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PHYSICAL ACTIVITY, NUTRITION, AND BONE HEALTH

review paper
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ABSTRACT
This review aims to describe the roles that physical activity and nutrition have in bone metabolism and to examine their effects on bone in a situation of altered metabolism as a consequence of inadequate nutrition and/or excessive physical activity. Referring to the recent studies and the main guidelines in the literature on athlete nutrition, the paper also focuses on essential nutrients for bone health during performance. Finally, it discusses the negative effect of some nutrients on bone mineral density.
Key words: osteoporosis, nutrition, bone metabolism, physical activity

Introduction

Bone tissue consists of specialized cells located in a mineralized matrix containing collagen fibres. The specific architecture and composition provides bone with exceptional solidity and resistance to pressure and traction. In spite of these characteristics and structural functions, bone is a living tissue, continuously changing during the phases of life. Bone remodelling takes place thanks to the balance between the demolition of the tissue by osteoclasts and its reconstruction by osteoblasts [1]. This process varies with age: during preadolescence, more than 50% of adult total bone mineral content (BMC) is obtained [2]; with aging, the activity of osteoblasts, producing new bone, can no longer completely replace bone tissue destroyed by osteoclasts, which leads to a loss of bone mass (i.e. osteopenia). When this loss is accentuated, the normal skeletal function becomes compromised, thus establishing a pathological condition known as osteoporosis. Osteoporosis is characterized by a decrease in the protein and mineral component of bone, with consequent skeletal microstructure alteration and fragility of bone, highly predisposed to fractures [3]. In particular, bone not only has the function of supporting and protecting the body, but it also intervenes in the balance of minerals, in the production of blood cells, and in numerous metabolic processes [4]. Furthermore, owing to its ability to produce osteocalcin, it can be defined as a true endocrine organ [5–7]. Being considered a metabolically active tissue, bone is in turn influenced by several factors such as sex hormones, growth hormone, insulin, diet (calcium, phosphate, vitamin D and A [8, 9]), and physical activity [10–12].

This review outlines the involvement of physical activity and nutrition in bone homeostasis.

Physical activity and bone

It is well established that many diseases can be prevented through physical activity [13]. Physical activity has a protective role against metabolic diseases, such as diabetes; furthermore, it helps prevent cardiovascular diseases (CVD) or manage hypertension [13]. Most studies have verified the influence of exercise on CVD mortality. Regarding bone metabolism, physical activity

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is also important to stimulate bone growth and help maintain and restore adequate bone mineral density (BMD), both in pathological and non-pathological conditions, supporting the regeneration of bone tissue. Exercise stimulates the production of electric fields in the bone that activate osteoblasts, causing new bone matrix synthetization [14]. Therefore, as it has been demonstrated, moderate physical activity increases bone mass [15] and can provide an important contribution in cases of low BMD [16]. In turn, bone loss results from the removal of mechanical loading [17], caused by sedentary life [18], bed rest, low body weight [17], or significant weight loss due to excessive physical exercise without adequate nutrition. Therefore, mechanical signals generated by exercise can prevent a reduction in the musculoskeletal system, and exercise-related improvement in cortical thickness can be effective in increasing the bone mass of bone structure sites, especially the trabecular and cortical sites [15]. Physical activity influences bone metabolism also through hormone secretion and local factors [15]. Besides, intestinal Ca^{++} absorption, energy metabolism, and the volume of skeletal muscles improved as a result of moderate exercise [19]. Therefore, the right amount and intensity of exercise combined with proper nutrition can be considered key factors to maintain adequate BMD. Although physical activity produces both mechanical and hormonal stimuli, the exact mechanisms underlying the exercise-related effect on bone metabolism are not clear.

How mechanical stress regulates bone metabolism: a possible explanation

Regarding mechanical stimulation, recent studies have shown that mechanical stress stimulates proliferation and differentiation of osteoblasts (the key cells involved in bone regulation) and inhibits the proliferation and activity of osteoclasts (the cells that regulate bone resorption and are essential for the balance of bone metabolism), modulating the anabolic and anticatabolic gene expression in bones, thus improving bone metabolism [20–22]. The mechanical stimulus provided by physical exercise seems to directly influence microRNA (miRNA), an abundant class of short non-coding RNA, molecules composed of about 22 nucleotides [23]. MiRNA and protein translation are involved in multiple biological processes including cell proliferation, differentiation, survival, transposing silencing [24], and self-renewal of stem cells [25]. MiRNA has been shown to play a regulatory role in bone metabolism [26, 27], in mesenchymal bone marrow stem cells (BMSC) and in osteoblasts [28], which suggests that miRNAs could be one of the main mechanisms by which exercise or mechanical load regulate bone metabolism and promote bone formation. MiRNAs regulate the proliferation and differentiation of osteoblasts and osteoclasts and, subsequently, bone metabolism [29]. However, the numerous miRNAs can play different and opposite roles: while some promote osteoblast proliferation and differentiation, others have been shown to inhibit osteoblast proliferation and differentiation [30]. Lack of mechanical stimuli, as experienced by patients bedridden or under microgravity conditions, results in osteoporosis [17, 31, 32], although miRNAs are not the only mechanism by which mechanical stress regulates bone metabolism. However, it is shown that they are influenced by mechanical loading effects on bone formation by modulating the expression of osteogenic factors or bone resorption factors. The response of bone cells to a mechanical stress stimulus is negatively affected when critical miRNAs are lacking.

Adequate physical activity and bone metabolism

Although numerous studies report that trained subjects have a greater BMD (osteogenic effect) compared with untrained ones [33, 34], it is crucial to identify the volume, intensity, and frequency of training suitable for stimulating osteogenic activity. Below, some of the different types of training responsible for the osteogenic effect are described.

Resistance training vs. aerobic activities

Recent studies show that resistance training helps maintain homeostasis and has numerous metabolic effects [35].

Bone deformation during resistance training is associated with higher improvement in BMD as compared with exercise performed at a lower intensity, e.g. running results in more mechanical stress than aerobic activity [36–39]. As the magnitude of the stimulus proved to be more important than its frequency [37–40], a relationship between BMD and the level of muscular strength could be hypothesized [39, 41, 42], although the type of muscular contraction also plays a key role. In particular, an eccentric contraction stimulates the bone more than a concentric contraction [43, 44], and it is therefore more effective in BMD increasing [45]. For example, comparing concentric and eccentric contractions trainings for the knee extensors and flexors,

Hawkins et al. [45] showed that only subjects who administered eccentric training had a increase of 3.9% in the femoral BMD. These results were confirmed in a recent study [46] in which cyclic mechanical stretch was shown to up-regulate the protein expression of Runx2 and promote osteoblast proliferation, which explains the biomolecular mechanisms in the bone during the eccentric and elongation phase.

Osteoporosis prevention with physical activity

As strength training is an important form of exercise for bone growth, there are other activities recommended for the prevention of osteoporosis by health organizations [47, 48]. Weight-bearing exercises, high impact exercises such as jumping, plyometric training (jumping/hopping), and weight lifting [49] have positive effects on bone, regardless of age [50]. The subject's age is another important factor of physical exercise effect on bone metabolism because the bone response to mechanical stress changes during lifetime. In adolescence, resistive exercise can increase bone strength [51], whereas during middle age and after puberty it can help to reduce loss of bone mass and density [50]. The combination of high impact or weight-bearing and aerobic training can prevent age-related bone loss [52] but aerobic activities, such as cycling, walking, yoga, and swimming, are not osteogenic [52]. Therefore, to provide the magnitude of load necessary to maintain bone mass and density, it is crucial to combine low-load activities, such as aerobics, with resistance exercises.

Possible negative effects of excessive physical activity on bone

Physical activity inadequate in volume and intensity could have negative effects on bone metabolism, leading to a loss of BMD up to osteoporosis when very intense physical exercise is associated with inadequate caloric intake (in particular, that of specific nutrients) [53] and low starting BMD. Bone stress as a consequence of high-intensity physical activity can be more easily manifested in women. As female sex hormones (oestrogens) play a key role in bone metabolism and their concentration can be influenced by physical exercise [54], high intensity of endurance training might lead to an early bone loss due to an excessive decrease in body fat. Therefore, low level of oestrogen synthesis substrate and the effects of the female sexual hormones on the bone homeostasis are altered [54]. Although there is a bone strengthening effect of physical activities with overload, intense training may cause low hormonal production, with a negative effect on the axial bone health, mainly in women. However, the bone loss in this case occurs because of a caloric deficit, and an appropriate nutritional diet could help avoid these hormonal disturbances in female athletes [55–57].

Nutrition effects on physical activity and bone. General considerations for athletes' nutrition

To guarantee the necessary energy for intense physical activity and to help avoid the aforementioned problems, adequate diet must include the right contribution of all the main nutrients, as enumerated below.

Fat

Lipids (or fats) are organic compounds widely diffused in nature, representing one of the four main classes of organic compounds of biological interest, together with carbohydrates, proteins, and nucleic acids. They constitute an important energy reserve, especially during long-term exercise, being the main sources of skeletal muscle adenosine triphosphate (ATP) production [58]. Chronic exercise training results in favourable mitochondrial adaptations in adults, which enhance lipid metabolism as well [59], although gender differences in relative fat and carbohydrate oxidation during exercise exist [60]. Dietary lipids are essential for the absorption of vitamins and for sex hormones homeostasis [61]. In terms of caloric requirements, most sources recommend that lipid intake should be limited to 25–30% of the total caloric intake. Nonetheless, caloric demands are increased in athletes [62], and lipids are important to produce hormones involved in healthy growth, maturation, and bone metabolism [63]. Ingested lipids differ in the composition of the hydrocarbon chain and this can affect the metabolism [64, 65]. In particular, monounsaturated fatty acids can potentially have a favourable effect on body composition [66]; fish oil and conjugated linoleic acid could exert ergogenic and anabolic effects on exercise, being also related to increased testosterone synthesis.

Protein

Proteins are biological macromolecules made up of chains of amino acids linked to one another by a peptide bond. Their functions are mainly structural and synthesis-related, but they also play a role in energetic processes, although in a lower percentage compared with carbohydrates and fats, with a greater thermic

effect [67]. Consequently, they are fundamental to guarantee a good physical performance. The adequate protein intake indicated by the American College of Sports Medicine (ACSM) is 1.2–1.8 g/kg of body mass for active adults [68, 69], with athletes requiring higher protein intake to maintain protein synthesis [70]. In particular, a recent study has shown that the ingestion of 20 g of protein post-exercise helps maintain positive protein balance following exercise [71].

Carbohydrate

Glucides or glycides are organic chemical compounds formed of carbon, hydrogen, and oxygen atoms, constituting the carbohydrate biomolecule class. On the basis of their chemical structure, carbohydrates are classified into simple and complex and some confusion exists in athletes' understanding of specific carbohydrate needs. General carbohydrate intake recommendations suggest adult athletes to consume 5–12 g of carbohydrate per kilogram per day but this dependent on different exercise/activity, its intensity, duration, and volume, as well as the environmental conditions in which physical activity takes place. Moreover, as men and women are biologically different, they react differently to physical exercise and consequently the caloric intake, especially from carbohydrates, should be adapted to their needs [72]. It is therefore difficult to suggest the exact carbohydrate intake necessary for an athlete during particular activities. However, Burke et al. [72] suggested that carbohydrate ingestion during activities lasting 45 minutes or longer provides an ergogenic effect with doses varying from small ones up to 90 g/hour, whereas ACSM recommends that athletes should ingest simple sugars at the rate of 30–60 g/hour for exercise lasting longer than 60 minutes. Additionally, Amato et al. [69] showed that gymnastics performance improved after eating a carbohydrate snack compared with a different pre-exercise meal.

Micronutrients

Micronutrients, subdivided into vitamins and minerals, are ingested substances whose main function is not directly related to energy production and growth. Among vitamins most important for homeostasis, vitamin A is involved in immune function, vision, reproduction, and cellular communication [73–75], also supporting cell growth and differentiation [76], whereas vitamin B_{12} helps keep the nerve and blood cells healthy and supports DNA synthesis, also preventing megaloblastic anaemia, which makes people tired and weak [77]. Furthermore, being important in the cross-linking of collagen fibres in bone [77], vitamin C (ascorbic acid) is a cofactor in the hydroxylation of lysine and proline, whereas vitamin K is a cofactor in the gamma-carboxylation of glutamic acid, important in the production of osteocalcin [78, 79].

One of the most important minerals for homeostasis is magnesium, involved in bone and mineral homeostasis, crucial for bone crystal growth and stabilization. Magnesium, along with other nutrients found in fruit and vegetables, contributes to an alkaline environment and may promote bone health through a variety of mechanisms, therefore it is difficult to examine the effects of magnesium alone. The recommended dietary allowances (RDAs) for magnesium are 400–420 mg daily for males and 300–320 mg daily for females [80].

Phosphorus is an essential bone-forming element and, as in the case of calcium, an adequate supply of phosphorus to bone is necessary throughout life. Both calcium and phosphorus are required for an appropriate mineralization of the skeleton, and a depletion of serum phosphate leads to impaired bone mineralization, compromising osteoblast function [81]. Furthermore, a combined supplement of calcium, zinc, manganese, and copper produced increases in BMD [82]. Finally, boron has effects on urinary calcium excretion and associations with BMD have been reported [83].

As higher BMD has been associated with a higher dietary potassium intake [80], the electrolytes of sodium and potassium play an important role in the development and prevention of osteoporosis. The adequate intake for potassium is 4700 mg daily for males and females [80].

Another essential component is iron, involved in erythrocyte protein, haemoglobin, which transfers oxygen from the lungs to the tissues [84]. It is also necessary for growth, development, normal cellular functioning, and synthesis of some hormones and connective tissue [75, 85]. The RDAs for iron are 8–11 mg daily for males and 8–15 mg daily for females [75]. Athletes will likely find additional benefit from including other iron-rich foods, such as peanuts, dried fruit, and iron-fortified cereals as regular snacks. Furthermore, the inclusion of foods higher in ascorbic acid with these nonheme iron sources will improve iron absorption from these snacks [85].

Athletes' nutrition for bone health

Low energy availability due to exhausting physical exercise linked with failure of diet intake of the above-

mentioned nutrients can impair bone health. In particular, values below the minimum energy threshold (30 kcal · kg lean body mass [LBM]$^{-1}$ · d^{-1}) [86] can alter physiological mechanisms such as cell repair, thermoregulation, immunity, growth, and bone turnover through the distorted levels of metabolic hormones and substrates, such as growth hormone, cortisol, fatty acids, and glucose among the most important ones [87]. Under this threshold, the levels of carboxyterminal propeptide of type 1 procollagen (P1CP) and osteocalcin, the matrix mineralization measure, were significantly reduced [88]. The minimum energy threshold for athletes' population has been identified as 45 kcal · kg LBM^{-1} · d^{-1} [86], depending on many factors, such as the different types of physical activities, environmental conditions, and physical characteristics of each athlete. As an example, elite runners need 6 kcal · kg LBM^{-1} · d^{-1} [88], while triathletes require 24–33 kcal · kg LBM^{-1} · d^{-1} [89].

Carbohydrate and protein intake

With a mixed meal, calcium, glucose, protein can supresses bone resorption at rest [90]. Gastric inhibitory polypeptide (GIP) and glucagon-like peptide-2 (GLP-2) are potential mediators of the post-prandial regulation of bone turnover [91]. Henriksen et al. [90] showed that only GLP-2 was secreted with glucose and protein ingestion and was in parallel with the suppression of beta C-terminal telopeptide (β-CTX). The effects of carbohydrate supplementation during intermittent running is bound with bone turnover markers (a carbohydrate beverage including 1 g · kg body mass [BM]$^{-1}$ of maltodextrin reduced β-CTX, increased bone formation, and decreased resorption) [92]. Another study demonstrated that a carbohydrate drink (glucose) before, during, and after running exercise at 70% VO_{2max} attenuated procollagen type 1 amino-terminal propeptide (P1NP) responses [93]. The same author showed that a carbohydrate drink attenuated the rise in the circulating interleukin 6 (IL-6), an osteoclastogenesis activator associated with exercise. Moreover, eating in close proximity to exercise also suppresses bone resorption at rest but can cause gastrointestinal discomfort, impairing performance [94]. Simple carbohydrates and proteins are not likely to cause gastrointestinal complaints as they contain little fibre or fat, which means that digestion is quick [95]. A carbohydrate + protein recovery drink consumed immediately post-exercise is beneficial for endurance athletes [96], in whom the ingestion of a carbohydrate + protein solution (containing 1.5 g · kg BM^{-1} of carbohydrate and 0.5 g · kg BM^{-1} of protein) immediately after an exhaustive run suppressed β-CTX concentrations, although a delayed ingestion of the carbohydrate + protein solution (2 hours post-exercise) also resulted in a large suppression of β-CTX concentrations.

Ca^{++} and vitamin D intake

Calcium is a key factor to keep human body homeostasis. It is involved in many vital functions, such as cellular processes including exocytosis, neurotransmitter release, muscle contraction, and the proliferation of action potentials through the cardiac muscle. Bone is the largest reservoir of calcium in the body and reductions in serum ionized calcium are therefore mitigated by demineralization of bone, a process stimulated by increases in the parathyroid hormone (PTH). The cross-linked C-telopeptide of type I collagen (CTX-I) and, more recently, cross-linked C-telopeptide of type II collagen (CTX-II) have been indicated as sensitive markers of osteoclastic bone resorption, while the procollagen I N-terminal propeptide (PINP) is determined as a marker of osteoblastic bone formation [97]. Furthermore, calcium absorption is dependent on adequate levels of vitamin D [98]. Vitamin D is obtained either from the diet or by synthesis in the skin under the action of sunlight. The report on dietary reference intakes for calcium and vitamin D by Ross et al. [98] shows that all individuals meet their needs at RDAs for vitamin D, at 25-hydroxyvitamin D (25(OH)D) levels of at least 20 ng/ml (50 nmol/l) even under conditions of minimal sun exposure [98]. Associations have been reported between plasma 25(OH)D and BMD in middle-aged and older women [99, 100]. Supplementation with calcium and vitamin D together resulted in sizeable reductions BMD loss; bone loss was limited to subjects with a daily calcium intake below 400 mg [77, 101]. However, it is not clear what the pre-exercise meal able to guarantee the right amount of calcium to an athlete is, especially during long-lasting and high-intensity sports, when there is a great sweat calcium loss. For example, it has been observed that ~1000 mg calcium supplement pre- or post-exercise reduces bone resorption markers levels [94, 102]. A recent study by Haakonssen et al. [94] shows that a calcium-rich pre-exercise meal can maintain serum ionised calcium and reduce post-exercise increase of PTH and CTX-I, especially among endurance athletes.

Good foods and bad foods for bone health

The interaction between food supplementation, sport, and bone health is complex. Recent studies show that

in addition to the integration of 'positive' nutrients for bone homeostasis, there are some foods that, on the contrary, can be negatively related to BMD if taken in excess. For athletes with chronic energy deficiency, an excess of fibre, phytic and oxalic acids, isoflavones, and vegetable proteins with an imbalance of other essential macro- and micronutrients can be detrimental to bone health [67]. Dietary fibre can influence the energy availability and digestibility of complex foods. It can interact with proteins and fats and decrease the metabolizable energy of a diet, influencing the digestibility of these components [103]. Because dietary fibre increases most intestinal contents and accelerates calcium and other minerals transit time in the intestine, it causes loss of time to absorb these nutrients. Foods rich in phytic acid, such as wheat bran, legumes, seeds, nuts, and soy isolates, can reduce bioavailability and thus prevent the beneficial effects of nutrients such as calcium, magnesium, and protein on the bones [67]. Dietary fibre is inversely associated with the levels of the luteinizing hormone, follicle-stimulating hormone, oestradiol, and progesterone [104], and oestrogen plays a significant defensive role in oxidative stress [105] and attenuates bone endocortical reabsorption [106]. Moreover, it is already clear that reactive oxygen species (ROS) induce the apoptosis of osteoblasts and osteocytes; this inhibits osteogenesis, favouring osteoclastogenesis. Antioxidants like polyphenols and anthocyanins, the most abundant antioxidants in the diet, counteract the action of oxidants, contributing to the prevention of bone loss [107]. Specific nutritional approaches suggest the antioxidant use to counteract the resorption. Excess consumption of such foods is predominant in sports in which aesthetics and the maintenance of adequate weight are essential. However, further studies are needed to provide understanding of the recommended quantity of this type of food and the athlete's starting condition that can cause osteopenia.

Conclusion

The objective of this review was to point out how nutrition and physical activity interact with each other and how they affect bone metabolism. This issue is important for the prevention of bone disease such as osteoporosis. Bone health constitutes a crucial aspect for an athlete. Bone metabolism is the basis of good musculoskeletal system function and thus favourable performance, which is in turn strongly related to the right energy derived from nutrients intake. Recent studies show how bone metabolism, diet, and training are interconnected and crucial for elite athletes. Although the purpose of this review was to clarify how these elements interact with each other, further studies are necessary to illustrate some other key elements, such as adequate bone markers to be used to monitor bone health, the exact quantity and quality of nutrients in the diet, and the correct volume, frequency, and intensity of training with the consideration of the biological characteristics of an athlete.

Ethical approval

The conducted research is not related to either human or animal use.

Disclosure statement

No author has any financial interest or received any financial benefit from this research.

Conflict of interest

The authors state no conflict of interest.

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