Bone Density Measurements and Biomarkers in Nutrition: DXA (Dual X-ray Absorptiometry), Osteopenia, and Osteoporosis

51

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Contents

Abstract

The continuous interest of researchers for osteopenia, as well as osteoporosis, has resulted in an enrichment of existing knowledge with new scientific findings. The purpose of this chapter is to provide a concise and critical summary of published research literature concerning the epidemiology, etiology, bone physiology and pathophysiology, clinical manifestations and diagnosis, and prevention and management of these "insidious" diseases. While osteopenia is a clinical condition where bone mineral density is below normal, osteoporosis is a severe systemic

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skeletal disorder characterized by decreased bone mass and disruption of bone microarchitecture resulting in reduced endurance, fragility, and propensity to fracture. Osteopenia and osteoporosis are age related and manifest more often after menopause in women and later in men. Osteoporosis can be compared to other serious health problems, because bone fractures are associated with a high degree of morbidity, mortality, and disability. Fractures have usually impairment in activities of daily living and, not uncommonly, are the beginning of an institutionalized life. Clinically, the symptoms are bone deformation and diffused pain, especially in the spine, but osteoporosis and osteopenia could be asymptomatic. In the last 15 years, osteoporosis has become a major focus. The first step for an efficacious cure is the early diagnosis through measurement of bone density with DXA, before fracture risk becomes too high. Accordingly, prevention of bone fractures is of utmost importance at advanced age and is directly related to bone health. Optimization of bone condition must be the main concern throughout life for both men and women. Stepping-stone for this is the regulation of all the parameters that affect vitally the quality of life, mostly nutrition and exercise.

Keywords

Osteoporosis · Osteopenia · Bone mineral density · Bone mass · Nutrition · Biomarkers · DXA

Abbreviations

BMC	Bone mineral content
BMD	Bone mineral density
BMI	Body mass index
DXA	Dual-energy X-ray absorptiometry
NOF	National Osteoporosis Foundation
QCT	Quantitative computed tomography
WHO	World Health Organization

Introduction

Osteopenia and osteoporosis, both defined as states of abnormally low bone mineral density (BMD), are common musculoskeletal disorders, especially in the elderly. In particular, osteopenia is a clinical term that describes a decrease in bone mineral density below normal reference values (but not low enough to meet the diagnostic criteria for osteoporosis) (Table 1). As defined by the World Health Organization (2007), a T-score between −1 and −2.5 defines osteopenia (while values less than −2.5 are diagnostic for osteoporosis) (Table 2). Decreasing BMD values are indicative of an underlying disruption in the microarchitecture of bone and quantitative disorder of bone mineralization (Porter and Varacallo 2021). A combination of physical, metabolic, and/or endocrine factors is considered to be the cause for osteopenia (Raisz 2005). Generally, decreased daily living activities reduce the

Table 1 Differences between osteopenia and osteoporosis

Osteopenia	Osteoporosis
Low bone mass below normal	Too low bone mass
$-1 > T > -2.5$	$T \leq -2.5$
Higher prevalence than osteoporosis	Lower prevalence than osteopenia
Low fracture risk	High fracture risk
May progress to osteoporosis	Osteoporosis is established
No fragility fracture	Presence of fragility fracture in severe cases
Medication is necessary only in the presence of risk factors	Medication is always necessary

Table 2 Diagnostic criteria for osteoporosis

Classification	*T-score*
Normal	$T \geq -1$ (SD*)
Osteopenia	$-1 > T > -2.5$
Osteoporosis	$T \leq -2.5$
Severe (or established) osteoporosis	≤ -2.5 and osteoporotic fragility fracture

[a]SD = standard deviation below the young adult female reference mean

mechanical loading to both bone and skeletal muscle and may result in a decrease of BMD as osteopenia (Toshima et al. 2018).

Conversely, osteoporosis is a severe systemic skeletal disorder characterized by reduced bone mass, microarchitectural deterioration of bone tissue, and a propensity to fracture (National Osteoporosis Foundation [NOF] 2013). Osteoporosis is one of the major and growing healthcare problems around the world, largely related to the general aging of societies (World Health Organization [WHO] 2007). In the last 15 years, age-related osteoporosis has become a major focus, and significant progress has been made both in defining this disorder and in understanding its complex pathogenesis. Most importantly, a consensus has emerged concerning the strength of the association between low bone mineral density and fracture risk (Kanis, 1994, 2002; NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy 2001).

Osteoporotic bone fractures are associated with a severe degree of disability and a high direct cost for rehabilitation and have an adverse impact on mortality (Cole et al. 2008a; WHO 2007). Thus, prevention of osteopenia and osteoporosis is of utmost importance, especially for the elderly.

The purpose of this chapter is to provide a concise and critical summary of published research literature concerning the epidemiology, etiology, bone physiology and pathophysiology, clinical manifestations and diagnosis, and prevention and management of osteopenia and osteoporosis. This will help researchers, physicians, and other health professionals to keep current on the evidenced-based research about theses "insidious" diseases.

Epidemiology

Osteoporosis affects more than 75 million people in the USA, Europe, and Japan, while worldwide it is involved in approximately 8 to 9 million fractures annually, of which 4,5 million were in the USA and Europe (WHO 2007). Osteoporotic fractures account for 0.83% of the global burden of non-communicable disease, and the 1.75% of the global burden is in Europe (Johnell and Kanis 2006). In 2000, the total disability-adjusted life years (DALYs) lost were 5.8 million, of which 51% were due to osteoporotic fractures that occurred in Europe and the Americas. The annual financial cost in Europe (approximately 48 billion dollars) is higher than that of cancer or cardiovascular diseases (Kanis and Johnell 2005).

Epidemiologic studies have subsequently provided insight into the prevalence of osteoporosis in the elderly population (Cole et al. 2008a; Umland 2008). Although fractures of the hip, wrist, and spine are often focused upon almost any bone can fracture, virtually, all fractures in the elderly can be attributed to osteoporosis, whether primary or secondary, and evidently, the occurrence of these fractures increases exponentially with age (Gooren 2007; WHO 2007).

Osteoporosis affects both women and men and has an impact comparable to, if not greater than, the major health problems, such as cardiovascular disease and malignancy. The female-to-male ratio of hip fractures is approximately 2:1 (DeLaet and Pols 2000; NOF 2013). Men, probably due to their larger accrual of bone mass in puberty, suffer bone fractures approximately 10 years later in life than their female counterparts, and using a delay of approximately 10 years for comparison with women, incidence and prevalence rates in men are not very different from the rates in women. But, men's clinical condition at that age has usually also deteriorated, and it is not surprising that morbidity associated with fractures and their (surgical) treatment is considerably greater than in women.

Morbidity and mortality following bone fracture have been the focus of many research efforts carried out over the last few decades (Tosteson et al. 2007). These endeavors concern mainly the hip fractures, which have a detrimental effect on quality of life, after only 30% of the elderly retrieves the level of functionality that was before fracture. Almost 1/3 of patients with hip osteoporotic fracture are hospitalized even for 1 year, and it is remarkable that one of five patients departs within the first year after the fracture. Fractures in hips and the vertebrae occur mainly in women aged over 70 or 80 years, and fractures in the wrist occur mostly in women between 50 and 70 years, while all other fractures, such as in the pelvis, can occur throughout life after menopause (NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy 2001).

Osteoporosis has become a major problem even in developing countries. The prevalence of osteoporosis and incidence of fracture vary by gender and race/ethnicity. The incidence of hip fractures in relation with age is higher in Caucasians than in Asians, but there is a lot of variation even between the different communities of the same race (Eisman 1999; NOF 2013). The probability for a 50-year-old white woman or man to sustain hip fracture, during lifetime, is 14% and 5–6%, respectively. Over 50% of postmenopausal white women will have an osteoporotic-related fracture (Porter and Varacallo 2021). The risk for African Americans is very less, 6%

and 3% for a 50-year-old woman or man, respectively (NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy 2001). The difference in frequency between ethnic and racial groups may be related to environmental factors but can also reflect heritable differences in vulnerability.

Etiology

From birth to adulthood, there is a bone mineral acquisition that follows a predictable trend specific to an individual's age and sex. During puberty, bone mineral gain increases to its maximum level, and this bone mineral accretion rate remains the greatest for males and females for about 4 years after the peak gain rate is achieved. The 95% of adult bone mass is achieved by age 17 for females and 21 for males; thus, peak bone mass is normally achieved by the third decade of life. After the age of 30, there is a gradual and natural bone mass reduction that continues for the later life (Weaver et al. 2016). Failure to reach peak bone mass in adolescence and adulthood results in early-onset conditions of decreased bone mass (or osteopenia) and increased risk of osteoporosis and fragility fractures in later life.

Heritable factors contribute up to 80% to the ability to attain and maintain optimal bone mineral density level (Varacallo et al. 2021). Natural bone mass reduction in adulthood occurs gradually due to modifiable factors which include body mass, nutrition status (adequate calcium and vitamin D daily intake), weight-bearing exercises, and hormonal status. This natural bone loss is considered to be the cause of primary forms of osteopenia and osteoporosis, while secondary causes accelerate this process (including lifestyle factors like smoking, abuse of alcohol, and sedentary lifestyle).

Primary osteoporosis is related to the aging process in conjunction with decreasing sex hormones. There is deterioration in bone microarchitecture, leading to loss of bone mineral density. Secondary osteoporosis and low bone mass state (osteopenia) are caused by other diseases or their treatments (e.g., hyperthyroidism, hyperparathyroidism, anorexia, malabsorption syndromes, hypogonadism, chronic renal failure, Cushing syndrome, non-estrogen hormonal therapy, secondary amenorrhea/oligomenorrhea). White or Asian race, low body weight (BMI under 18.5 kg/m^2), smoking, family history, early menopause, calcium and/or vitamin D deficiency, low levels of physical activity, and any disease or condition that can affect overall mobility level with long-term immobilization (such as spinal cord injuries) can also lead to rapid loss of bone mass and are risk factors for osteoporosis (Varacallo and Fox 2014) (Table 3). Also, medications like glucocorticoids, long-term steroid use, anti-epileptics, and chemotherapy agents can lead to secondary osteoporosis or are suspected to contribute to osteopenia and osteoporosis (Varacallo et al. 2021).

Bone Physiology and Pathophysiology

Bone is a complex organ. It contains an organic matrix that serves as frame and calcium as mineral distributed in a pattern, which provides structure and serves as an ion stock for the body. Within this complex tissue reside specialized bone cells,

Table 3 Risk factors for osteoporosis and fragility fracture

Gender (female > male)
Asian or Caucasian race
Aging
Low peak bone mass
Low BMI
Thyroid diseases
Vitamin D deficiency
Low calcium intake
Early menopause
Primary or secondary amenorrhea/oligomenorrhea
Hypogonadism
Neuromuscular disorders
Abuse of alcohol
Smoking
Medications (e.g., glucocorticoids)
Low levels of physical activity or immobilization

including osteoblasts, osteocytes, and osteoclasts (Seeman and Delmas 2006). Bone is also a dynamic organ and continually models-remodels itself throughout life ("bone modeling-remodeling"). This process involves removal or resorption of bone from one surface of bone and the subsequent deposition of new bone on another nearby surface. These two specific actions, bone resorption and formation, are performed by the specialized bone cells, and these events are tightly coupled in time and space (Becker 2006; Umland 2008).

In osteoporosis, there is a decrease in unit volume in both the organic part of bone and calcium, without changing the ratio of one to another, unlike in osteomalacia. Hence, the composition and volume of bone remain normal, but the bone mass in proportion to volume, the thickness of cortical bone, and the number and size of trabeculae in cancellous bone decrease (bone trabeculae with normal composition but sparser), as well as the connections among them, thereby impairing the bone microarchitecture (Simon, 2005). Eventually, osteoporosis leads to bone with diminished tensile strength and significantly more susceptibility to fracture with less force. At some point, the amount of bone available for mechanical support falls below a certain threshold, and the patient may sustain a fracture.

Many factors, more or less interdependent on each other, participate in the setting of the above procedures and influencing the accumulation of bone mass during growth (Raisz 2005). These factors may be genetic, which quantitatively seems to be the most important, dietary (calcium, phosphorus, proteins), hormonal (sex steroids, calcitonin, factor IGF-1), mechanical (exercise, body weight), and also the gender, race, and exposure to risk factors (Frost 1997; Becker 2006; Rizzoli et al. 2001). Most of these factors are involved in both the maintenance of bone mass in adulthood and loss of bone later, although in different proportions compared to their role in the acquisition of peak bone mass.

Estrogens, the female sex hormones, appear to be necessary not only for both men and women to reach the peak bone mass during puberty but also for its preservation in adulthood. These hormones control bone remodeling during reproductive life in females and later on in elderly men (Weitzmann and Pacific 2006). Pathologic conditions associated with premature estrogen deficiency (e.g., anorexia nervosa, secondary amenorrhea due to arduous exercise) further support the concept of a causal link between estrogen inadequacy and increased bone loss (Rizzoli et al. 2001). Estrogen deficiency is the main cause of postmenopausal osteoporosis and probably plays an important role in male osteoporosis. Consequently, estrogen deficiency is directly implicated in the age-related increase in the incidence of fractures (Riggs et al. 2002).

Vitamin D is important in the maintenance of skeleton integrity in adults. Elderly people tend to have poor dairy calcium and vitamin D intakes and decreased sunlight exposure and dermal production of vitamin D. Also, vitamin D and calcium supplementation has been demonstrated to significantly increase BMD and decrease the incidence of osteoporotic fractures in the elderly (Bischoff-Ferrari et al. 2006; Jackson et al. 2006).

In the matter of bone mass, there is no consistent difference between genders before puberty, at any skeletal site (Rizzoli et al. 2010). On the contrary, there is no evidence for a gender-related difference in bone mineral density at birth, and this sameness in bone mass between males and females is maintained until the onset of pubertal maturation. In adolescence, bone mineral mass of various skeletal sites, such as the lumbar spine, doubles, and this increase occurs approximately 2 years earlier in females than in males. Meantime, a gender-related difference in peak bone mass becomes detectable and appears to result essentially from a longer period of bone mass gain in males than in females, resulting in a larger increase in bone size and cortical thickness in the former (Seeman 1997). Thus, at the end of puberty, the peak bone mineral content at the lumbar spine and the proximal femur is higher in males than in females, while bone mineral density does not differ significantly (Gilsanz et al. 1988, 1997).

The gain in length and the gain in bone mass do not occur simultaneously. The peak of growth in stature precedes the peak of maximal bone mass gain. In males, the greatest difference occurs in the age of 13–14 years and is more pronounced for the lumbar spine and femoral neck than for the mid-femoral shaft, while in females, it occurs in the age of 11–12 years (Theintz et al. 1992; Fournier et al. 1997). Peak bone mass is reached by men and women about in the middle of the third decade of life, is probably genetically predetermined, and remains constant in the subsequent plateau period of bone turnover, with equal rates of bone formation and resorption (Riggs et al. 2002; Mora and Gilsanz 2003). This lifelong and dynamic remodeling process in the adult skeleton occurs on all bone surfaces, including the periosteal, trabecular, cortical, and endosteal surfaces, in order to maintain the strength of bone (Bonjour et al. 2007).

Following the aforementioned plateau phase, a period of net bone loss equivalent to about 0.3% to 0.5% per year begins for both genders (Simon 2005; Becker 2006). Beginning with the decrease in estrogen in association with the menopause, women

accelerate this net bone loss about tenfold for approximately 5–7 years. The steady loss of bone affects equally men and women after the age of 70 years, while dominant problem remains the reduced production of new bone (The North American Menopausal Society [NAMS] 2010).

Bone size varies little throughout life, except a slight expansion of bone cortex, mainly in men. This periosteal expansion is less than the increase in bone marrow space due to endosteal resorption, which increases with age in both genders, resulting in a thinner bone cortex. These conditions, combined with an increment in cortical bone and a destruction of trabecular bone, account for the age-dependent bone loss. It is well documented that bone loss does not drop with age, but continues throughout life, at least in peripheral skeletal sites (Ensrud et al. 1995; Seeman 1997; Rizzoli et al. 2001).

The strength of bone depends on the total size, the volume and density, as well as its structural characteristics. The total bone mass of each person in each phase of his life depends on the amount of bone formed during adolescence or even in the third decade and by the subsequent loss due to aging and menopause (Riggs et al. 2002; Mora and Gilsanz 2003). Usually, there is a misperception that osteoporosis is always the result of bone loss that commonly occurs in men and women because of aging. However, someone who does not reach its optimal, peak bone mass during childhood and adolescence may develop osteoporosis without the occurrence of increased bone loss. Therefore, sub-optimal bone growth before adulthood is as important as bone loss to the development of osteoporosis (NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy 2001). The factors that determine the peak bone mass, bone turnover, and loss of bone are the main objectives wherein the research of osteoporosis focuses.

Clinical Manifestations and Diagnosis

Clinically, the symptoms of osteoporosis manifest mostly in women after menopause with main characteristic the deformities, loss of height, and widespread pain in bones but could be also asymptomatic (Becker 2006). Sometimes, pain is more acute, and movements in the vertebral column are limited and painful, a condition that reveals compressive fractures of the vertebrae, largely in low thoracic and lumbar spine. The typical osteoporotic fractures occur suddenly and sometimes after a fall, sudden movement, weight-lifting, jump, or even cough. The pain is chronic and may be severe and is typically located mainly at the region of fracture but may radiate to the abdomen or flanks. Elderly over 65 years of age suffer mainly from fractures of the femoral neck, and incidence increases as people age. Most patients with osteoporotic fracture sustain other fractures within the next few years (Simon 2005; NAMS 2010).

Osteoporosis can occur as a primary disorder or as a disorder associated with various diseases (NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy 2001). Primary osteoporosis is a disease of the elderly, particularly among older women, with most cases occurring in the sixth and later decades of life. This form of osteoporosis is sometimes referred to as “involutional”

osteoporosis. Secondary osteoporosis is a series of abnormalities and diseases that may manifest with effects in bone. Those disease states associated with osteoporosis include endocrine disorders, systemic inflammatory diseases (like rheumatoid arthritis), bone mineral and metabolic defects, and other chronic illnesses.

The aims of screening the individuals who are at risk for osteoporosis is to put the diagnosis on the basis of the assessment of bone mass, to determine fracture risk, and to take decisions regarding the appropriate treatment. Typical radiological examinations permit identification of architecture of bone. In reality, however, the X-rays, although inexpensive and simple, allow only partial quantitative evaluation of bone mass and provide little information for the cancellous bone, which is the most active metabolically and is involved in postmenopausal osteoporosis. For that reason, more appropriate methods have been developed for quantifying both the cortical and trabecular bone mass and assessing fracture risk (Simon 2005).

Dual-energy X-ray absorptiometry, abbreviated as "DXA" (although usually abbreviated in older literature as "DEXA"), was first introduced in 1987 (Hologic QDR-1000 system, Hologic, Inc) and immediately made all previous forms of radiation-based BMD measurement systems obsolete (Miller 2017). Since then, there have been many generations of the technology, with the main US manufacturers in 2017 being Hologic, Inc. and GE Lunar.

Nowadays, DXA is recognized as the reference method ("gold standard") to measure bone mineral density with acceptable accuracy errors, good precision, and reproducibility. The examination with DXA has become the best choice for measurement and accurate diagnosis of osteoporosis as this technique is used for measuring bone mass and density and identifies individuals whose osteoporosis is so severe as to be qualified at potential fracture risk (NOF 2013) (Table 4). It is also used to monitor patients undergoing treatment by performing serial assessments. Areal BMD is expressed in absolute terms of grams of mineral per square centimeter scanned (g/cm^2). The measurement of bone mass is also provided by DXA technique through the expression of bone mineral content (BMC) in terms of grams (g).

The diagnosis of normal, low bone mass (or osteopenia), osteoporosis, and severe or established osteoporosis is based on the WHO's diagnostic classification through BMD (WHO 2007). By using population standards, osteoporosis is defined by BMD at the hip or spine that is less than or equal to 2.5 standard deviations (*SD*) below the mean of a reference population of young, normal, white women ("*T*-score"). In the same manner, osteopenia is defined as a bone density between 1.0 and 2.5 *SD*s below

Table 4 Why BMD measurement with DXA ("gold standard") for diagnosis of osteoporosis?

Osteoporosis is a severe systemic disorder
Osteoporosis causes fragility fractures
Osteoporosis is associated with increased morbidity, hospitalization, and mortality
Easy to put early the diagnosis of osteoporosis
Prevention and reduction in fracture risk with early management and treatment
Low cost
Low level of radiation

Table 5 Indications for BMD measurement

Women ≥65 yrs of age
Men ≥70 yrs of age
Postmenopausal women <65 yrs of age with risk factors
Adults with osteoporotic fragility fracture
Adults with a disease or condition for secondary osteoporosis
Adults under treatment that causes bone loss (e.g., glucocorticoid therapy)
Individual under treatment for low bone mass or bone loss ("follow-up")
Individual not receiving therapy in whom evidence of bone loss would lead to treatment

the bone density of the same reference population. Thus, patients do not have to sustain a fracture to be diagnosed with this insidious problem. Additionally, another norm, the "*Z*-score," provides similar information regarding a patient's BMD in relation to age-matched controls. Thence, with this calculation, it is possible to screen for prominent causes of accelerated bone loss. WHO has established DXA as the best densitometric technique for assessing BMD in postmenopausal women and has based the definitions of osteopenia and osteoporosis on its results (Table 5).

However, currently, there is no accurate measure of overall bone strength. The BMD is frequently used as a proxy measure and accounts for approximately 70% of bone strength; therefore, it might be an excellent predictor of future fracture risk. There is an exponential correlation between the decrease in BMD and increase in fracture risk. Usually, 1 *SD* equals 10–15% of the BMD value in g/cm^2 (NOF 2013). Almost all population studies have now confirmed that for a single *SD* below young normal mean BMD (at virtually any skeletal site), there is a nearly twofold greater risk of an eventual hip fracture (Kanis 1994, 2002; WHO 2007; Kanis et al. 2008).

According to the point of view of the "Utah Paradigm," regarding updated bone physiology, "whole-bone" strength ranks above bone "mass" in physiologic importance and depends strongly on the amount and kind of bone tissue in a bone, the distribution of bone tissue, and the bone's longitudinal and cross-sectional size and shape (Frost 2003b). The measurement with DXA can evaluate the bone "mass" factor in terms of BMC and BMD. However, bone "mass" alone cannot reliably evaluate "whole-bone" strength; hence, currently popular BMD values provide very unreliable indicators of whole-bone strength and a poor evaluation of it, weakening many arguments that depend on such BMD data. Conversely, another method, the quantitative computed tomography (QCT), can evaluate both the "mass" and "architectural" factors in whole-bone strength.

Although available technologies (e.g., peripheral DXA (pDXA), QCT, peripheral QCT (pQCT), quantitative ultrasound (QUS)) measuring central (spine and hip) and peripheral (forearm, heel, fingers) skeletal sites provide site-specific and global (overall risk at any skeletal site) assessment of future fracture risk, DXA measurement at the hip is the best predictor of future hip fracture risk (Singer 2006). However, it is not clear how to apply the diagnostic criterion of *T-score* to men, to children, and across ethnic groups. Because of the difficulty in accurate measurement and standardization between instruments and sites, controversy exists among

experts regarding the continued use of this diagnostic criterion (NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy 2001). In accordance with the guidance of the National Osteoporosis Foundation (NOF 2013), the WHO bone mineral density diagnostic classification should not be applied in premenopausal women, men less than 50 years of age, and children (NAMS 2010). In these groups, the diagnosis of osteoporosis should not be made based on densitometric criteria alone (see also the recommendations of the International Society for Clinical Densitometry [ISCD] in ISCD 2007).

Prevention and Management

Osteoporosis and osteoporotic bone fractures are associated with a severe degree of disability, and also their impact on mortality cannot be ignored (Tosteson et al. 2007; Cole et al. 2008a). Furthermore, fractures are usually a forewarning of a handicapped life with impairment in activities of daily living and, sometimes, the beginning of an institutionalized life (Gehlbach et al. 2007; Umland 2008).

Therefore, prevention of osteopenia and osteoporosis and bone fractures is of utmost importance, mostly at advanced age. Patient awareness of the potential risks associated with falling down is also important. Many elderly people are at risk for falling as a result of poor coordination, poor vision, muscle weakness, confusion, and the use of hypnotics or other medications (Cole et al. 2008b). Because they are at a higher risk of falling, they are also at an increased risk of sustaining a fracture.

Osteopenia and osteoporosis are to a great extent preventable and treatable, because of significant scientific progress in the field of diagnosis and treatment and in understanding of their pathogenesis. It must be kept in mind that in the case of osteoporosis, there is no complete cure in the meaning of bringing back the bone mass in normal levels. The first step for an effective treatment is an appropriate diagnosis. Because there are no warning signs prior to a fracture, many people are not being diagnosed in time to receive effective therapy during the early phase of the disease. The goal is to diagnose the patients with osteopenia and osteoporosis before they have sustained enough bone loss to be at risk for a fracture (Cole et al. 2008b). Therefore, people who are at risk for future fracture should be identified early, based on their family history and other known risk factors. Accordingly, they should undergo a bone densitometry examination to determine their bone mass (WHO 2007).

Many factors have been associated with an increased risk of osteoporosis-related fracture. Since the majority of osteoporosis-related fractures result from falls, it is also important to evaluate risk factors for falling (such as a personal history of falling, along with muscle weakness and gait, balance, and visual deficits). Consequently, strategies to reduce falls are essential and should include, but are not limited to, checking and correcting vision and hearing, evaluating any neurological problems, reviewing prescription medications for side effects that may affect balance, and providing a checklist for improving safety at home (NOF 2013).

The main therapeutic goal is the retardation of the disease's progress by decreasing bone resorption and increasing the bone mass. The treatment strategies include

Table 6 Nutritional factors in osteoporosis

Calcium
Vitamin D
Phosphorus
Vitamins K, C, B12, and B6 and folic acid
Proteins
Magnesium
Sodium chloride
Caffeine
Fluoride
Boron
Minerals (zinc, copper, potassium)

medications, such as calcium and vitamin D supplementation, hormone replacement therapy (e.g., estrogens), calcitonin, and bisphosphonates (Simon 2005; Gooren 2007). A good and adequate nutrition is essential for normal growth and also important for all individuals with osteopenia and osteoporosis (Table 6). A balanced diet with the adequate calories and appropriate nutrients is the foundation for the development of all tissues, including bone. Controlled clinical trials have demonstrated that an optimal diet for bone health (for patients older than age 50) must include a sufficient intake of supplemental calcium (at least 1200 mg per day) and vitamin D (800 to 1000 IU per day) and this combination can reduce the risk of fracture (NOF 2013). Additionally, it is recommended to abstain from smoking and the abuse of alcohol and caffeine.

Another therapeutic goal is also the treatment of pain; so, medications for this purpose are useful (e.g., analgesics, anti-inflammatory, and muscle relaxants). The role of physical therapy is also important in pain management, improving muscle function, and reducing the risk of falls by the use of electrotherapy, hydrotherapy, and mild heat and with appropriately adapted exercises of regular weight-bearing and muscle-strengthening (Lange and Uhlemann 2008; Preisinger 2009; Bautmans et al. 2010; Bennell et al. 2010; Dusdal et al. 2011; Lange et al. 2012). For example, special therapeutic exercise programs for dorsal muscle-strengthening in women with kyphosis and lumbar spine vertebral fractures had positive effects in muscle force, mobility, reducing pain, better sleep, and quality of life (Hongo et al. 2007; Qvist et al. 2011).

Physical activity, in general, can play an important role in the prevention and treatment of osteopenia and osteoporosis. A key factor for the bone mass and density is the mechanical loading applied to the bone, which is achieved by special physical activity that involves exercises of weight transfer (Bailey and Brooke-Wavell 2008). In fact, active people with intense daily activity have greater bone density than non-active persons, while the lack of mechanical loading and the long lying-in bed have devastating effects on bones (Zhang et al. 2008; Humphries et al. 2000; Rizzoli et al. 2010). The specific benefits of lifelong physical activity on bone health have been investigated in numerous randomized clinical trials and observational studies (Kohrt et al. 2004; Vicente-Rodriguez 2006; Marcu et al. 2010).

Some evidence indicates that resistance and high-impact exercise are likely the most beneficial (Martyn-St James and Carroll 2009; Vicente-Rodriguez et al. 2007). Moreover, there is convincing evidence that exercise in elderly people also improves function and delays loss of independence by increasing muscle mass and strength, agility, body posture, and balance and thus contributes to quality of life by reducing the risk of falls (approximately 25%) and possibly fracture risk (Cole et al. 2008b; de Kam et al. 2009; Guadalupe-Grau et al. 2009).

However, the most important parameter in the treatment of osteoporosis is prevention, which is directly related to bone health. Optimization of bone health is a process that must occur during lifetime of both men and women. Factors that affect the good condition of the bones at all ages are essential for the prevention of osteoporosis and its consequences. Therefore, prevention strategies should be based on the formation of these determinants, especially those involved in bone mineral density and its changes with increasing age (Vicente-Rodriguez et al. 2008). Consequently, the most important determinant of bone health is the peak bone mass that is achieved until the third decade of life. Of course, genetic factors play a strong and dominant role on peak bone mass, but the modifiable factors that are related to quality of life, such as nutrition, diet, and physical activity, are also crucial. Moreover, childhood is a critical period for adopting habits and lifestyles which promote the preservation of the good condition of the bones. For example, smoking that usually starts in adolescence can have a deleterious effect on the acquisition of peak bone mass. Proper and balanced diet with enough calories and nutrients, with the calcium being in predominant position, is also essential for normal development.

Overall, the implementation of specific exercise programs in critical younger ages helps the achievement of the ideal peak bone mass (Wang et al. 2007; Pate et al. 2010; Gracia-Marco et al. 2011a, 2011b). This enables a substantial advantage to individuals who are at risk of osteopenia, since the bone loss, though it will increase due to the disorder, will start by higher prices for bone density having as a result the reduced negative consequences of osteoporosis (Rizzoli et al. 2010).

Finally, according to the still-evolving skeletal-biologic Utah Paradigm, there are some different aspects regarding osteoporosis, namely, its pathophysiology and biomechanical pathogenesis, classification, diagnosis, prevention, management, and treatment. For the paradigm's specific suggestions and further definitions in reference with osteopenia and osteoporosis, there is a specialized bibliography by Harold M. Frost (1985, 1987, 1991, 1992, 1994, 1997, 1998, 1999, 2001a, 2001b, 2003a, 2003c), José Luis Ferretti, and Webster S. S. Jee (Ferretti et al. 1995, 2003; Frost et al. 1998; Jee 2000, 2006).

Mini-Dictionary of Terms

- Biomarker (A portmanteau of "biological marker") = A broad subcategory of medical signs – that is, objective indications of biological state observed from outside the body – which can be measured accurately and reproducibly.

- Body Mass Index = A person's weight in kilograms divided by the square of height in meters.
- Bone Mass = A function of bone size and volumetric bone mineral density.
- Bone Mineral Content (BMC) = A measurement of the amount of minerals (mostly calcium and phosphorus) contained in a specific area of bone.
- Bone Mineral Density (BMD) = A measure of the amount of minerals (mostly calcium and phosphorus) contained in a certain volume of bone.
- Dual-Energy X-ray Absorptiometry (DXA or DEXA) = An imaging technique that measures bone mineral density by passing X-rays with two different energy levels through the bone.
- Quantitative Computed Tomography (QCT) = An imaging technique that measures bone mineral density using a standard X-ray computed tomography (CT) scanner with a calibration standard to convert Hounsfield units of the CT image to bone mineral density values.
- Quantitative Ultrasound (QUS) = An imaging technique that measures bone mineral density measuring the velocity and attenuation of ultrasonic sound waves as they pass through bone tissue.
- Osteopenia = A condition where bone mineral density is lower than normal; however, not yet as low as osteoporosis and falls in the "T"-score range of −1.1 to −2.5.
- Osteoporosis = Osteoporosis is a systemic bone disease characterized by low bone mass and microarchitectural deterioration of bone tissues.

Summary Points

- Osteoporotic bone fractures are associated with a severe degree of disability, a high direct cost for rehabilitation, and an adverse impact on mortality.
- Virtually, all fractures in the elderly can be attributed to osteoporosis, whether primary or secondary, and evidently, the occurrence of these fractures increases exponentially with age.
- This natural bone loss is considered to be the cause of primary forms of osteopenia and osteoporosis, while secondary causes accelerate this process (including lifestyle factors like smoking, abuse of alcohol, and sedentary lifestyle).
- The strength of bone depends on the total size, the volume and density, as well as its structural characteristics.
- The typical osteoporotic fractures occur suddenly and sometimes after a fall, sudden movement, weight-lifting, jump, or even cough.
- According to the "Utah Paradigm," "whole-bone" strength ranks above bone "mass" in physiologic importance and depends strongly on the amount and kind of bone tissue in a bone, the distribution of bone tissue, and the bone's longitudinal and cross-sectional size and shape.
- Although available technologies (e.g., peripheral DXA (pDXA), QCT, peripheral QCT (pQCT), quantitative ultrasound (QUS)) measuring central (spine and hip) and peripheral (forearm, heel, fingers) skeletal sites provide site-specific and

global (overall risk at any skeletal site) assessment of future fracture risk, DXA measurement at the hip is the best predictor of future hip fracture risk.

- Osteopenia and osteoporosis are to a great extent preventable and treatable, because of significant scientific progress in the field of diagnosis and treatment and in understanding of their pathogenesis.

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