ISSN 2564-0127 (Print)
ISSN 2564-0135 (Online)

Canadian Journal of Medicine 3(2021)99-104

Canadian Journal of Medicine

WWW.CIKD.CA

Review Article

Risk Factors and Therapeutic Interventions for Osteoporosis

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Keywords:
Osteoporosis, DEXA, Bone mineral density, Fracture Body mass index (BMI)

Received
11 June 2021
Received in revised form
22 June 2021
Accepted
22 June 2021

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ABSTRACT

Osteoporosis is a disease of the bone characterized by a loss in bone mineral density. Although this disease is commonly diagnosed in adults, it is not directly associated with increasing age. There are many links and potential risk factors to developing osteoporosis, including hormonal imbalances, nutrient deficiency, cardiovascular health, and exercise. This review examines how osteoporotic fractures are diagnosed using bone imaging techniques, including dual-energy X-ray absorptiometry scans. The quality of life for patients with osteoporosis is discussed concerning the protective and risk factors associated with osteoporosis. Specifically, the risk factors for osteoporosis include genetic inheritance patterns, BMI, age, and lifestyle choices (including alcohol consumption, smoking, and physical exercise). There are many protective factors for preventing osteoporotic fractures, including natural bone supplements and prebiotics. These supplements can be found in most dairy products, which are fortified with vitamin D, which can be consumed in the diet to support bone health. Prebiotics can also be used to increase the healthy proliferation of commensal gut bacteria that are used to improve the bone-building process, relieving bone breakdown during the stages of bone turnover. These therapeutic interventions can be applied to support existing patient care to prevent and maintain overall bone health.

Introduction

Osteoporosis is derived from the Greek term for “porous bone” [1]. Commonly referred to as the “silent bone disease”, osteoporosis often goes undiagnosed in individuals for long periods. This disease slowly weakens bones by degenerating the bone microarchitecture, results in loss

of bone mass and decreased bone mineral density (BMD), leading to an increased risk of bone fracture [2].

The pathogenesis of osteoporosis is linked to endocrine factors, including parathyroid hormone (PTH), vitamin D, calcitonin, and estrogen. PTH promotes osteoclast activity, which increases the absorption of calcium through the kidneys, bone, and intestine. PTH also activates vitamin D, which forms the active metabolite known as calcitriol. Vitamin D is an important factor in maintaining the rate of bone remodelling by promoting intestinal calcium absorption [1]. Low calcium levels in the body increase the risk of developing osteoporosis because osteoclasts break down bone to release calcium into the bloodstream. During menopause, the loss of estrogen in women significantly increases the rate of bone remodelling by increasing osteoclast function and decreasing osteoblast function. This impact of estrogen on the rate of bone turnover creates an imbalance that speeds up bone loss and slows down bone formation, leading to the onset of osteoporosis [3].

Bone Density Imaging Techniques

Dual-energy X-ray absorptiometry (DEXA) is a diagnostic tool capable of identifying patients with osteoporosis. When DEXA screening is used accurately and effectively, it can help guide early clinical intervention which is critical to prevent patients from suffering an osteoporotic fracture, along with the induced morbidity and increased rate of mortality [4]. However, many factors can influence the misinterpretation of the DEXA results. These factors include the patient's previous fracture history, osteoarthritis (joint pain associated with bone), osteomalacia (the softening of the bone), and metal implants [5]. X-ray imaging for osteoarthritis shows narrowing joint spaces and marginal osteophytes [6]. DEXA assessments showed reduced BMD at relevant sites in patients with osteomalacia, including the spine, hip, and forearm [7]. Therefore, alternate methods of diagnosis should be used to confirm the correct patient diagnosis and rule out other diseases that share common pathologies and symptoms as osteoporosis.

Canadian statistics obtained from *Osteoporosis Canada* (2017) showed that the development of osteoporosis is most common among Canadians over 50 years of age, although the onset of this disease can be capable of affecting people at any age. Osteoporosis has a very high prevalence in the global population, where approximately 2 million Canadians are affected by this bone disease. Data showed that at least 1 in 3 women and 1 in 5 men would have an osteoporotic-related fracture during their lifetime. Patients diagnosed with osteoporosis have a lifetime fracture risk of at least 40% [8]. The major osteoporotic fractures occur in the spine, hip, forearm, and humerus [9].

Adjusting to a Lifestyle with Osteoporosis

Patients with osteoporosis commonly suffer from a decreased quality of life (QOL) due to loss of mobility and autonomy. Severe osteoporotic fractures occurring in the hip and spine require hospitalization time and carry a 20% increase in mortality rate [8]. Studies have shown that men with hip fractures have a higher mortality rate than women [10]. Correlational studies between the risk of osteoporotic fracture and mortality rates showed that 30% of patients with hip fracture die within one year [11]. Patients commonly feel socially isolated, and they show signs of feeling anxious about their health and changing lifestyles after being diagnosed with osteoporosis. Most patients have fears and concerns regarding when they will

get their subsequent fractures. After a fracture, patients have decreased mobility in their body, which makes it difficult for these individuals to complete their activities of daily living (e.g., personal hygiene, getting dressed, continence management, cleaning, cooking, etc.) [12]. In the elderly population, anthropometric factors (e.g., hypertension, diabetes, obesity, low physical activity, and obstructive sleep apnea) are associated with a decreased BMD and increased risk of severe bone fractures [13].

Risk Factors for Osteoporosis

It is important to be educated about osteoporosis and the risks associated with this disease. The prevalence of this disease makes many of us very susceptible to potential fractures, which can be very detrimental to our overall health and well-being. Individuals who were well-educated on osteoporosis using focus groups were able to report changes in their health behaviors. In addition, it was found that they were able to make lifestyle changes that would reduce the risk of osteoporotic fractures in the future [14].

There are many risk factors commonly associated with osteoporosis. There is a genetic basis of inheritance for developing an osteoporotic disease. If a family member has osteoporosis or suffered a fracture, their offspring may be more susceptible to inheriting the disease. Using twin studies, researchers have been able to find genetic markers that influence the development of osteoporotic disease. Meta-analyses have been used to look for individual polymorphisms that may predispose an individual to osteoporosis [15]. Low bone mass density leads to weaker bones by reducing the bone microarchitecture, one of the characteristic features of an osteoporotic disease. Age is also a risk factor, as increased age is associated with increased bone resorption by osteoclasts and decreased bone formation by osteoblasts [16]. Peak bone density is achieved by 30 years of age, and bone density decreases shortly after due to increased osteoclast (bone resorption) activity. As we age, humans experience reduced testosterone (in men) and estrogen (in women), which limits osteoblast activity. Measuring a patient's Body Mass Index (BMI) is sometimes used as an osteoporosis screening tool, as low BMI (<28) is a major risk factor for diagnosing osteoporosis [4]. Previous fragility fractures have been defined to be a common risk factor for having another osteoporotic fracture. If a patient has had a prior fragility fracture, they are more susceptible to having more compression fractures in the future. Post-menopausal women are at a higher risk of developing osteoporotic fractures [8]. Many lifestyle factors such as smoking, overconsumption of alcohol, and physical inactivity are risk factors for osteoporosis.

The Role of Exercise in Maintaining Bone Health

A common protective factor commonly prescribed for osteoporosis prevention is exercise. Staying active and doing weight-bearing exercises builds muscle, which stimulates bone formation because the bones and muscles need to remain strong enough to support increased weight load [17]. It was also found that BMD could be improved by engaging in aerobic dance therapy, thus, decreasing the risk of bone fracture [18]. It is highly recommended that exercise interventions should be tailored with the help of a healthcare professional to support improved bone health status and quality of life [19]. Pharmacologic therapies can be used to support the bone remodelling process. Teriparatide is an anabolic agent for treating osteoporosis, as approved by the Food and Drug Administration (FDA) in the United States; it is a recombinant hormone-containing parathyroid hormone (PTH). Through multiple

signaling pathways, PTH is capable of increasing osteoblast function, which are the bone-building cells crucial for maintaining bone turnover homeostasis. It has also been shown that teriparatide lowers the risk of hip and vertebral fractures by increasing bone strength and BMD [20].

Natural Bone Supplements

Physicians may also prescribe natural remedies to reduce pain for patients with osteoporosis. Although many pharmacologic treatments can be used, many of them are associated with unwanted side effects if prescribed for long periods. Natural remedies are based on compounds that are already found in our bodies, so many side effects are limited. A general recommendation for patients is to consume a diet rich in dairy products that are high in vitamin D, protein, calcium, magnesium, potassium, zinc, and phosphorus [21].

Vitamin D (also known as calciferol) is a group of fat-soluble sterols, where the two major forms are vitamin D_2 and vitamin D_3 [22]. Data obtained from *Statistics Canada* revealed that only 68% of Canadians had sufficient vitamin D intake [23]. Everyone should be conscious of adequate vitamin D intake as it helps with the reabsorption of calcium into the systemic circulation, promoting strong bone health. Vitamin D has a positive role in supporting calcium absorption from the bone. Vitamin D can also be converted from ultraviolet (UV) sunlight exposure and absorbed into the skin [24]. The amount of vitamin D absorbed into the skin depends on a few factors, including the temperature season, skin pigmentation, sunscreen use, clothing, and the amount of exposed skin [22]. For Canadians, the temperate seasons make it difficult to absorb natural vitamin D as we typically stay indoors for almost half the year. Natural sources of vitamin D in food include fatty fish, liver oil, and egg yolks. Fortified foods, such as milk, cheese, and yogurt products are high in vitamin D content [25].

Prebiotics Support Bone Health

Prebiotics are very beneficial for many of the microorganisms contained within our gut microbiome. These non-living, indigestible fibers stimulate the growth and proliferation of gut microbes [26]. It has been shown that short-chain fatty acids (SCFAs) help regulate osteoclast metabolism and bone mass *in vivo* [27]. The microbiota-bone axis needs to be regulated to allow the gut microbes to increase bone mass, reducing the risk of developing an osteoporotic disease. The mechanism behind the onset of osteoporosis is linked to the inhibition of osteoclast proliferation and differentiation. The benefits of this process are reduction of apoptosis (cell death), reduction of bone resorption, as well as promotion of osteoblast proliferation and maturation [28]. Prebiotics are stable in acidic solutions, such as gastric juice, which makes them resistant to gastrointestinal enzymes and can be fermented by intestinal microorganisms [29]. The use of prebiotics in clinical healthcare has been shown to promote the proliferation of healthy gut microbiota, which leads to immunomodulatory effects on the host cells. It has been discovered that the receptor activator of nuclear factor kappa B ligand, known as RANKL, is important in the role of osteoclast formation. This knowledge has been used to facilitate the development of monoclonal antibodies that target RANKL to supplement the treatment of osteoporosis [30].

Conclusion

Osteoporosis is a common bone degenerative disease that affects millions of people worldwide. Many of the risk factors associated with osteoporotic disease affect the quality of life for patients with osteoporosis. Patients are generally concerned for their health and well-being following an osteoporotic fracture. However, protective factors can be implemented into a patient's lifestyle as a preventative action for avoiding the risk of future fractures. Regular exercise and physical activity are capable of stimulating the process of bone remodelling, as small micro-bends in the bone are experienced during exercise. Osteoclast (bone breakdown) and osteoblast (bone formation) cells are initiated by exercise, which slowly builds stronger bones over time. Many natural bone supplements are currently available in the market for supporting overall bone health. Vitamin D and prebiotics are common supplements that are recommended by physicians as early preventative measures towards osteoporosis.

Conflict of interest

None

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