health-related physical activities. However, to our knowledge, no randomised trials of the effects of exercise on osteoporosis have been done among premenopausal women.

The purpose of this randomised intervention trial was to investigate whether an 18-month regimen of high-impact loading exercise would beneficially modify axial and lower-limb BMD, muscular performance, and dynamic balance in healthy premenopausal women. We used a high-impact regimen because a high magnitude of forces, high rate of force production, and exceptional loading directions and patterns are essential in maximising the skeletal adaptive response.[14] This approach also allowed training of different movement skills and muscular performance, such as balance, coordination, muscle strength, and power.[15]

Methods

Design and participants

Premenopausal women aged 35–45 years were recruited through a local newspaper advertisement for inclusion in a prospective, randomised controlled trial. Of the 242 women who responded, 140 were excluded after telephone interviews. The exclusion criteria were: cardiovascular, musculoskeletal, respiratory, or other chronic diseases that might limit training or testing; medication that could affect the skeleton; menstrual irregularities; special diet; smoking; obesity (body-mass index >30 kg/m^2); regular exercise more than twice a week; and a willingness to participate only in the training group. After baseline measurements (102 women), a screening examination by a physiotherapist (MR) and a medical examination (when suggested by the physiotherapist), four additional women were excluded because of concurrent breastfeeding, neck and shoulder

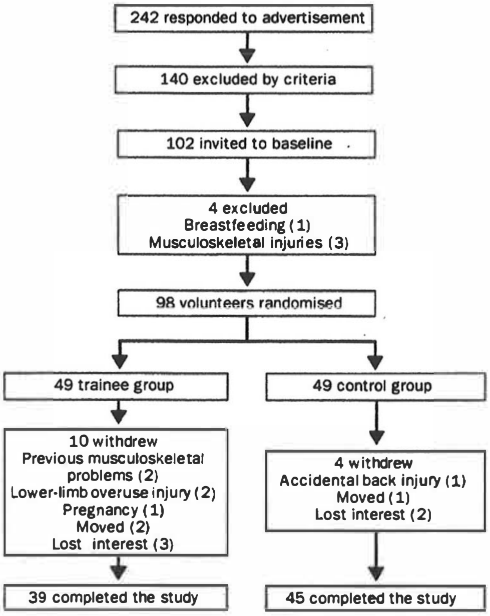

Figure 1: **Trial profile**

complaints, and a previous ankle and knee injury. The remaining 98 women were randomly assigned to an exercising group (n=49) or a non-exercising control group (n=49) within 2×2 strata of weight and oral-contraceptive use (figure 1). The success of randomisation was confirmed by checking the mean weight, height, BMD at the femoral neck, and daily calcium intake in the groups. Baseline characteristics are given in table 1. Percentage fat was assessed at four sites; biceps, triceps, subscapularis, and suprailiac with a Harpenden skinfold calliper (John Bull, British Indicator Ltd, Pembrokeshire UK). The anthropometric characteristics did not change in either group during the study. The study was approved by the ethics committee of our institute, and all participants gave their informed consent.

BMD (g/cm^2) measurements were done at baseline and at 12 and 18 months in the lumbar spine (L_2–L_4), right femoral neck, trochanter, distal femur, patella, proximal tibia, calcaneus, and dominant distal radius by dual-energy X-ray absorptiometry (XR-26, Norland Corporation, Wisconsin, USA). All scanning and analyses were done by the same operator; the coefficient of variation of the BMD measurement in our laboratory ranges from 0·5% to 0·8%. The scanner was calibrated daily and its performance was followed with our quality assurance protocol.[16] There was no significant machine drift during the study.

The maximum isometric strength of the trunk extensors and flexors and dominant elbow flexors was measured with an arm dynamometer (Digitest, Muurame, Finland), and that of the leg extensors with a leg press dynamometer with a knee angle of 90° (Tamtron, Tampere, Finland).[17] The leg-extensor power or lower-limb explosive performance capacity was evaluated with a vertical counter-movement jump test—first without extra weight and then with an additional weight of 10% of the volunteer's body mass.[18] The tests were performed on a contact platform (Newtest,

	Training group (n=49)	Control group (n=49)
Age (years)	39 (3)	39 (3)
Height (cm)	164 (6)	165 (5)
Weight (kg)	62 (7)	62 (7)
Body-mass index (kg/m^2)	23·2 (2·6)	22·9 (2·3)
Percentage body fat	30·9 (3·7)	30·4 (4·3)

Data are given as mean (SD).

Table 1: **Mean (SD) baseline characteristics of volunteers**

	Mean (SD) baseline BMD (g/cm^2)		Training effects after 18 months	
	Training group (n=49)	Control group (n=49)	Adjusted mean difference in g/cm^2 (95% CI)*	p
Lumbar spine	1·027 (0·141)	1·021 (0·116)	0·015 (0·005 to 0·025)	0·002
Femoral neck	0·882 (0·104)	0·862 (0·107)	0·012 (0·003 to 0·020)	0·006
Trochanter	0·939 (0·108)	0·909 (0·114)	0·006 (−0·002 to 0·015)	0·13
Distal femur	1·224 (0·108)	1·193 (0·106)	0·017 (0·010 to 0·024)	<0·001
Patella	1·035 (0·097)	1·032 (0·103)	0·007 (0·001 to 0·014)	0·036
Proximal tibia	1·081 (0·099)	1·050 (0·093)	0·026 (0·019 to 0·034)	<0·001
Calcaneus	0·606 (0·075)	0·590 (0·066)	0·010 (0·005 to 0·015)	<0·001
Distal radius	0·630 (0·070)	0·601 (0·065)	−0·002 (−0·007 to 0·003)	0·37

*Post-training difference between training and control groups adjusted for baseline values.

Table 2: **Baseline and training effects on BMD in entire study groups**

Oulu, Finland), which recorded the flying time of the vertical jump. Dynamic balance was tested by a figure-of-eight running test, around two poles placed 10 m apart.[19] The running time was recorded with photoelectric cells. A 2 km walking test was used to assess cardiorespiratory fitness.[20] The oxygen consumption per min at maximum exercise ($\dot{V}O_2max$) was predicted by the walking time and heart rate at the finish line. The heart rate was measured by a portable heart-rate monitor (Sport Tester PE 3000, Polar Electro, Kempele, Finland).

Total dietary intake, including calcium, and the use of vitamin and mineral supplements were estimated from complete 3-day dietary records at baseline, and after 9 and 18 months. The food composition was calculated with Micro-Nutrica software (Social Insurance Institution, Helsinki, Finland).

All training sessions, three times a week for 18 months, were supervised by one of four experienced exercise leaders. Each workout included 15 min warm-up, 20 min multidirectional high-impact exercises (jump training), 15 min callisthenics (stretching and non-impact exercises), and 10 min cooling down. The high-impact part of the session consisted of either an aerobic jump programme or a step programme, which alternated every 2 weeks.

The exercises in the aerobic and step programmes were selected on the basis of a pilot study; use of a force platform (Reute OY, Lahti, Finland), identified peak forces in 130 different types of exercise movements. In the aerobic jumping exercises, the magnitude of the ground reaction forces was gradually increased by raising the height of the foam fences from 10 to 25 cm. In the step exercises, the magnitude of loading was similarly increased by increasing the number of step benches (total height from 10 to 25 cm). The pilot study showed that the peak forces varied between 2·1 and 5·6 times body weight in these described exercises.

During the first 4 months, the trainees accustomed themselves to the jump training. In this period, the exercises involved no fences or only one step bench. After each 4-month period, the

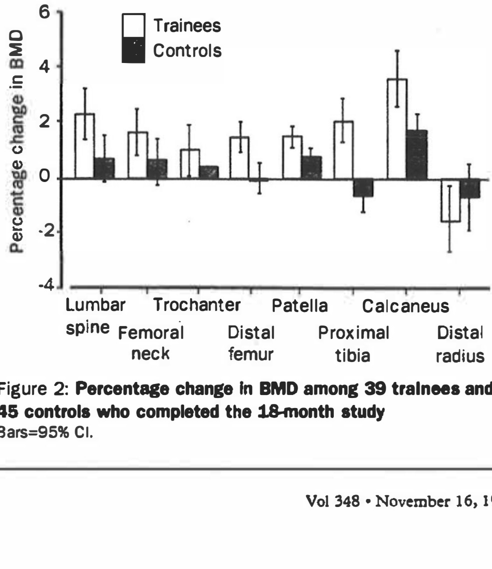

Figure 2: **Percentage change in BMD among 39 trainees and 45 controls who completed the 18-month study**
Bars=95% CI.

	Mean (SD) baseline		Training effects after 18 months*	
	Training group (n=49)	Control group (n=49)	Adjusted mean difference (95% CI)*	p
Isometric strength (kg)				
Trunk extension	58·0 (7·3)	56·3 (8·7)	−0·6 (−4·8 to 3·6)	0·787
Trunk flexion	40·5 (7·9)	39·2 (7·0)	2·6 (−1·6 to 6·9)	0·228
Leg press, 90°	142·1 (22·4)	137·5 (26·5)	7·5 (−0·9 to 16·0)	0·081
Elbow flexion	21 (25·9)	17·2 (3·8)	17·2 (−4·3 to 38·6)	0·117
Vertical jump flight time (ms)				
Without extra weight	444 (38)	437 (38)	21 (6 to 36)	0·007
Plus 10% body weight	410 (37)	407 (36)	36 (24 to 56)	<0·001
Figure-of-eight running (s)	6·4 (0·5)	6·6 (0·6)	−0·3 (−0·7 to 0·4)	0·082
$\dot{V}O_2max$ (ml kg^{-1} min^{-1})	36·4 (3·1)	37·6 (3·3)	3·1 (2·0 to 4·3)	<0·001

*Post-training difference between training and control groups adjusted for baseline values.

Table 3: **Baseline and training effects on muscular performance, dynamic balance, and cardiorespiratory fitness**

jumping height was gradually increased. Along with the continuous increase in jumping height, the number of jumps decreased so that the number of jumps was more than 200 during the first and second 4-month periods then 150, 120, and 100 in the following periods. Over the entire study period, the trainees kept a continuous exercise diary with consecutive 7-day forms for type and duration of all physical activities.

The women in the control group were asked to maintain their current physical activity during the 18 months and were interviewed every 4th month to monitor any changes in their exercise habits.

At 8 and 12 months all the women wore pedometers on two occasions for 3 consecutive days to assess daily physical activity.

Statistical analysis

General linear models with the restricted maximum likelihood estimation were used to assess the effects of exercise intervention at 12 and 18 months on the BMD, muscular performance, dynamic balance, and cardiorespiratory fitness.[21] This type of analysis allows incorporation of incomplete data into the models. The training effect was calculated as a group difference in the post-training BMD, muscular performance, dynamic balance, and cardiorespiratory fitness; the difference was adjusted for baseline values.

With an acceptance of an equal dropout rate of ten subjects per group, the sample size of the study provided 90% statistical power to detect a difference between the groups of about 2% in BMD at a significance level of $p<0·05$.

Results

39 women in the training group and 45 controls completed the study (figure 1). The other participants withdrew because of aggravation of previous musculoskeletal problems, pregnancy, accidental back injury, lower-limb overuse injury, loss of interest, or moving from the study area. During the study period, the trainees consulted the attending physician (PK) 16 times for the following reasons; mild ankle distortion (one), knee-overuse injuries (four), Achilles-tendon inflammation (one), unspecified foot pain (one), aggravated low back pains (eight), and partial calf muscle rupture (one). The training was interrupted for at most 1 or 2 weeks as a result of these injuries.

The reported training compliance, defined as the percentage of completed exercise sessions of the prescribed sessions, was 83% (2·5 times per week). The mean daily physical activity, which did not change during the study, was 10 000 steps per day (SD 2400) in the training group and 9800 steps per day (2800) in the control group. The estimated mean distance walked per day was 8 km (2) in both groups; the means did not change during the 18 months.

The baseline values and the training effect on BMD are given in table 2. After 18 months, BMD was significantly greater in the training than the control group at the lumbar spine, femoral neck, distal femur, patella, proximal tibia, and calcaneus. At the trochanter and distal radius, the difference was not significant.

The percentage change in BMD over the whole study period among women who completed the study (39 subjects in training group and 45 subjects in the control group) is presented in figure 2. In general, at the loaded sites of the skeleton the BMD increases were larger in the trainees than in the controls. The proportion of sessions attended did not correlate with the BMD changes at any site.

There were no significant differences between the groups in the change of maximum strength in any of the isometric strength tests (table 3). In the vertical jump test, the trainees did significantly better than the controls after training, both with ($p<0·001$) and without extra weight ($p=0·007$). There was no significant difference in the figure-of-eight running ($p=0·082$). The percentage changes in leg press, vertical jump, and figure-of-eight running among women who completed the study are given in figure 3.

The post-training predicted $\dot{V}O_2max$ was significantly higher in the trainees than in controls (table 3, figure 3).

The 9-day (three occasions of 3 days each) calcium intake was sufficient in both groups—1125 mg/day (240) in the training group and 1102 mg/day (264) in the control group. Total daily energy intakes were 7822 kJ (963) and 7824 kJ (1656), respectively. There were no changes in the energy or calcium intakes between the groups during the study period.

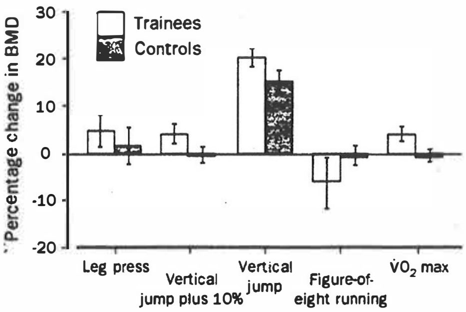

Figure 3: **Percentage changes in isometric leg press, vertical jump (with and without 10% additional weight), figure-of-eight running, and cardiorespiratory fitness ($\dot{V}O_2$max) among 39 trainees and 45 controls who completed the 18-month study**
Bars=95% CI.

Discussion

In this study we have shown that high-impact exercise has a systematic, positive effect on the loaded axial and leg bones in conjunction with improvements in muscle power and dynamic balance. This exercise regimen was able to modify favourably multiple risk factors for osteoporosis and osteoporotic fractures, and proved to be feasible judged from the high attendance (80%), high compliance (83%), and the minimum need for medical services (16 visits over the entire study period).

Despite the commonly accepted role of physical activity in determining BMD and thus risk of osteoporotic fractures,[6] few prospective studies have investigated whether exercise can influence bone mass and density.[22,23]

Information on premenopausal women, who are an important target group for the prevention strategies of osteoporosis, is scarce. Notelovitz et al[24] reported resistance training to be an effective modality for increasing spinal BMD in oestrogen-replete women with a mean age of 43 years.

Our findings are in agreement with those of Nelson et al[22] who observed in postmenopausal women a positive exercise effect on several risk factors for osteoporotic fractures—including femoral-neck and lumbar-spine BMD, muscle strength, and balance. On the other hand, others[25,26] have reported that different training regimens effectively increase muscular strength but not lumbar-spine or hip BMD. These apparently conflicting results on the effects of exercise training on BMD may be due to differences in the exercise regimen (eg, type, intensity, frequency, duration) or in the characteristics of the volunteers participating (eg, age, nutrition, hormonal status), or both. Finally, the training effects are likely to disappear once training is discontinued[27] and therefore, the exercises described here should become a part of the premenopausal women's lifestyle to prevent osteoporosis and osteoporotic fractures in later life.

In addition to improving muscular performance and dynamic balance, our training regimen was focused on providing a rapidly rising force profile on the bones of the legs and lumbar spine. Cross-sectional studies support the concept that high-impact training, especially if producing high strain rates and high peak forces in movements to which bones are unaccustomed, is most effective in enhancing bone formation in young women.[28-30] These data and the results of our study suggest that high-impact weight-bearing training is undoubtedly beneficial for bone accumulation. Longitudinal studies, which used an exercise regimen with a rapidly rising force profile (jumping),[31,32] have shown an increase in trochanteric BMD in premenopausal women[31] and maintenance of lumbar BMD in early postmenopausal women.[32] Together with our results these findings indicate that high-impact exercise is efficient in improving and maintaining bone mass and preventing age-related bone loss. Moreover, aerobic and step exercises are popular among premenopausal women, a point which suggests good feasibility in the general population.

The commonest cause of osteoporotic fracture is falling.[3,4,7,10] Disturbed balance and poor muscle strength and power in the legs have an essential role in the propensity to fall.[6] Consequently, a reduction in the number of falls may be achieved by exercise programmes that increase leg performance—ie, improving and maintaining balance and neuromuscular response mechanisms.[9] We have shown that high-impact training positively influences the muscular performance of the trainees. Training with high-velocity movements (jumping) can improve the speed of body movements and reflex times, which in turn can be beneficial in terms of movement skills, balance, coordination, reaction time, muscle strength, and power.[15] Therefore, high-impact training seems to be suitable for increasing BMD and neuromuscular performance simultaneously. However, as evident in this study, impact training is not able to increase maximum isometric muscle strength, although it was effective in increasing leg explosive performance capacity and BMD. The impact loading of a tennis stroke is very effective for increasing bone mineral content and BMD in the playing arm, but only moderately effective in increasing maximum isometric strength.[11]

Because osteoporotic fractures have a complex aetiology, our study design intentionally included more than one outcome measure and, in theory, the subsequent multiple testing of the results could introduce error. However, for this reason our outcome variables were limited in number and carefully selected before the study, and thus we feel we can interpret the results as above.

We conclude that high-impact exercise is effective in improving skeletal integrity and promoting muscular performance and dynamic balance in premenopausal women. If done on regular basis, this type of training may be an efficient, feasible, and inexpensive way to prevent osteoporosis and osteoporotic fractures.

We thank Virpi Nieminen for BMD measurements, Sanna Roine for help with the ground reaction force measurements, Katriina Ojala, Riita Pulli, Teija Lempinen, and Hannele Hiilloskorpi for professional guidance of the exercises, and Taru Malminen for help in volunteer recruitment. Financial support was provided by the Ministry of Education, Finland.

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