Open Access

The Effect of Physical Activity on Bone Accrual, Osteoporosis and Fracture Prevention

Anna Nordström*[,1,2], Taru Tervo[1] and Magnus Högström[1]

[1]*Sports Medicine, Department of Surgical and Perioperative Science, Umeå University, S-901 85 Umeå, Sweden*

[2]*Department of Community Medicine and Rehabilitation, Rehabilitation Medicine, Umeå University, S-901 85 Umeå, Sweden*

Abstract: *Background*: Physical activity has been recommended for the prevention and even treatment of osteoporosis because it potentially can increase bone mass and strength during childhood and adolescence and reduce the risk of falling in older populations. However, few reports have systematically investigated the effect of physical activity on bone in men and women of different ages.

Purpose: The goal of this study was to review the literature relating to the effect of physical activity on bone mineral density in men and women of various ages.

Method: This review systematically evaluates the evidence for the effect of physical activity on bone mineral density. Cochrane and Medline databases were searched for relevant articles, and the selected articles were evaluated.

Results: The review found evidence to support the effectiveness of weight bearing physical activity on bone accrual during childhood and adolescence. The effect of weight bearing physical activity was site-specific. In contrast, the role of physical activity in adulthood is primarily geared toward maintaining bone mineral density. The evidence for a protective effect of physical activity on bone is not as solid as that for younger individuals.

Conclusions: The effect of weight bearing physical activity is seen in sites that are exposed to loading. There also seems to be a continuous adaptive response in bone to loading. Additional randomized, controlled studies are needed to evaluate the effect of physical activity in the elderly.

Keywords: BMD, BMC, osteoporosis, fractures, physical activity, DEXA, pDEXA,QUS, pQCT.

INTRODUCTION

Osteoporosis is an increasing global health care problem. It is characterized by a reduction in bone mass and micro-structural changes that lead to increased fracture susceptibility. Given that fractures are a significant cause of mortality and painful impairment in the Western World, the identification and optimization of factors affecting the incidence of osteoporosis are critical [1-3].

Physical activity is considered to be the most important modifiable environmental factor with the potential to increase or maintain bone mineral density (BMD) in both children and adults [4-13] and to reduce the risk of falling in older populations. Physical activity has therefore been recommended for the prevention and treatment of osteoporosis [14, 15].

Mechanical loading, such as physical activity, stimulates bone formation and thus aids in regulating bone size, shape and strength. Bending loads causes deformations in the bone matrix, generating fluid pressure differences from the compression side to the tension side through extracellular spaces in canaliculi and lacunae. This fluid shear stress may be a way by which the bone cell network senses mechanical loading [16, 17]. The fluid flow generated by loading causes shearing stresses on the cell membranes in osteoblastic and osteocytic cell lines, disrupts junctional communication, rearranges junctional proteins, and determines the *de novo* synthesis of specific connexins to an extent that depends on the magnitude of the shear stress. The disconnection that results from fluid shear stress on the bone cell network may be part of the signal whereby the disconnected cells or the remaining network initiates focal bone remodeling [18]. Experimental studies in rats suggest that there is an immediate and delayed response in bone formation following mechanical stimulation [19, 20]. The immediate response results from the activation of bone lining cells into osteoblasts [20], and the delayed response occurs due to preosteoblast proliferation and differentiation into osteoblasts [19].

High magnitude strains from different angles and with fairly few repetitions have been suggested to induce the most pronounced increases in bone mass [21-26]. Typically, ground reaction forces during activities such as jumping can reach 6-7 times the body weight; in especially osteogenic sports, such as gymnastics, the ground reaction forces can be as high as 10-15 times the body weight. Normal daily activities, such as walking or running typically exert forces up to 1-2 times the body weight and are applied with the

*Address correspondence to this author at the Sports Medicine Unit, Department of Surgical and Perioperative Sciences, Umeå University, 901 85 Umeå, Sweden; Tel: +46-90-7853951; Fax: +46-90-135692; E-mail: anna.nordstrom@idrott.umu.se

same angle every time [27]. It has been suggested the loading related to high-impact and odd-impact activities like racket games, soccer and gymnastics best stimulates the bone formation [28-30].

The importance of weight-bearing loading to maintain bone strength becomes apparent in studies investigating the effects of skeletal unloading. Indeed, microgravity-induced bone loss is a model that is frequently used to study disuse osteoporosis. One review estimates a 1-2% loss of BMD each month (depending on the skeletal site) when the skeleton is exposed to micro-gravity [31]. Studies, although with small cohorts, have shown BMD losses predominantly at weight-bearing sites, such as the calcaneus and tibia, whereas there have been no measurable losses of bone in non-weight-bearing sites, such as the radius [32]. Bed rest is another model often used to study disuse osteoporosis [33-35]. LeBlanc *et al.* studied 6 patients that were confined to bed rest for 17 weeks [35]. The patients exhibited BMD losses of approximately 0.4% per month in their legs. Zerwekh *et al.* found BMD decreases of 0.95% per month in the greater trochanter, but no decrease was detected at the radius after 12 weeks of bed rest in healthy subjects [33]. However, there are a few studies showing that treadmill exercise within a lower body negative pressure chamber in a supine position counteracts the negative effects of stimulated microgravity on bone. Smith *et al.* and Cao *et al.* show that weight-bearing axial loads stimulated by a lower body negative pressure chamber improve some of the negative effects on bone metabolism and lumbar spine deconditioning during a 4-week bed rest [36, 37].

Thus, indirect evidence supports the theory that physical activity positively affects bone mass. However, more evidence of the beneficial effects of physical activity is needed before recommending physical activity as a community-based prevention strategy. This review aims to examine the current evidence for the effects of physical activity on the development of bone mass, peak bone mass and osteoporosis and fracture prevention. Tables **1-6** summarize the current literature regarding such benefits.

METHODS

A comprehensive systematic search was undertaken in the PubMed, Medline, EMBASE, and the Cochrane controlled trials databases to identify studies of physical activity and bone parameters such as bone accrual, bone mineral density, bone mineral content, bone area, osteoporosis and fractures. Medical subject headings used were "physical activity" or "exercise". These subject headings were then combined with dual-energy X-ray absorptiometry (DEXA or DXA), pheripheral dual-energy X-ray absorptiometry (pDEXA or pDXA), QUS quantitative ultrasound (QUS) and pheripheral quantitative computed tomography (pQCT). Search terms were explored. Reference lists from retrieved publications and review articles identified by the outlined search strategy were reviewed to identify further studies. From the relevant papers included in the search, a further search was undertaken by choosing the connection "related manuscripts". The computerized searches covered the period January 1966 to November 2009. Hard copies of retrieved publications were obtained. Publications were eligible for inclusion if information on the effects of physical activity on bone mass and strength was presented. Excluded were non-English language publications and papers that had been published outside of peer review journals.

RESULTS

Literature Review

Physical Activity and Infants

Even in such young ages as infancy, there have been documented positive effects of physical activity programs on bone growth and mineralization [38-42] (Table **1**). Interven-

Table 1. Randomized, Controlled Intervention Studies of the Effects of Physical Activity on Bone Parameters in Infants

Author	Participants	Study period	Intervention/ Exercise	Measurements	Results
Nemet [38] *et al.*	24 low birth weight premature infants	4 weeks	Passive range of motion exercise and gentle compression 5-10 min per day, 5 days per week	BSAP, PICP, ICTP, weight	Weight, BSAP, PICP increased significantly in Ig compared to Cg, ICTP decreased significantly compared to Cg
Moyer-Mileur [40] *et al.*	33 low birth weight premature infants	4 weeks	Passive range of motion exercise and gentle compression 5-10 min per day, 5 days per week	Forearm BA, BMC, BMD, BAP, Pyd	Forearm BA BMC greater in intervention groups compared in Cg. serum BAP decreased in Cg but not intervention groups
Moyer-Mileur [41] *et al.*	32 low birth weight premature infants	4 weeks	Passive range of motion exercise and gentle compression 5-10 min per day, 5 days per week	Forearm length, weight, pDEXA of forearm BA, BMC, BMD PICP, Pyd, PTH, 1,25(OH) vitamin D3	Ig gain significantly in forearm length, weight, BA, BMC, fat free mass. PICO constant in Ig and decreased in Cg
Litmanovitz [39] *et al.*	24 low birth weight premature infants	4 weeks	Passive range of motion exercise and gentle compression 5-10 min per day, 5 days per week	QUS of mid tibial shaft, BSAP, ICTP	SOS decreased in controls but not in Ig
Litmanovitz [42] *et al.*	16 low birth weight premature infants	8 weeks	Passive range of motion exercise and gentle compression 5-10 min per day, 5 days per week	SOS, BSAP, ICTP	SOS decreased in controls but not in Ig

BMD=bone mineral density, BMC=bone mineral content, BA=bone area, TB=total body, LS=lumbar spine, FN=femoral neck, QUS=quantitative ultrasonography, SOS=speed of sound, BAP=bone alkaline phosphatase, BSAP=bone-specific alkaline phosphatase, ICTP=carboxy-terminal telopeptide of type-I collagen, PICP=procollagen type I C-terminal propeptide, Ig=Intervention group, Cg=Control group, PreM=pre menarcheal group, PostM=post menarcheal group, PF=proximal femur, TR=trochanter, NS=non significant, BUA=broadband ultrasound attenuation.

Table 2a. Cross-Sectional and Observational Studies of the Effects of Physical Activity on Bone Modeling in Children 51

Reference	Design	Participants	Study period	Intervention/ Exercise	Measurements	Results
Haapasalo [54] *et al.*	Cross-sectional	91 girls, age 7-17 + 58 controls		Tennis players + Cg	BMD, dominant, non dominant arms, LS	BMD of playing and non playing arms significant in tennis players. In non-dominant distal radius, no differences between groups
Bailey [51] *et al.*	Observational longitudinal	60 boys, 53 girls, age 8-14 years	6 years	Divided into inactive average active and active	BMC of TB, LS, PF	TB, FN, BMC increased significantly in active *vs*. inactive
Lehtonen-Veromaa [48] *et al.*	Observational longitudinal	155 girls, age 9-15 years Tanner stage registered	1 year	Gymnasts, runners, Cg	BMD, BA of PF, LS	FN, Tr BMD increased significantly in gymnasts than Cg and runners
Slemenda [58] *et al.*	Observational longitudinal	90 twins, 6-14 years Tanner stage registered	3 years	Correlation analysis	BMD of R, PF, LS R, PF, LS BMD	Significantly correlated to physical activity
Bass[29] *et al.*	Observational longitudinal	45 female gymnasts, age 10 yrs 50 controls	12 months	Gymnastics	BMD of TB, spine, legs	Gymnast increased more at all sites compared to Cg

BMD=bone mineral density, BMC=bone mineral content, BA=bone area, TB=total body, LS=lumbar spine, FN=femoral neck, PF=proximal femur, Tr=trochanter, R=radius, Cg=Control group.

tion studies have been performed on premature infants who were at risk of osteopenia due to early birth and subsequent hospitalization in a neonatal intensive care unit. Moyer-Mileur *et al*. designed range-of-motion exercises against passive resistance, which were performed in all extremities for 5 to 10 min daily, resulting in greater gains in bone mineral content (BMC) and bone area (BA) in the treatment group compared to controls [40, 41].

Physical Activity and Children

Physical activity has been described as one of the best strategies to optimize skeletal development in children. The childhood period is thought to be an opportune time to potentiate bone modeling and enhance peak bone mass; therefore, it is of great importance to study the impact of physical activity on the growing skeleton.

Consistent findings from several randomized, controlled intervention studies, as well as cross-sectional and observational studies, have shown that weight bearing physical activity increases both bone size and BMD at weight bearing sites in 6 – 12-year-old boys and girls [4-7, 10, 29, 43-46] (Table **2a** and **b**). One randomized, controlled study, however, did not show any positive effects of physical activity in girls. In this study, 87 girls took part in 10 minutes of high impact training 3 times per week over a period of 7 months,

Table 2b. Intervention Studies of the Effects of Physical Activity on Bone Modeling In Children

Reference	Design	Participants	Study period	Intervention/ Exercise	Measurements	Results
Mckay [6] *et al.*	RCT	144 children 6-10 years	8 months	High impact 3 times a week, school intervention	BMD, BMC, BA of TB, LS, PF	Tr BMD increased significantly more in the Ig than Cg
Fuchs [7] *et al.*	RCT	51 boys, 38 girls 5.9-9.8 years	7 months	High impact 3 times a week, school intervention	BMD, BMC, BA of LS, FN	FN, LS BMC, LS BMD and FN BA increased significantly
Morris [4] *et al.*	RCT	71 girls 9-10 years	10 months	High impact 3 times a week, school intervention	BMC, BMD, BA of PF, FN, LS, TB	All BMD, BMC sites and FN BA increased significantly in Ig than Cg
Bradney [5] *et al.*	RCT	40 boys 8.4-11.8 years	8 months	Weight bearing 3 times a week, school intervention	BMD, BMC of TB, LS	TB, LS, legs BMD increased significantly in Ig than Cg
Alwis [45] *et al.*	RCT	7-9 years 80 boys	2 years	General physical activity school based intervention, 40 min, 3 times a week	BMC of TB, LS, FN	LS BMD increased significantly more in Ig than Cg
MacKelvie [47] *et al.*	RCT	87 girls Ig + 90 in C, 8.7 -11.7	7 months	10 min high impact, 3 times a week	BMD, BMC of TB, LS, PF, FN, Tr, vBMD in FN	NS
MacKelvie [43] *et al.*	RCT	75 girls, 8.8-11.7 years	20 months	High impact, 3 times a week	BMC of TB, LS, PF	FN, LS BMC increased significantly more in Ig than in Cg
MacDonald [44] *et al.*	RCT	281 boys and girls, 129 controls	16 months	High impact, 5 times a week	BSI of dT and SSI at TMS with pQCT	BSI increased significantly more in prepubertal boys than postpubertal boys and girls
Heinonen [52] *et al.*	CT	139 girls 10-15 years	9 months	Step aerobics + extra jumping 2 times a week	BMC of LS, PF	LS, PF BMD increased significantly more in PreM than in PostM and Cg

BMD=bone mineral density, vBMD=volumetric bone mineral density, BMC=bone mineral content, BA=bone area, TB=total body, LS=lumbar spine, PF=proximal femur, LS=lumbar spine, FN=femoral neck, Tr=trochanter, dT=distal tibia BSI=bone strength index, DT=distal tibia, SSI=polar strength strain index, pQCT=Peripheral quantitative computed tomography, TMS=tibial midshaft, preM=pre menarcheal, postM=post menarcheal, Ig=Intervention group, Cg=Control Group.

compared to the 90 controls [47]. The girls who were early pubertal (Tanner stage 2 and 3) and took part in the intervention gained more BMD than the controls in both the femoral neck and lumbar spine when compared to controls in the same pubertal stage. In prepubertal girls (Tanner stage 1), there were no differences between the intervention group and controls. Lehtonen-Veromaa *et al.* showed a dose-response effect in peripubertal girls when studying a cohort of gymnasts, runners and controls [48]. The gymnasts had greater increases in the femoral neck BMD compared to both runners and controls during the 1-year observational study.

During the transitional period between childhood and adolescence, biological factors associated with bone growth and development varies noticeably depending on a child's level of physical maturity. This phenomenon is further complicated by the rapid biological changes observed during this relatively short time frame. Nonetheless, pre-adolescence (i.e., Tanner stages 2-4) is suggested to be an opportune time to intervene with physical activity, given that insulin-like growth factor 1 (IGF1) levels peak during this period; it has been suggested that IGF1 could be a mediator or promoter of the effects of physical activity [49, 50]. It has also been suggested that up to 26% of total body peak bone mass is acquired during this approximately two-year period [51]. Indeed, data from one intervention study [52] and two cross-sectional studies indicate that physical activity in girls is more beneficial for bone gain in early puberty than after [53, 54].

Physical Activity and Adolescents

The effects of physical activity on adolescents' bone gain are not as clear as those seen in children, and data are more limited (Table **3**). Cross-sectional studies have shown a higher bone mass in athletes of both genders involved in weight-bearing activities than in sedentary controls [55-57]. A cross-sectional study also found a larger bone size and a higher bone mineral content in adolescent boys participating in high-impact activities one hour or more per day, compared to those who were less active [56]. The limitations of these studies include small sample sizes, cross-sectional study designs, and the risk of selection bias due to a genetic predisposition to higher BMD in athletes. More consistent results from observational longitudinal studies suggest that participation in weight-bearing activities increases bone mass in both boys and girls [46, 58-61]. One 3-year observational study showed higher gains in bone mass in male athletes taking part in badminton and ice hockey compared to sedentary controls [60].

Results from intervention studies of the effects of physical activity on bone mass show a positive correlation in

Table 3. Effects of Physical Activity on Bone Modeling In Adolescents

Author	Study Design	Participants	Study period	Intervention/ Exercise	Measurements	Results
Heinonen [55] *et al.*	Cross-sectional	84 athletes and 25 controls, age 13-32		18 squash players, 27 aerobic dancers, 14 speed skaters, 25 active controls, 25 sedentary controls	BMD of LS, FN, distal femur, patella, prox tibia, calcaneus, dist radius	Squash players had sign higher BMD compared to sedentary Cg at LS, FN, prox tibia, calcaneus. Aerobic dancers and speed skaters had higher BMD at FN, prox tibia, calcaneus *vs*. sedentary Cg
Ginty [56] *et al.*	Cross-sectional	128 boys, 16-18 yrs		Questionnaire assessment of physical activity	BMD, BMC, BA of TB, hip, spine, forearm	Size adjusted BMC sign associated with time spent in high impact activities
Welten [57] *et al.*	Retrospective	84 boys, 98 girls, 27 years		Interview evaluating exercise levels	BMD of LS	LS association significant
Forwood [61] *et al.*	Observational longitudinal	109 males, 121 females, age 15-22	7 years	Inactive, average active, highly active	BMC of TB, PF, HAS, Z	PF, TB BMC, CSA, Z increased significantly in highly active vs. inactive
Gustavsson [60] *et al.*	Observational longitudinal	56 boys, age 16	3 years	Athletes Cg	BMD of TB, FN, H, LS vBMD of FN	Athletes gained significantly more in nondominant H, FN BMD than Cg
Nordström [59] *et al.*	Observational longitudinal	46 boys, age 17	4 years	Ice hockey players, badminton players Cg	BMD of FN, H, PF, LS BMC of FN, H, PF, LS	FN BMD, BMC and H BMC significantly higher gain in badminton players than in Cg, Greater gain in Hip BMC and ice hockey players
Blimkie [63] *et al.*	CT	36 girls, 14-18 years	6 months	Resistance training 3 times a week	BMC, BMD of TB, LS	NS
Witzke [62] *et al.*	CT	53 girls, age 13-15 years	9 months	High impact 3 times a week school intervention	BMC of TB, LS, PF	NS
Snow-Harter [8] *et al.*	RCT	52 women 19.9±0.7 years	8 month	Weight lifting or running 3 times a week + controls	BMD, BMC of the FN and LS	LS BMD increased significantly more in runners and weightlifters than in controls
Weeks[9] *et al.*	RCT	46 boys, 53 girls, 13.8 years	8 months	High Impact 2 times a week	Calcaneal BUA, BMC, BMD, BA of FN, TR, LS, TB	Size adjusted BMC sign associated with time spent in high impact activities

BMD=bone mineral density, BMC=bone mineral content, BA=bone area, LS=lumbar spine, FN=femoral neck, CSA=cross-sectional area, Z=section modulus, TB=total body, H=humerus, Ig=Intervention group, Cg=Control group, PreM=pre menarcheal group, PostM=post menarcheal group, PF=proximal femur, Tr=trochanter, NS=non significant, BUA=broadband ultrasound attenuation, HAS=hip strength analysis.

Table 4. Effects of Physical Activity Intervention Studies on Bone Parameters in Premenopausal Women

Reference	Design	Participants	Study period	Intervention/ Exercise	Measurements	Results
Heinonen [64] *et al.*	Follow up study	49 women, 35-45 years	8 months	High impact 3 times a week continued training	BMD of R, LS, FN	FN BMD increased significantly in Ig *vs*. Cg
Lohman [67] *et al.*	RCT	56 women 28-39 years	18 months	Resistance Calcium supplement	BMD of TB, LS, PF	Tr, LS BMD increased significantly in Ig *vs*. Cg
Gleeson [35] *et al.*	CT	68 women	12 months	Weight lifting Calcium supplement	BMD of LS	NS
Bassey [65] *et al.*	RCT	55 women, mean age 37.5 years	5 months	High impact 3 times a week	BMD of PF, LS	Tr BMD increased significantly in Ig *vs*. Cg
Sinaki [68] *et al.*	RCT	96 women, 30-40 years	3 years	Weight lifting Calcium supplement	BMD of LS, PF, R	NS
Winters [66] *et al.*	CT	65 women, 30-45 years	12 months	High impact	BMD of TB, Tr, FN, LS	Tr BMD increased significantly in Ig *vs*. Cg
Vainionpaa [12] *et al.*	RCT	120 women, 35-40 years	12 months	High impact 3 times a weekend daily home exercise program	BMD of FN, Tr, ITr, W, F, L1-L4, uR, R, U SOS of C	FN, Tr, ITr, F, L1 increased significantly in Ig *vs*. Cg
Kato [69] *et al.*	RCT	36 young women, mean 20 years	6 months	10 maximal jumps/day 3 times a week	BMD LS, FN, W, Tr	FN, LS BMD increased significantly more in Ig *vs*. Cg
Winters-Stone [13] *et al.*	RCT	35 interventions, 24 controls 34-45 yrs	12 months	Upper + lower body resistance activity + jumps or Lower body resistance activity + jumps, controls	BMD of hip, FN, LS, TB at 0, 6, 12 months	Greater trochanter BMD in activity groups *vs*. Cg

BMD=bone mineral density, LS=lumbar spine, FN=femoral neck, TB=total body, F=femur, PF=proximal femur, W= Ward´s triangle, Tr=trochanter, ITr=intertrochanter, C=calcaneus, R=radius, U=ulna, uR=ultradistal radius, SOS=speed of sound, Ig=Intervention group, Cg=Control group, NS= non significant.

both male and female adolescents [8, 9, 62, 63]. Consequently, weight bearing, high-impact activity during adolescence seems to be important for skeletal mineralization.

Physical Activity and Premenopausal Women

Positive osteogenic effects that seem to be site specific have been seen in high-impact physical activity intervention

Table 5. Effects of Randomized, Controlled Physical Activity Intervention Studies on Bone Parameters in Postmenopausal Women

Reference	Participants	Study period	Intervention/ Exercise	Measurements	Results
Kerr [75] *et al.*	56 women, 40-70 years	1 year	Endurance resistance or high load resistance, one side used as Cg	BMD of R, PF	PF, R BMD increased significantly in high load *vs*. Cg and R BMD in endurance resistance
Sinaki [77] *et al.*	65 women, 49-65 years	2 years	Resistance	BMD of LS	NS
Sandler [70] *et al.*	255 women, 49-65 years	3 years	Walking	BMD of R measured with CT	NS
Nelson [72] *et al.*	40 women, 50-70 years	1 year	Weight lifting 2 times a week	BMD, BMC of TB, FN, LS	FN, LS BMD increased significantly in Ig *vs*. Cg
Grove [71] *et al.*	15 women, 49-64 years	1 year	High impact, low impact, Cg	BMD of LS	LS BMD in Cg decreased significantly maintenance of Ig
Brooke-Wavell [76] *et al.*	84 women, 60-70 years	1 year	Walking or Cg	BMD of LS, FN, C	BMD C increased significantly in Ig *vs*. Cg
Karinkanta [80] *et al.*	149 women, 70-78 years	1 year	Resistance, balance. jumping or combination , Control	DEXA BMD, BMC and pQCT of the DT, TS, Rs, dR	TS bone strength index decreased significantly less in Ig than in Cg
Prince[65] *et al.*	168 women, 50-70 years	2 years	Weight lifting and/or calcium supplement	BMD of LS, PF	BMD of PF exercise + calcium increased significantly *vs*. calcium
Bassey [73] *et al.*	44 women, 50-60 years	1 year	Weight bearing or Cg	BMD of PF, LS, R	NS
Englund [78] *et al.*	48 women, 66-87 yrs	1 year	50 Combined weight bearing activity twice per week (strengthening, aerobic, balance, coordination)	BMD of TB, FN	BMD wards triangle increased significantly *vs*. controls
Korpeleinen [79] *et al.*	160 women, mean age 72 yrs	30 months	60 min balance, jumping, walking and 20 min home program daily	BMD FN, trochanter, tot hip, R, C at 0, 12, 30 months	BMD at FN, tr decreased significantly in Cg but not in Ig

BMD= bone mineral density, LS=lumbar spine, FN=femoral neck, TS=tibial shaft, dT= distal tibia, TB=total body, PF=proximal femus, C=calcaneus, R=radius, Rs=radial shaft, dR=distal radius, pQCT= Peripheral quantitative computed tomography, CT=computed tomography, Ig=Intervention group, Cg=Control group, NS=non significant.

studies [11-13, 64-69] (Table **4**). In the majority of the studies, the exercise intervention was conducted three times a week. In general, studies that used weight training as an intervention failed to show any effects on bone mass [35, 68]. However, one study did show small but significant increases in bone mass after 18 months of resistance training combined with calcium supplementation [67]. The inconsistency in these findings may be explained by the dissimilar ages represented in the different studies as well as differences in the performed activities; additionally, the study groups have been rather small and dropout rates relatively high in some of the studies. Moreover, it is possible that some of the training programs did not impose enough skeletal loading to increase BMD.

Physical Activity and Postmenopausal Women

Previous randomized studies investigating the effects of physical activity on BMD in postmenopausal women have yielded varying results [70-80] (Table **5**). Only one study used high-impact activity *versus* low-impact activity as an intervention [71]. In this study, there were no differences between the effects of high- and low-impact activity; both study groups maintained their lumbar BMD, whereas controls decreased. However, three randomized intervention studies have studied the effects of combined weight-bearing activity on bone mass in women in ages 66-87 [78-80]. These studies showed improvements in bone density and structure, as well as in functional capacity and muscle strength. It was also shown that these changes in bone structure and dynamic balance were partially maintained one year after cessation of supervised training [71, 80].

In postmenopausal women, no dose-response relationship between physical activity and BMD has been observed. The effect of physical activity on BMD in postmenopausal women seems to be modest. Most controlled trials use resistance training as the primary intervention. Possibly, some of the training programs have not imposed enough skeletal loading to increase BMD. It seems that, in some cases, physical activity might diminish BMD loss in sites that are exposed to mechanical loading. It is difficult to draw conclusions from these studies given the differences in study design, including duration of the interventions, limited and varying numbers of study subjects and the differences in types of assigned physical activity. Additionally, some studies were flawed with rather high dropout rates of up to

Table 6a. Cross-Sectional Studies of the Effects of Physical Activity on Bone Modeling in Men

Reference	Participants	Intervention/Exercise	Measurements	Results
Fredericson [82] *et al.*	45 men, 15 soccer players, 15 long distance runners, 15 c age 20-30		BMD of LS, hip, leg, TB, C	Soccer player had greater BMD at TB, LS, leg, C than Cg and higher hip, spine compared to runners. Runners had higher calcaneal BMD compared to Cg
Calbet [84] *et al.*	15 volley ball players, 15 controls		BMD, BMC of TB, LS, FN	TB BMC greater in V, *vs*. Cg BMD greater in TB, LS, FN
Calbet [85] *et al.*	9 tennis, 26+-6 yrs players, 17 controls 24+-3yrs		BMD, BMC of TB, LS, FN	BMC of arms greater in dominant *vs*. non dominant in tennis players. BMC greater in dominant arm vs. c. BMD of LS, FN greater in tennis players *vs*. Cg
Nevill [89] *et al.*	106 athletes, 15 C 27. 8 +-7.2 yrs	Cycling, keep fit, racquet sports, rowing, rugby, strength, triathlon, upper body	BMD of TB	Rugby players, strength athletes in TB, all sub measurements vs. Cg. Strength athletes. BMD in athletes greater in arms, legs, LS. Racquet players greater BMD at LS, pelvis, legs
Wittich [83] *et al.*	24 football players, 22 controls age 22 +-2.5 yrs		BMD, BMC, BA of TB	BMC TB, BMC, BMD, BA of pelvis, legs greater in football players *vs*. Cg
Magkos [87] *et al.*	52 men, 17-30 yrs: 21 runners, 16 swimmers, 15 controls		BMD of total body	Runners sign higher leg BMD *vs*. c Swimmers significantly lower leg, tot BMD *vs*. Cg
Morel [88] *et al.*	704 amateur athletes, mean age 30	14 different sports rugby, soccer, other team sports, endurance running, fighting sports, bodybuilding, multiple weight-bearing activities, swimming, swimming with flippers, biking, rowing, climbing, triathlon and multiple mixed activities	BMD of TB	Rowers, swimmers had lower leg and TB BMD. Participants in team sports, rugby, soccer and fighting sports had higher TB and leg BMD
Nichols [90] *et al.*	Male cyclists, older 27 age 51, 16 young adults age 32, 24 age matched controls		BMD of TB, LS,	Hip, Ls BMD lower in older cyclists *vs*. young cyclist and controls. TB BMD of older cyclists were lower compared to younger cyclists
Rector [91] *et al.*	27 cyclists, 16 runners, 20-59 yrs of age		BMD TB	Runners had significantly higher BMD of TB, spine
Daly [92] *et al.*	161 men, age 50-87		DEXA hip, spine, ultra distal BMD, QUS heel bone, QCT spine, mid femur	Osteogenic index calculated from previous physical activity during 1- 50 years was associated with greater mid femur total and cortical area, BMC, polar moment of inertia, heel VOS

BMD=bone mineral density, LS=lumbar spine, FN=femoral neck, TB=total body, C=calcaneus, Rs=radial shaft, udR=ultra distal radius, DEXA=dual energy x-ray absorptiometry QUS=Quantitative Ultrasonography, pQCT=Peripheral quantitative computed tomography, CT=computed tomography, VOS=velocity of sound, Ig=Intervention group, Cg=Control group.

Table 6b. Effects of Physical Activity Intervention Studies in Men

Reference	Study design	Participants	Study period	Intervention/ Exercise	Measurements	Results
Nguyen [94] *et al.*	Retrospective	690 men, age 60 years and above		Interview evaluating exercise levels	BMD of LS, FN	FN BMD association significant but not after adj. for age and BMI
Delvaux [93] *et al.*	Retrospective	126 men, age 40		Questionnaire evaluating exercise levels BMD, BMC	TB, LS BMD and BMC of TB, LS	BMD of TB, LS and BMC of LS significant associated with Baeckes sports index at 40yrs
Lynch [96] *et al.*	Retrospective	16 former professional football player + controls 66±6 years		Self reported questionnaire evaluating exercise levels	BMC, BMD of TB, LS, PF	TB BMC and BMD and LS, FN BMD significantly increased in Fp
Daly [86] *et al.*	Retrospective	152 males, 61.8±9 years at start	10 years	Interview-administered questionnaire	BMD of R	Significantly less bone loss in active *vs.* inactive
Neville [95] *et al.*	Retrospective	242 men, age 20-25 years		Questionnaire evaluating exercise levels	BMD, BMC of LS, FN	Sports activity was related to LS, FN BMD and BMC
Fujimura [97] *et al.*	RCT	17 males, 23-31 years	4 months	Weight training 3 times a week	BMD of TB, LS, FN, R	NS

BMD=bone mineral density, BMC=bone mineral content, LS=lumbar spine, PF=proximal femur, FN=femoral neck, TB=total body, NS= non significant, R=radius, Fp=football players, BMI=body mass index.

30%. Furthermore, in some studies, calcium supplements were used as an intervention together with physical exercise [80, 81]. Finally, ethnicity, hormone replacement therapy treatment, calcium substitution and smoking were not uniformly accounted for.

Physical Activity and Men

Cross-sectional studies have shown that male athletes involved in weight-bearing activities have higher BMD than inactive controls [82-86] or athletes in non-weight-bearing sports such as swimming [87, 88] or cycling [89-91] (Table **6a** and **b**). The data from two longitudinal observational studies [92, 93] and 3 retrospective studies indicate that weight-bearing physical activity and an active lifestyle appear to be associated with higher BMD and decreased bone loss at weight-bearing sites in men [94-96]. However, it must be kept in mind that there is always risk for recall bias in retrospective studies.

Only one randomized, controlled intervention study has investigated the effects of physical activity on bone mass in young men [97]. This 4-month study used weight lifting as the intervention activity and failed to show any significant differences in BMD between weight lifters and controls. An intervention time of 4 months is most likely too short to detect any changes in BMD measured by Dual Energy X-ray Absorptiometry (DEXA), since a single bone remodeling cycle is estimated to last 5-6 months [98].

Physical Activity and Fractures

When studying the possible effects of physical activity in the elderly, the focus has mainly been on associations between physical activity levels and fracture risk. Although most studies suggest that previous high levels of physical activity is associated with lower hip fracture incidence, there are no prospective studies evaluating whether lifelong exercise protects against fragility fractures in old age [99,

Table 7. Observational Studies of Physical Activity and Fracture Incidence

Reference	Participants	Study period	Intervention/Exercise	Results
Cummings [102] *et al.*	9516 women, 65 years or older	4.1 years	Questionnaire + interview to assess exercise levels	Significant fracture reduction associated with physical activity
Gregg [106] *et al.*	9704 women, 65 years or older	7.6 years	Questionnaire to assess exercise levels	Significant fracture reduction associated with physical activity
Farmer [104] *et al.*	3595 women, 40-77 years	10 years	Questionnaire to assess exercise levels	Significant fracture reduction associated with physical activity
Kujala [103] *et al.*	3262 men, 44 years or older	21 years	Questionnaire to assess exercise levels	Significant fracture reduction associated with physical activity
Paganini-Hill [101] *et al.*	5049 men, age 73 years	7 years	Questionnaire to assess exercise levels	Significant fracture reduction associated with physical activity
Wickham [100] *et al.*	983 men and women, age 65 and older	15 year prospective follow up of randomly selected population	Questionnaire and physician examination	Adjusted odds ratio for the lowest third of outdoor activity was 4.3 (0.7-26.8) compared to highest
Coupland [105] *et al.*	197 patients with hip fractures age 50 and older and 382 age, gender matched controls	Cross-sectional	Questionnaire to assess exercise levels	Physical inactivity associated with the risk of hip fracture in men and women

100] (Table 7). Observational studies focusing on physical activity and fracture risk reduction have shown that physical activity is associated with a reduced risk of fractures, especially hip fractures, both in men and in women [99, 101-104]; only one study disagreed with this conclusion [86]. Daly *et al.* prospectively investigated the effects of physical activity (assessed with a questionnaire) in 359 men and women who were then followed for 10 years. The BMD of the radius was measured. Even moderate levels of exercise and low-impact activities were shown to be associated with a lower risk of hip fracture. The authors speculate that the reduced fracture risk is not entirely associated with enhanced bone mass but could also be influenced by factors such as better neuromuscular function and enhanced muscle strength, balance and mobility. Several studies have also reported a dose-response relationship, when comparing the most active with the least active individuals, a conclusion which supports the theory that physical activity reduces hip fracture risk [101, 105, 106]. Thus, current physical activity seems to offer a protective effect against hip fracture in both men and women. However, it is also possible that the studies reflect the overall health of the participants, i.e., participants with worse health tend to exercise less and are more prone to falling and, therefore, are more susceptible to fractures [99].

Physical Activity and Falls

The risk of sustaining an osteoporotic fracture is largely commensurate with the risk of falling, with the force that the fall generates on the skeleton and with the strength of the skeleton. Factors associated with the risk of falling include advanced age, poor balance and vision and decreased muscle strength and mobility [107, 108]. The risk of falling may be influenced by many other factors such as medications and environmental factors such as stairs, carpets and thresholds.

The bulk of our knowledge to date about physical activity and the risk of falling stems from the FICSIT trials (Frailty and Injuries: Cooperative Studies of Intervention Techniques) [109]. The study was based on eight independent but coordinated investigations, and the results have been compiled in a meta-analysis. The results showed 10% fewer falls if the subjects were engaged in general training and a 17% reduction in falls if they were engaged in balance training. The largest single effect was observed after 2.5 months of Tai Chi training; in the intervention group, 47% fewer fall incidents were observed compared to the control group [110]. Physical activity in the form of endurance training actually increased the risk of falling. It could be speculated that the increased risk of falling reflected the increased exposure to situations in which falling was possible. Campbell *et al.* also observed a decreased risk of falls following participation in a training program focusing on balance and coordination [111]. The 30-min home-based training program, carried out 3 times a week for 1 year, consisted of training for the lower extremities, balance exercises such as toe walking and various coordination routines. The subjects were also encouraged to walk outside the home at least three times a week. The risk of falling at least 4 times during the study period was 32% lower in the intervention group, and the risk of falling and sustaining an injury was 39% less. Further research is needed to determine what type and quantity of physical activity is needed for optimal protection from falls and which are the populations that would most benefit from such an intervention.

CONCLUSIONS

The general concepts underpinning the potential use of physical activity to avoid fractures can be divided into three strategies: maximizing BMD gain during childhood and adolescence, minimizing the age-related decline in BMD and preventing injurious falls and fractures.

The most consistent data showing gains in BMD from physical activity come from studies performed during childhood and adolescence. From the studies published to date, we can conclude that physical activity is effective at increasing peak bone mass. It is well established that the activity should be weight-bearing and should result in high intensity loading being applied in unusual directions, resulting in a high-strain magnitude and rate. Activities that meet these criteria include gymnastics, racquet sports, and sports with a high content of jumping such as volleyball, soccer, and basketball. High impact activities can cause sports-related injuries such as tendinosis and muscle strains; the risk of osteoarthritis is low in moderate recreational sports but elevated in some professional athletes [112]. However, a discussion about these subjects is beyond the scope of this article.

With regard to the role of physical activity in adulthood, the focus is toward maintaining BMD. The evidence for a protective effect of physical activity in adults is not as solid as it is in younger individuals. More randomized, controlled studies are needed in both men and women to investigate the potential effects of physical activity. An important factor to examine is whether the potential effects are dose-dependent. The skeleton in adulthood is not likely to be as sensitive to loading and, at the same time, muscles and tendons start to lose strength; however the greatest loss in muscle strength and mass occurs after the age of 70 years [113]. The current advice is to maintain previous activity levels while engaging in weight-bearing activities that are more forgiving to the skeleton and tendons such as dancing, jogging and resistance training.

In the elderly, the focus has shifted from maintaining bone mass towards activities designed to improve balance and prevent falls. The evidence for a possible dose-dependent relationship between physical activity and improved bone health is lacking. However, it does seem that physical activity is important for the maintenance of BMD. Furthermore, the evidence to date suggests that physical activity is associated with a reduction in fracture risk. Both weight-bearing endurance exercise and resistance training are important, but specific balance training, such as Tai Chi, may offer the greatest benefit. Larger randomized, controlled studies are needed to further evaluate the effects of physical activity on fall and fracture risk reduction.

REFERENCES

[1] Browner WS, Pressman AR, Nevitt MC, Cummings SR. Mortality following fractures in older women. The study of osteoporotic fractures. Arch Intern Med 1996; 156(14): 1521-5.

[2] Cooper C, Atkinson EJ, Jacobsen SJ, O'Fallon WM, Melton LJd. Population-based study of survival after osteoporotic fractures. Am J Epidemiol 1993; 137(9): 1001-5.

[3] Nevitt MC, Ettinger B, Black DM, *et al.* The association of radiographically detected vertebral fractures with back pain and function: a prospective study. Annals of internal medicine 1998; 128(10): 793-800.

[4] Morris FL, Naughton GA, Gibbs JL, Carlson JS, Wark JD. Prospective ten-month exercise intervention in premenarcheal girls: positive effects on bone and lean mass. J Bone Miner Res 1997; 12(9): 1453-62.

[5] Bradney M, Pearce G, Naughton G, *et al.* Moderate exercise during growth in prepubertal boys: changes in bone mass, size, volumetric density, and bone strength: a controlled prospective study. J Bone Miner Res 1998; 13(12): 1814-21.

[6] McKay HA, Petit MA, Schutz RW, *et al.* Augmented trochanteric bone mineral density after modified physical education classes: a randomized school-based exercise intervention study in prepubescent and early pubescent children. J Pediatr 2000; 136(2): 156-62.

[7] Fuchs RK, Bauer JJ, Snow CM. Jumping improves hip and lumbar spine bone mass in prepubescent children: a randomized controlled trial. J Bone Miner Res 2001;16(1):148-56.

[8] Snow-Harter C, Bouxsein ML, Lewis BT, Carter DR, Marcus R. Effects of resistance and endurance exercise on bone mineral status of young women: a randomized exercise intervention trial. J Bone Miner Res 1992;7(7):761-9.

[9] Weeks BK, Young CM, Beck BR. Eight months of regular in-school jumping improves indices of bone strength in adolescent boys and Girls: the POWER PE study. J Bone Miner Res 2008; 23(7): 1002-11.

[10] Bailey DA, McKay HA, Mirwald RL, Crocker PR, Faulkner RA. A six-year longitudinal study of the relationship of physical activity to bone mineral accrual in growing children: the university of Saskatchewan bone mineral accrual study. J Bone Miner Res 1999; 14(10): 1672-9.

[11] Heinonen A, Kannus P, Sievanen H, *et al.* Randomised controlled trial of effect of high-impact exercise on selected risk factors for osteoporotic fractures. Lancet 1996; 348(9038): 1343-7.

[12] Vainionpaa A, Korpelainen R, Leppaluoto J, Jamsa T. Effects of high-impact exercise on bone mineral density: a randomized controlled trial in premenopausal women. Osteoporos Int 2005; 16(2): 191-7.

[13] Winters-Stone KM, Snow CM. Site-specific response of bone to exercise in premenopausal women. Bone 2006; 39(6): 1203-9.

[14] Kannus P. Preventing osteoporosis, falls, and fractures among elderly people. Promotion of lifelong physical activity is essential. BMJ 1999; 318(7178): 205-6.

[15] Nordstrom A, Karlsson C, Nyquist F, *et al.* Bone loss and fracture risk after reduced physical activity. J Bone Miner Res 2005; 20(2): 202-7.

[16] Weinbaum S, Cowin SC, Zeng Y. A model for the excitation of osteocytes by mechanical loading-induced bone fluid shear stresses. J Biomech 1994; 27(3): 339-60.

[17] Hsieh YF, Turner CH. Effects of loading frequency on mechanically induced bone formation. J Bone Miner Res 2001; 16(5): 918-24.

[18] Robling AG, Castillo AB, Turner CH. Biomechanical and molecular regulation of bone remodeling. Annu Rev Biomed Eng 2006; 8: 455-98.

[19] Turner CH, Owan I, Alvey T, Hulman J, Hock JM. Recruitment and proliferative responses of osteoblasts after mechanical loading *in vivo* determined using sustained-release bromodeoxyuridine. Bone 1998; 22(5): 463-9.

[20] Chow JW, Wilson AJ, Chambers TJ, Fox SW. Mechanical loading stimulates bone formation by reactivation of bone lining cells in 13-week-old rats. J Bone Miner Res 1998; 13(11): 1760-7.

[21] O'Connor JA, Lanyon LE, MacFie H. The influence of strain rate on adaptive bone remodelling. J Biomech 1982; 15(10): 767-81.

[22] Raab-Cullen DM, Akhter MP, Kimmel DB, Recker RR. Bone response to alternate-day mechanical loading of the rat tibia. J Bone Miner Res 1994; 9(2): 203-11.

[23] Rubin CT, Lanyon LE. Regulation of bone formation by applied dynamic loads. J Bone Joint Surg Am 1984; 66(3): 397-402.

[24] Rubin CT, Lanyon LE. Regulation of bone mass by mechanical strain magnitude. Calcif Tissue Int 1985; 37(4): 411-7.

[25] Lanyon LE, Rubin CT, Baust G. Modulation of bone loss during calcium insufficiency by controlled dynamic loading. Calcif Tissue Int 1986; 38(4): 209-16.

[26] Lanyon LE. Control of bone architecture by functional load bearing. J Bone Miner Res 1992; 7 Suppl 2: S369-75.

[27] McNitt-Gray JL. Kinetics of the lower extremities during drop landings from three heights. J Biomech 1993; 26(9): 1037-46.

[28] Nikander R, Kannus P, Rantalainen T, *et al.* Cross-sectional geometry of weight-bearing tibia in female athletes subjected to different exercise loadings. Osteoporos Int 2010; 21(10): 1687-94.

[29] Bass S, Pearce G, Bradney M, *et al.* Exercise before puberty may confer residual benefits in bone density in adulthood: studies in active prepubertal and retired female gymnasts. J Bone Miner Res 1998; 13(3): 500-7.

[30] Tervo T, Nordstrom P, Nordstrom A. Effects of badminton and ice hockey on bone mass in young males: A 12-year follow-up. Bone 2010; 47(3): 666-72.

[31] Holick MF. Perspective on the impact of weightlessness on calcium and bone metabolism. Bone 1998; 22(5 Suppl): 105S-11S.

[32] Vico L, Collet P, Guignandon A, *et al.* Effects of long-term microgravity exposure on cancellous and cortical weight-bearing bones of cosmonauts. Lancet 2000; 355(9215): 1607-11.

[33] Zerwekh JE, Ruml LA, Gottschalk F, Pak CY. The effects of twelve weeks of bed rest on bone histology, biochemical markers of bone turnover, and calcium homeostasis in eleven normal subjects. J Bone Miner Res 1998; 13(10): 1594-601.

[34] Watanabe Y, Ohshima H, Mizuno K, *et al.* Intravenous pamidronate prevents femoral bone loss and renal stone formation during 90-day bed rest. J Bone Miner Res 2004; 19(11): 1771-8.

[35] Gleeson PB, Protas EJ, LeBlanc AD, Schneider VS, Evans HJ. Effects of weight lifting on bone mineral density in premenopausal women. J Bone Miner Res 1990; 5(2): 153-8.

[36] Smith SM, Davis-Street JE, Fesperman JV, *et al.* Evaluation of treadmill exercise in a lower body negative pressure chamber as a countermeasure for weightlessness-induced bone loss: a bed rest study with identical twins. J Bone Miner Res 2003; 18(12): 2223-30.

[37] Cao P, Kimura S, Macias BR, *et al.* Exercise within lower body negative pressure partially counteracts lumbar spine deconditioning associated with 28-day bed rest. J Appl Physiol 2005; 99(1): 39-44.

[38] Nemet D, Dolfin T, Litmanowitz I, *et al.* Evidence for exercise-induced bone formation in premature infants. Int J Sports Med 2002; 23(2): 82-5.

[39] Litmanovitz I, Dolfin T, Friedland O, *et al.* Early physical activity intervention prevents decrease of bone strength in very low birth weight infants. Pediatrics 2003; 112(1 Pt 1): 15-9.

[40] Moyer-Mileur LJ, Ball SD, Brunstetter VL, Chan GM. Maternal-administered physical activity enhances bone mineral acquisition in premature very low birth weight infants. J Perinatol 2008; 28(6): 432-7.

[41] Moyer-Mileur LJ, Brunstetter V, McNaught TP, Gill G, Chan GM. Daily physical activity program increases bone mineralization and growth in preterm very low birth weight infants. Pediatrics 2000; 106(5): 1088-92.

[42] Litmanovitz I, Dolfin T, Arnon S, *et al.* Assisted exercise and bone strength in preterm infants. Calcif Tissue Int 2007; 80(1): 39-43.

[43] MacKelvie KJ, Khan KM, Petit MA, Janssen PA, McKay HA. A school-based exercise intervention elicits substantial bone health benefits: a 2-year randomized controlled trial in girls. Pediatrics 2003; 112(6 Pt 1): e447.

[44] Macdonald HM, Kontulainen SA, Khan KM, McKay HA. Is a school-based physical activity intervention effective for increasing tibial bone strength in boys and girls? J Bone Miner Res 2007; 22(3): 434-46.

[45] Alwis G, Linden C, Ahlborg HG, *et al.* A 2-year school-based exercise programme in pre-pubertal boys induces skeletal benefits in lumbar spine. Acta Paediatr 2008; 97(11): 1564-71.

[46] Bailey DA, Faulkner RA, McKay HA. Growth, physical activity, and bone mineral acquisition. Exerc Sport Sci Rev 1996; 24: 233-66.

[47] Mackelvie KJ, McKay HA, Khan KM, Crocker PR. A school-based exercise intervention augments bone mineral accrual in early pubertal girls. J Pediatr 2001; 139(4): 501-7.

[48] Lehtonen-Veromaa M, Mottonen T, Irjala K, *et al.* A 1-year prospective study on the relationship between physical activity,

markers of bone metabolism, and bone acquisition in peripubertal girls. J Clin Endocrinol Metab 2000; 85(10): 3726-32.
[49] Mora S, Pitukcheewanont P, Nelson JC, Gilsanz V. Serum levels of insulin-like growth factor I and the density, volume, and cross-sectional area of cortical bone in children. J Clin Endocrinol Metab 1999; 84(8): 2780-3.
[50] Libanati C, Baylink DJ, Lois-Wenzel E, Srinvasan N, Mohan S. Studies on the potential mediators of skeletal changes occurring during puberty in girls. J Clin Endocrinol Metab 1999; 84(8): 2807-14.
[51] Bailey DA, Martin AD, McKay HA, Whiting S, Mirwald R. Calcium accretion in girls and boys during puberty: a longitudinal analysis. J Bone Miner Res 2000; 15(11): 2245-50.
[52] Heinonen A, Sievanen H, Kannus P, *et al.* High-impact exercise and bones of growing girls: a 9-month controlled trial. Osteoporos Int 2000; 11(12): 1010-7.
[53] Kannus P, Haapasalo H, Sankelo M, *et al.* Effect of starting age of physical activity on bone mass in the dominant arm of tennis and squash players. Ann Intern Med 1995; 123(1): 27-31.
[54] Haapasalo H, Kannus P, Sievanen H, *et al.* Effect of long-term unilateral activity on bone mineral density of female junior tennis players. J Bone Miner Res 1998; 13(2): 310-9.
[55] Heinonen A, Oja P, Kannus P, *et al.* Bone mineral density in female athletes representing sports with different loading characteristics of the skeleton. Bone 1995; 17(3): 197-203.
[56] Ginty F, Rennie KL, Mills L, *et al.* Positive, site-specific associations between bone mineral status, fitness, and time spent at high-impact activities in 16- to 18-year-old boys. Bone 2005; 36(1): 101-10.
[57] Welten DC, Kemper HC, Post GB, *et al.* Weight-bearing activity during youth is a more important factor for peak bone mass than calcium intake. J Bone Miner Res 1994; 9(7): 1089-96.
[58] Slemenda CW, Reister TK, Hui SL, *et al.* Influences on skeletal mineralization in children and adolescents: evidence for varying effects of sexual maturation and physical activity. J Pediatr 1994; 125(2): 201-7.
[59] Nordstrom A, Hogstrom M, Nordstrom P. Effects of different types of weight-bearing loading on bone mass and size in young males: A longitudinal study. Bone 2008; 42(3): 565-71.
[60] Gustavsson A, Thorsen K, Nordstrom P. A 3-year longitudinal study of the effect of physical activity on the accrual of bone mineral density in healthy adolescent males. Calcif Tissue Int 2003; 73(2): 108-14.
[61] Forwood MR, Baxter-Jones AD, Beck TJ, *et al.* Physical activity and strength of the femoral neck during the adolescent growth spurt: a longitudinal analysis. Bone 2006; 38(4): 576-83.
[62] Witzke KA, Snow CM. Effects of plyometric jump training on bone mass in adolescent girls. Med Sci Sports Exerc 2000; 32(6): 1051-7.
[63] Blimkie CJ, Rice S, Webber CE, *et al.* Effects of resistance training on bone mineral content and density in adolescent females. Can J Physiol Pharmacol 1996; 74(9): 1025-33.
[64] Heinonen A, Kannus P, Sievanen H, *et al.* Good maintenance of high-impact activity-induced bone gain by voluntary, unsupervised exercises: An 8-month follow-up of a randomized controlled trial. J Bone Miner Res 1999; 14(1): 125-8.
[65] Bassey EJ, Rothwell MC, Littlewood JJ, Pye DW. Pre- and postmenopausal women have different bone mineral density responses to the same high-impact exercise. J Bone Miner Res 1998; 13(12): 1805-13.
[66] Winters KM, Snow CM. Detraining reverses positive effects of exercise on the musculoskeletal system in premenopausal women. J Bone Miner Res 2000; 15(12): 2495-503.
[67] Lohman T, Going S, Pamenter R, *et al.* Effects of resistance training on regional and total bone mineral density in premenopausal women: a randomized prospective study. J Bone Miner Res 1995; 10(7): 1015-24.
[68] Sinaki M, Wahner HW, Bergstralh EJ, *et al.* Three-year controlled, randomized trial of the effect of dose-specified loading and strengthening exercises on bone mineral density of spine and femur in nonathletic, physically active women. Bone 1996; 19(3): 233-44.
[69] Kato T, Terashima T, Yamashita T, *et al.* Effect of low-repetition jump training on bone mineral density in young women. J Appl Physiol 2006; 100(3): 839-43.
[70] Sandler RB, Cauley JA, Hom DL, Sashin D, Kriska AM. The effects of walking on the cross-sectional dimensions of the radius in postmenopausal women. Calcif Tissue Int 1987; 41(2): 65-9.
[71] Grove KA, Londeree BR. Bone density in postmenopausal women: high impact *vs.* low impact exercise. Med Sci Sports Exerc 1992; 24(11): 1190-4.
[72] Nelson ME, Fiatarone MA, Morganti CM, *et al.* Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures. A randomized controlled trial. JAMA 1994; 272(24): 1909-14.
[73] Prince R, Devine A, Dick I, *et al.* The effects of calcium supplementation (milk powder or tablets) and exercise on bone density in postmenopausal women. J Bone Miner Res 1995; 10(7): 1068-75.
[74] Bassey EJ, Ramsdale SJ. Weight-bearing exercise and ground reaction forces: a 12-month randomized controlled trial of effects on bone mineral density in healthy postmenopausal women. Bone 1995; 16(4): 469-76.
[75] Kerr D, Morton A, Dick I, Prince R. Exercise effects on bone mass in postmenopausal women are site-specific and load-dependent. J Bone Miner Res 1996; 11(2): 218-25.
[76] Brooke-Wavell K, Jones PR, Hardman AE. Brisk walking reduces calcaneal bone loss in post-menopausal women. Clin Sci (Lond) 1997; 92(1): 75-80.
[77] Sinaki M, Wahner HW, Offord KP, Hodgson SF. Efficacy of nonloading exercises in prevention of vertebral bone loss in postmenopausal women: a controlled trial. Mayo Clin Proc 1989; 64(7): 762-9.
[78] Englund U, Littbrand H, Sondell A, Pettersson U, Bucht G. A 1-year combined weight-bearing training program is beneficial for bone mineral density and neuromuscular function in older women. Osteoporos Int 2005; 16(9): 1117-23.
[79] Korpelainen R, Keinanen-Kiukaanniemi S, Heikkinen J, Vaananen K, Korpelainen J. Effect of impact exercise on bone mineral density in elderly women with low BMD: a population-based randomized controlled 30-month intervention. Osteoporos Int 2006; 17(1): 109-18.
[80] Karinkanta S, Heinonen A, Sievanen H, *et al.* Maintenance of exercise-induced benefits in physical functioning and bone among elderly women. Osteoporos Int 2009; 20(4): 665-74.
[81] Holm L, Olesen JL, Matsumoto K, *et al.* Protein-containing nutrient supplementation following strength training enhances the effect on muscle mass, strength, and bone formation in postmenopausal women. J Appl Physiol 2008; 105(1): 274-81.
[82] Fredericson M, Chew K, Ngo J, *et al.* Regional bone mineral density in male athletes: a comparison of soccer players, runners and controls. Br J Sports Med 2007; 41(10): 664-8; discussion 8.
[83] Wittich A, Mautalen CA, Oliveri MB, *et al.* Professional football (soccer) players have a markedly greater skeletal mineral content, density and size than age- and BMI-matched controls. Calcif Tissue Int 1998 ; 63(2): 112-7.
[84] Calbet JA, Diaz Herrera P, Rodriguez LP. High bone mineral density in male elite professional volleyball players. Osteoporos Int 1999; 10(6): 468-74.
[85] Calbet JA, Moysi JS, Dorado C, Rodriguez LP. Bone mineral content and density in professional tennis players. Calcif Tissue Int 1998; 62(6): 491-6.
[86] Daly RM, Ahlborg HG, Ringsberg K, *et al.* Association between changes in habitual physical activity and changes in bone density, muscle strength, and functional performance in elderly men and women. J Am Geriatr Soc 2008; 56(12): 2252-60.
[87] Magkos F, Yannakoulia M, Kavouras SA, Sidossis LS. The type and intensity of exercise have independent and additive effects on bone mineral density. Int J Sports Med 2007; 28(9): 773-9.
[88] Morel J, Combe B, Francisco J, Bernard J. Bone mineral density of 704 amateur sportsmen involved in different physical activities. Osteoporos Int 2001; 12(2): 152-7.
[89] Nevill A, Holder R, Stewart A. Do sporting activities convey benefits to bone mass throughout the skeleton? J Sports Sci 2004; 22(7): 645-50.
[90] Nichols JF, Palmer JE, Levy SS. Low bone mineral density in highly trained male master cyclists. Osteoporos Int 2003; 14(8): 644-9.
[91] Rector RS, Rogers R, Ruebel M, Hinton PS. Participation in road cycling vs running is associated with lower bone mineral density in men. Metabolism 2008; 57(2): 226-32.
[92] Daly RM, Bass SL. Lifetime sport and leisure activity participation is associated with greater bone size, quality and strength in older men. Osteoporos Int 2006; 17(8): 1258-67.

[93] Delvaux K, Lefevre J, Philippaerts R, *et al.* Bone mass and lifetime physical activity in Flemish males: a 27-year follow-up study. Med Sci Sports Exerc 2001; 33(11): 1868-75.
[94] Nguyen TV, Center JR, Eisman JA. Osteoporosis in elderly men and women: effects of dietary calcium, physical activity, and body mass index. J Bone Miner Res 2000; 15(2): 322-31.
[95] Neville CE, Murray LJ, Boreham CA, *et al.* Relationship between physical activity and bone mineral status in young adults: the Northern Ireland young hearts project. Bone 2002; 30(5): 792-8.
[96] Lynch NA, Ryan AS, Evans J, Katzel LI, Goldberg AP. Older elite football players have reduced cardiac and osteoporosis risk factors. Med Sci Sports Exerc 2007; 39(7): 1124-30.
[97] Fujimura R, Ashizawa N, Watanabe M, *et al.* Effect of resistance exercise training on bone formation and resorption in young male subjects assessed by biomarkers of bone metabolism. J Bone Miner Res 1997; 12(4): 656-62.
[98] Hadjidakis DJ, Androulakis, II. Bone remodeling. Ann NY Acad Sci 2006; 1092: 385-96.
[99] Gregg EW, Cauley JA, Seeley DG, Ensrud KE, Bauer DC. Physical activity and osteoporotic fracture risk in older women. Study of Osteoporotic Fractures Research Group. Ann Intern Med 1998; 129(2): 81-8.
[100] Wickham CA, Walsh K, Cooper C, *et al.* Dietary calcium, physical activity, and risk of hip fracture: a prospective study. BMJ 1989; 299(6704): 889-92.
[101] Paganini-Hill A, Chao A, Ross RK, Henderson BE. Exercise and other factors in the prevention of hip fracture: the Leisure World study. Epidemiology 1991; 2(1): 16-25.
[102] Cummings SR, Nevitt MC, Browner WS, *et al.* Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group [see comments]. N Engl J Med 1995; 332(12): 767-73.
[103] Kujala UM, Kaprio J, Kannus P, Sarna S, Koskenvuo M. Physical activity and osteoporotic hip fracture risk in men. Arch Intern Med 2000; 160(5): 705-8.
[104] Farmer ME, Harris T, Madans JH, *et al.* Anthropometric indicators and hip fracture. The NHANES I epidemiologic follow-up study. J Am Geriatr Soc 1989; 37(1): 9-16.
[105] Coupland C, Wood D, Cooper C. Physical inactivity is an independent risk factor for hip fracture in the elderly. J Epidemiol Commun Health 1993; 47(6): 441-3.
[106] Gregg EW, Pereira MA, Caspersen CJ. Physical activity, falls, and fractures among older adults: a review of the epidemiologic evidence. J Am Geriatr Soc 2000; 48(8): 883-93.
[107] Nevitt MC, Cummings SR, Kidd S, Black D. Risk factors for recurrent nonsyncopal falls. A prospective study. JAMA 1989; 261(18): 2663-8.
[108] Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med 1988; 319(26): 1701-7.
[109] Buchner DM, Hornbrook MC, Kutner NG, *et al.* Development of the common data base for the FICSIT trials. J Am Geriatr Soc 1993; 41(3): 297-308.
[110] Wolf SL, Barnhart HX, Kutner NG, *et al.* Reducing frailty and falls in older persons: an investigation of Tai Chi and computerized balance training. Atlanta FICSIT Group. Frailty and Injuries: Cooperative Studies of Intervention Techniques. J Am Geriatr Soc 1996; 44(5): 489-97.
[111] Campbell AJ, Robertson MC, Gardner MM, *et al.* Randomised controlled trial of a general practice programme of home based exercise to prevent falls in elderly women. BMJ 1997; 315(7115): 1065-9.
[112] Buckwalter JA, Lane NE. Athletics and osteoarthritis. Am J Sports Med 1997; 25(6): 873-81.
[113] Berger MJ, Doherty TJ. Sarcopenia: prevalence, mechanisms, and functional consequences. Interdiscip Top Gerontol 2010; 37: 94-114.

Received: January 27, 2011 Revised: February 25, 2011 Accepted: March 07, 2011