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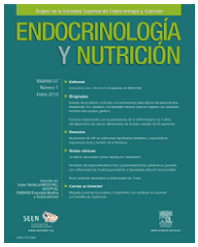

SHORT REVIEW

High bone density and bone health

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Abstract The aim of this paper is to review the main aspects related to high bone density (HBD) as well as to discuss the physiologic mechanisms involved in bone health. There are still no well-defined criteria for identification of individuals with HBD and there are few studies on the topic. Most studies demonstrate that overweight, male gender, black ethnic background, physical activity, calcium and fluoride intake and use of medications such as statins and thiazide diuretics play a relevant and positive role on bone mineral density. Moreover, it is known that individuals with certain diseases such as obesity, diabetes, estrogen receptor-positive breast or endometrial cancer have greater bone density than healthy individuals, as well as athletes having higher bone density than non-athletes does not necessarily mean that they have healthy bones. A better understanding of risk and protective factors may help in the management of patients with bone frailty and have applicability in the treatment and in the prevention of osteoporosis, especially intervening on non-modifiable risk factors.

PALABRAS CLAVE
Hueso y huesos;
Dieta;
Densidad ósea

Densidad ósea elevada y salud ósea

Resumen El objetivo de este artículo es revisar los aspectos principales relacionados con la Densidad Ósea Elevada (DOE) y analizar los mecanismos fisiológicos implicados en la salud ósea. No existen aún criterios bien definidos que sirvan para identificar a los individuos con DOE, y los estudios sobre el tema son escasos. La mayoría de los estudios demuestran que el exceso de peso, el sexo masculino, la raza negra, la actividad física, la ingesta de calcio y flúor y el uso de medicamentos como las estatinas y los diuréticos tiazídicos desempeñan un papel relevante y positivo en la Densidad Mineral Ósea (DMO). Además, se ha observado que los individuos con enfermedades tales como obesidad, diabetes, cáncer de mama positivo para receptores de estrógenos o cáncer del endometrio tienen mayor DMO que los individuos sanos; del mimo modo, se observa una mayor DMO en atletas frente a los que no lo son, sin que

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ello necesariamente sea sinónimo de salud ósea. Un mejor entendimiento de los factores de riesgo y de protección podría ayudar a mejorar el tratamiento de los pacientes con fragilidad ósea e incidir en la prevención de la osteoporosis, especialmente en los factores de riesgo no modificables.

Introduction

The high prevalence of osteoporosis and fractures due to bone frailty worldwide underscores the importance of seeking new prevention and treatment strategies,[1] such as the identification of factors involved in the increase of bone mineral density (BMD) for possible applicability in high risk populations. Few studies have addressed the prevalence of high BMD or the main clinical and laboratory aspects of individuals with high BMD. Most of these studies indicate that the following factors seem to have a positive influence on bone density: anthropometric factors (weight and body mass index [BMI] above 30 kg/m^2),[2] demographic factors (male gender, black ethnic background),[3] genetic factors (LRP 5 mutations),[4] healthy lifestyle habits (regular physical activity,[5] calcium intake above 1500 mg/day)[6] and use of medications such as statin[7] and thiazide diuretics.[8] Moreover, individuals with certain diseases as obesity, estrogen receptor-positive breast or endometrial cancer[9,10] and type II diabetes[11] have greater BMD than that of healthy individuals and among healthy subjects as athletes have greater bone density than non athletes.[12] Based on the items addressed in the studies cited above, the aim of this paper is to review and discuss the aspects related to high BMD and to bone health.

High bone mineral density

The occurrence of high bone density (HBD) has been described in the literature in the last ten years. However, yet there are no well-defined criteria for adequate and precise identification of HBD. In 1994, the World Health Organization defined criteria to characterize normal and low bone density (osteopenia and osteoporosis).[13] However, there is currently no consensus on the cutoff point for the definition of individuals with high BMD.

A cohort study involving more than 1800 women[14] suggests that the cutoff point for high BMD is 1.209 g/cm^2 for the femoral neck and 1.228 g/cm^2 for the lumbar spine (upper quartiles). Assessing more than ninety six thousand bone densitometry exams, Gregson et al.[15] defined *Z*-score equal to or greater than 3.5 standard deviations for spine and/or hip for the characterization of such individuals; based on this criterion, only 169 individuals with HBD were found (approximately 0.2% of the overall sample). Beginning with the premise that a *T*-score less than or equal to −2 standard deviations indicates low bone density and so a greater risk for fractures, it is reasonable to assume that a *T*-score above +2 standard deviations in the absence of fractures or diseases known to affect bone quality to define HBD.

However, there is no reference in these definitions regarding the relation between high bone mass and bone health reflected by a lower rate of stress or bone frailty fractures and better bone quality and strength. In other words, it is not known if higher BMD is truly associated with bone healthy.

The main factors associated to HBD are unknown.[4] Genetic, mechanical, environmental, nutritional and endocrine factors are among the determinants related to the acquisition peak bone mass, to bone health and potential factors associated with HBD are discussed below.

Genetic factors

Genetic factors account for 75–80% of the variation in bone mass peak.[16] An increase in bone mass may be caused by rare (often hereditary) osteochondrodysplasias and a variety of dietetic, metabolic, endocrine, hematological, infectious and neoplastic disorders.[17]

Low-density lipoprotein receptor-related protein 5 (LRP5) gene mutations and some other mutations are among the most studied genetic factors.

LRP5 is involved in the Wnt canonical signaling pathway, in which it acts as a coreceptor and regulator of the intracellular signaling of β-catenin. Expressed in various tissues, LRP5 is considered a key protein for the physiology of bone tissue as well as in different pathological processes that include bone formation or neoformation.[18] Mutations in the LRP5 gene are responsible for bone abnormalities, such as high bone mineral density and osteoporosis-pseudoglioma syndrom.[4]

Genetic mutations and gene polymorphisms may cause either positive or negative phenotype modifications in bone tissue. Thus, it is of clinical importance to know whether an excess in expression or gain in function of a particular gene, such as VDR, could be associated to high BMD or to a lesser risk of fractures.

Non-genetic factors

Non-genetic factors account for 20–25% of peak bone mass and may change over time. The main modifiable factors and physiopathogenic mechanisms suggested for health and increase in bone mineral density are displayed in Table 1.

Details on the positive influence of these factors on bone tissue are provided below.

Anthropometrics and body composition

The vast majority of studies include body weight as a positive factor for bone density with 10–20% of the variation in bone density related with high BMI.[19] In a cohort study carried out with more the sixteen thousand women over