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# The role of physical activity in bone metabolism and osteoporosis prevention

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### Abstract

**Introduction.** The attainment of peak bone mass in childhood and early adolescence can be ensured by proper diet, which includes a high intake of calcium and vitamin D, and by an adequate level of physical activity. During the period of skeletal involution physical exercise can reduce the rate of bone resorption, and improve motor coordination and prevention of falls. **Aim of Study.** The aim of the review is to discuss present-day views regarding the effects of physical activity on bone metabolism, and in particular, on osteoporosis prevention. Authors studying the effects of physical activity on bone tissue often classify physical exercises according to the volume of mechanical loads related to gravity and muscle strength. The reaction of bone tissue to mechanical loading depends on the frequency and intensity of the loads. Different forms of physical activity can be classified into *weight-bearing*, in which the athlete's skeleton is loaded by the athlete's own body weight, and *non-weight-bearing*. The forces acting on bone tissue in result of muscle contractions may additionally affect bone metabolism in loaded sites, and the resulting bone deformations inhibit resorption during bone remodeling. At later stages of life, prevention of falls becomes highly significant, that is why physical exercise should be aimed at the development of mass and muscle strength. In recent years there has been a growing interest in the role of vitamin D in proper bone mineralization and regulation of muscle strength and functional state of muscles. The intake of sufficient levels of vitamin D significantly lowers the risk of falls. **Conclusion.** Physical activity is a very important determinant of proper bone metabolism, both in pubescence and during skeletal involution. Physical activity is also conducive to the maintenance of muscle mass, which is an important element of osteoporosis prevention. Due to the crucial role of vitamin D in maintaining the proper condition of the musculoskeletal system various forms of outdoor physical activity are highly recommended.

**KEYWORDS:** bone, physical activity, vitamin D.

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### What is already known on this topic?

Physical activity is a very important factor in maintenance of proper bone metabolism and muscle mass, in pubescence as well as during skeletal involution. That can potentially increase or maintain bone mass and strength, and reduce the risk of falls in older populations, which is associated with the prevention of sarcopenia.

Osteoporosis, which is characterized by low bone mass and distortions of bone microarchitecture entailing an increased risk of fractures, is a serious social problem. The growing prevalence of osteoporosis is associated with the rising population of elderly people and lifestyle changes. In 2010, about 22 million women and 5.6 million men suffered from osteoporosis in the European Union. In the same year, there were 3.5 million reported bone fractures, including the hip fractures (610,000 cases), vertebral fractures (520,000 cases), the forearm fractures (560,000 cases), and other parts of the skeleton, e.g. the pelvis, rib, humerus, tibia, fibula, clavicle, scapula, sternum, and femur [1].

There are two general strategies of making the skeleton more resistant to fracture: 1) maximizing the gain in BMD in the first three decades of life; and 2) minimizing the decline in BMD after the age of 40 due to endocrine changes, aging, or other factors such as decline in physical activity [2].

The attainment of peak bone mass in childhood and early adolescence can be ensured by proper diet, which includes a high intake of calcium and vitamin D, and by a high level of physical activity [3, 4]. Michalopoulou et al. [5] showed that a high level of physical activity before puberty has a greater effect on long bone geometry, the size of cortical bone, and that the density of cortical and cancellous bone in girls with high levels of physical activity is higher than in their more physically passive counterparts. Bielemann et al. [6] noted a significant correlation between participation in sport activity of young people aged 11-15 years and the BMD of the femoral neck and lumbar spine measured after 18 years of age.

During the period of skeletal involution an inactive lifestyle leads to a faster decrease in bone mass, while increased physical activity can inhibit this decline [2, 7]. Feskanich et al. [8] in their study of postmenopausal women noted a reduced risk of hip bone fracture along with increasing physical activity. Furthermore, the undertaking of regular physical exercise by the elderly improves muscle strength and motor coordination, which reduces the risk of falls and fall-related bone fractures [2, 9, 10, 11]. Sarcopenia, i.e. the degenerative loss of skeletal muscle mass associated with aging, impairs muscle strength, general fitness and quality of life [12].

The significant impact of physical activity on bone metabolism has been confirmed by numerous studies on animals and humans [2, 13, 14, 15, 16]. Many authors show that after years of training athletes do have higher bone mineral density than non-training individuals at a similar age [17, 18, 19, 20, 21]. Significantly higher BMD in different parts of the skeleton was found in athletes representing such sports as gymnastics [22, 23], modern dance [24], jogging [25], tennis [26, 27], judo [20, 28], water polo [28], wrestling [20], basketball [29], volleyball [30], rugby [31, 32], handball [33], and soccer [34].

Numerous studies point to bone mass losses when bone tissue is deprived of the impact of the gravity force, e.g. during long-term immobilization. This is associated with the lack of mechanical loading of bones as well as losses in muscle mass [35]. According to some authors, the mechanical loads of bones result from the impact of

gravity and ground-reaction forces as well as muscle-reaction forces [19].

Osteocytes are regarded as the primary sensors of mechanical loads in bone tissue [36, 37]. Under the mechanical impact bone tissue is subject to stress and compressive forces causing tissue deformations, which induces an increased flow of the intraosseous fluid and generates streaming electric potentials [37, 38]. The latter stimulate osteocytes, regardless of the stimulation by the osseous fluid flux, which exerts a pressure on bone cell membranes [39]. Both factors contribute to the processing of mechanical stimulus into cellular response which leads to changes in the bone tissue structure [40]. The effect of mechanotransduction is the mechanism of bone tissue remodeling [41].

The skeleton is sensitive to mechanical stimulation at each stage of life; however, the bone tissue is more adaptable to structural changes before attaining the peak bone mass. The positive effects of physical activity are also observable at later stages of life, during which physical exercise usually leads to a decreased bone resorption rate, and improves motor coordination and fall prevention [42, 43]. The response of bone tissue to mechanical loading also depends on sex, genetic determinants, comorbidities, available nutrients, used drugs, or other biochemical factors [44].

The response of bone to mechanical loading depends on the type of mechanical stimuli. An important determinant of bone remodeling is the load size [45]. According to Harold Frost's Mechanostat theory in order to induce bone growth reaction the strength of the stimulus should exceed the threshold of tissue sensitivity to mechanical loads [46]. Skerry [47] points out that the stimulated bone mass growth is the result of tissue adaptation to increased mechanical loads. Rubin and Lanyon [45] found in their study on an animal model that this mechanism is not only determined by the volume of mechanical loads but also by the type of tissue tensions, in particular, the impact of compressive forces. Moreover, dynamic loads were shown to be of greater significance to the stimulation of bone remodeling than static loads [48]. An important role is also played by the load frequency [49, 50]. The sensitivity of bone to mechanical loads decreases during steady loading, and this is why interval stimulation is more effective than continuous stimulation [51].

The significance of mechanical loads for bone growth has been confirmed by studies on athletes representing different sports. BMD is greatly affected by physical activity that significantly loads the skeleton [19, 52, 53]. Examples of such activity include resistance

training [54, 55, 56, 57] and exercises involving great movement dynamics [20, 58]. In the comparison of BMD of the lumbar spine and the femoral neck in athletes of different sports Platen et al. [20] observed the greatest bone growth effects in athletes of sports involving quick, intense, and diverse body movements (jumps, short accelerations, quick stoppages). Exercises of lower loads, e.g. cycling, swimming, shooting, horse riding, water polo, bowling and billiards were shown to have a less significant impact on BMD changes [22, 59, 60, 61].

The effects of mechanical loads on bone tissue are confirmed by authors who observed that the bone mass of the dominant limb was significantly greater than the bone mass of the non-dominant limb in athletes after many years of training or on completion of their sports career. This was in particular noted in squash [62], tennis [63], volleyball [64] and basketball players [29]. Moreover, Kannus et al. [65] in a study of tennis and squash players noted that the difference in bone mass between the dominant and non-dominant arms was two-times to four-times bigger in athletes who began their sports career before or during puberty than in athletes who took up training about 15 years later. The aforementioned research confirms that bone sensitivity to mechanical loads depends on the stage of life. Thus such factors as the age of training commencement and sporting experience are crucial for bone mass growth [34, 66, 67].

As far as the significance of body weight for bone cell response is concerned some authors distinguish between weight-bearing sports in which the athlete's skeleton is loaded with the athlete's own body weight, e.g. volleyball, basketball, dance, soccer, rugby and squash; and non-weight-bearing sports in which the athlete's skeleton is offloaded or supported, e.g. cycling or rowing [19, 68].

Impact exercise, i.e. exercise consisting of overcoming one's own body weight, is to a large extent associated with the effects of ground forces on bone tissue. In the resistance exercises or exercises during which the athlete's body is supported, the main bone growth stimuli are contracting muscles [69, 70]. Yung et al. [70] observed that the most beneficial for bone tissue are weight-bearing exercises and exercises involving significant impact of the ground forces.

Despite the confirmed significance of physical activity for proper bone metabolism, some authors reveal a negative impact of training, especially with large training loads, on bone mineral density in some parts of the skeleton [71, 72, 73]. Such studies concerned

long-distance runners who displayed lower bone mineral content and BMD in the lumbar spine than non-training controls [74, 75]. Excessive training volume and intensity in endurance sports may disturb hormonal balance, e.g. the level of sex hormones, and thus impair bone metabolism [76, 77, 78]. Moreover, it is assumed that the imbalance between the presence of microdamages in bone due to frequent loading and the rate of bone remodeling is the cause of frequent fractures in athletes [79]. A study on an animal model showed that training with big loads, even exceeding 100% of athlete's body weight, can be less advantageous to bone metabolism than training with smaller loads (8% of athlete's body weight) [80]. Lower BMD was also noted after exercises in a body mass reduction program [81, 82]. Physically active girls and women also feature low BMD, which is one of components of female athlete triad. The Triad is a medical condition involving any one of the three components: 1) low energy availability (EA) with or without disordered eating (DE); 2) menstrual dysfunction; and 3) low bone mineral density (BMD) [83]. Depleted energy resources contribute significantly to the disorders of the menstrual cycle. Low estrogen levels can have a negative impact on musculoskeletal health [84]. Female athletes with irregular menstruation and/or low BMD display bone stress injuries, including a spectrum of stress reactions and stress fractures [85, 86]. In prevention of osteoporosis physical activity is an intervention that can potentially 1) increase or maintain bone mass and strength, and 2) reduce the risk of falls in older populations, which is associated with the prevention of sarcopenia [87].

In recent years the contribution of vitamin D to the regulation of muscle strength and function has been noted [88]. The main source of vitamin D in the human body (about 80%) is its dermal synthesis from 7-dehydrocholesterol (provitamin D) with UVB radiation at wavelengths between 290 and 315 nm. In Poland the optimal insolation for endogenous production of vitamin D occurs only from June to September. Dietary sources meet the human body's demand of vitamin D only to some extent (about 20%). In the human body previtamin D follows a long metabolic pathway. First, cholecalciferol is transported in the bloodstream to the liver, where in the process of hydroxylation it is converted into 25-hydroxycholecalciferol (calcidiol) [89, 90], which is the main vitamin D metabolite in the bloodstream. Calcidiol is also the most commonly used marker of vitamin D status in the human body, because it has a relatively long half-life of 2–3 weeks [91]. It is then converted in

the mitochondria of the proximal convoluted tubules of the nephrons into 1,25-dihydroxycholecalciferol (calcitriol) – the hormonal active metabolite of vitamin D, whose concentration is 1000 times higher than calcidiol, however, with the half-life of only 4-6 hours [89, 90]. Hydroxylation in the proximal tubules is the only source of the active metabolite of vitamin D. The activity of mitochondrial 1  $\alpha$ -hydroxylase was observed in other human cells such as macrophages, keratinocytes, the placenta, parathyroid glands, malignant cells, and smooth muscle tissue of blood vessels. It has not been detected in the heart, liver, or adrenal cortex. Outside the kidneys, locally synthesized 1,25-dihydroxycholecalciferol regulates (in an auto and paracrine fashion) important physiological functions of the aforementioned tissues [92].

Biologically active calcitriol, as well as its analogs, affect the target cells through the vitamin D receptor. VDR (55-56kDa) is a ligand activator regulating gene transcription together with other receptors such as glucocorticoids, retinoids, thyroxine, sex steroids, fatty acids and eicosanoids, and is classified as a receptor of steroid hormones [93]. VDR can be found in more than 30 tissues and organs of the human body: bone, kidneys, intestines, heart, blood vessels, brain, adrenal glands, pituitary gland, smooth muscle and striated muscle [94].

The discovery of VDR in skeletal muscle led to the recognition of its role as a regulator of muscle metabolism [95, 96]. There are three proposed mechanisms by which vitamin D affects muscle strength. The first comprises the direct role of 1,25(OH)<sub>2</sub>D in protein biosynthesis. By binding to nuclear VDR calcitriol regulates the process of transcription [97, 98]. The second is the modification of calcium transportation in the sarcoplasmic reticulum by increasing the effectiveness and/or the number of binding sites of calcium during muscle contraction [97]. The third mechanism is the contribution of vitamin D to aerobic energy processes as confirmed by a significant relationship between vitamin D and mitochondrial function [99]. Garcia et al. [100] indicated that calcitriol can also increase the amount of VDR in muscle cells and reduce myostatin expression.

Vitamin D deficiency is quite common and related to the geographical latitude (in moderate climate zones the sun exposure (UVB radiation) is not enough to produce sufficient amounts of dermal vitamin D), season of the year, skin pigmentation, air pollution and elevation [101, 102]. Furthermore, the high risk of vitamin D deficiency is observed in individuals suffering from malabsorption, nephritic syndrome, liver diseases, and

those who take some medicines increasing vitamin D metabolism, e.g. glucocorticosteroids, anticonvulsants, or immunosuppressants [103, 104].

The level of vitamin D in the human body is marked by the blood level of calcitriol. A 25OHD level below 75 nmol/l (30 ng/ml) is considered a state of insufficiency. Vitamin D deficiency is defined as a 25OHD level below 75 nmol/l (30 ng/ml), and its level below 50 nmol/l (20 ng/ml) is considered severe deficiency [94].

Many authors show that a low 25(OH)D blood level increases the risk of falls in the elderly, while proper vitamin D supplementation (700-1000 IU/day) lowers the risk for up to 19% [105, 106]. Calcitriol regulates the expression of vitamin D receptors in muscle cells and can also promote the diversity of these cells by intensifying the expression of IGF-II follistatin and reducing the myostatin expression [100, 107]. The number of VDR receptors decreases with age, which probably reduces muscle strength in the elderly. In conditions of vitamin D deficiency the muscle function and muscle performance can deteriorate before the appearance of any clinical and biochemical symptoms of bone disease [108]. The calcitriol level as shown by different studies is correlated with muscle contraction force and morphological characteristics of skeletal muscle [109, 110]. Grimaldi et al. [109] in their research on a large population of men and women, found a significant correlation between calcitriol and the isometric and isokinetic force of the upper and lower limbs. In another study on a population of elderly women with the 25(OH)D levels lower than 39 nmol/L in the gluteus medius muscle, the diameter of type II muscle fibers was smaller than in individuals with the correct levels of the metabolite [110]. Snijders et al. [111] in their study on an elderly population observed that the higher 25(OH)D concentration and lower PTH concentration increase the risk of sarcopenia.

Literature data show that physical exercise increases the demand for vitamin D, and the problem of vitamin D deficiency is also visible in athletes. Hamilton et al. [112] indicated that 91% of Middle Eastern male athletes had an insufficient level of 25(OH)D (<20 ng/ml). In their study population they found no associations between calcitriol levels and sun exposure, wearing clothes, or skin pigmentation. Lovell [113] noted a vitamin D deficiency (below 20 ng/ml) in 33% of studied Australian female gymnasts. Constantini et al. [114] showed that 73% of athletes had an insufficient level of vitamin D: in 80% of indoor athletes and in 48% of outdoor athletes. The most serious vitamin D deficiency was found among dancers (94%), basketball

players (94%) and taekwondo practitioners (67%). Hamilton [115], in a study of athletes representing various sports, observed an exceptionally high deficiency of vitamin D in athletes under heavy training loads. Similar conclusions were drawn by Willis et al. [116], who recommended monitoring of vitamin D levels for physically active individuals, since regular exercise does lead to vitamin D deficiency in the human body. On the other hand, Close et al. [117] concluded that vitamin D supplementation ensures the optimal functioning of muscles of athletes in winter time.

In conclusion, physical activity is a very important determinant of proper bone metabolism, both in pubescence and during skeletal involution. Physical activity is also conducive to the maintenance of muscle mass, which is an important factor of fractures prevention. Due to the crucial role of vitamin D in maintaining the proper condition of the musculoskeletal system various forms of outdoor physical activity are highly recommended.

#### What this study adds?

Vitamin D is necessary for the maintenance of structural integrity and function of the musculoskeletal system, therefore, various forms of outdoor physical activity are highly recommended to improve bone health.

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