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OSTEOPOROSIS - "A SILENT KILLER". A REVIEW OF THE CURRENT LITERATURE FROM CLINICIAN AND PHYSIOTHERAPIST PERSPECTIVE

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SUMMARY

Osteoporosis is a disease characterized by low bone mass and deterioration of bone structure that causes bone fragility and increases the risk of fracture. Individuals with osteoporosis are at high risk of suffering one or more fractures, which are often physically debilitating and can potentially lead to a downward spiral in physical and mental health. Article attempts to discuss this issue from the clinical and rehabilitation perspective. Following contents were included: diagnosis, types of osteoporosis, epidemiology, burden of osteoporosis, types of fractures, treatment and rehabilitation of osteoporosis.

Key words: osteoporosis, porous bone, low bone mass, silent disease.

DEFINITION AND DIAGNOSIS

Osteoporosis is a disease characterised by low bone mass and micro-architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk. The cornerstone for the diagnosis of osteoporosis lies in the assessment of Bone Mineral Density (BMD). The measure represents the average concentration of mineral (primarily calcium hydroxyapatite) per unit area of bone. Based on World Health Organisation (WHO) diagnostic criteria, a BMD value that falls below 2,5 standard deviation (a T-score less than or equal to -2.5 SD) from the young adult mean value denotes osteoporosis. In case of severe osteoporosis (established), one or more fragility fractures is also presence [1,2].

The primary limitations to this approach is the fact that there is no clear threshold or cut-point of BMD that divides individual's who have fracture from these and who do not. Moreover, bone mass is not the only factor that contribute to bone fragility. Other factors such as bone size, cross-sectional area as well as micro-architecture, also contribute to fractural resistance [3,4].

Decreased BMD has been recognised by plain radiographic examination for a long time. Now, the most widely validated technique to measure BMD is dual energy X-ray absorptiometry (SXA, DXA), and diagnostic criteria based on the T-score for BMD are a recommended entry criterion for the development of pharmaceutical interventions in osteoporosis [5,6]. Although, quantitative computed tomography (QCT) providing a true measure of mineral content per unit volume, requires greater amount of radiation exposure

and is more costly than X-ray absorptiometry. In the peripheral areas, such as the calcaneus or tibia, quantitative ultrasound (QUS) is also used. The advantage of this method is a lower cost and radiation-free [7].

TYPES OF OSTEOPOROSIS

One of the classification system categorizes osteoporosis as primary - typical age-related loss of bone from skeleton and secondary - results from the presence of other diseases or conditions that predispose to bone loss. They are three types of osteoporosis. Other allows to distinguish three types of osteoporosis. Type 1 or postmenopausal osteoporosis occurs in 5% to 20% of women, affecting those within 15 to 20 years of menopause, with a peak incidence in the 60s and early 70s. Estrogen deficiency is thought to underlie this form of osteoporosis, rendering the skeleton more sensitive to parathyroid hormone (PTH), resulting in increased calcium resorption from bone. Type 2 or senile osteoporosis occurs in women or men more than 70 years of age and usually is associated with decreased bone formation along with decreased ability of the kidney to produce $1,25(OH)_2D_3$. Type 3 or secondary osteoporosis occurs equally in men and women and at any age. This type of osteoporosis is associated with a variety of conditions, including hormonal imbalances, cancer, gastrointestinal disorders, drug use, chronic renal failure, hyperthyroidism, hypogonadism in men, immobilization, inflammatory arthritis and poor nutrition [8-11].

EPIDEMIOLOGY

Osteoporosis is major health problem and one that affects a large segment of the population. Currently it is estimated that over 200 million people worldwide suffer from this disease [12]. Approximately 22 million women and 5.5 million men aged between 50-84 years of age are estimated to have osteoporosis in the European Union (UE). Due to changes in population demography the number of men and women with osteoporosis in the EU will rise from 27.5 million in 2010 to 33.9 million in 2025, corresponding to an increase of 23% [13]. The overall prevalence of osteoporosis in the general population was in the range of 3,7% (Cyprus, Ireland) to 6,3% (Italy). Of all 27 countries, Germany was estimated to have the highest number of individuals with osteoporosis with approximately 1 million osteoporotic men and 4 million osteoporotic women. In women aged 50 years or more, the prevalence of osteoporosis varied from under 19,5% in Cyprus and Slovakia to 23,4% in Italy. The corresponding data for males were 5,7% in Slovakia to 6,9% in Italy, Greece and Sweden. In case of Poland, it is estimated that 1,8 milion people (approximately 338 000 women and over 1,5 milion men) suffer from osteoporosis, what represents 4,8% of the overall population [13,14]. In addiction, osteoporosis affects approximately 1,4 million Canadians [15]. In USA, 44 milion people with osteoporosis represent 55 percent of the people aged 50 and older [16]. In Australia, 2.2 million people are affected by osteoporosis. About 11% of men and 27% of women aged 60 years or more are osteoporotic, and 42% of men and 51% of women are osteopenic [17]. Osteoporosis is greatly underdiagnosed and undertreated in Asia. "*Porous bones*" seems to be a significant problem due to major nutritional issues as well as limited and underutilised diagnostic facilities. The problem is particularly acute in rural areas. Almost 70 million Chinese over the age of 50. The overall prevalence of osteoporosis in mainland China might be approximately 7% among adults, 10-20% in urban areas, 22.5% among men aged 50 years or more, and 50.1% among women aged 50 years or more [18].

BURDEN OF OSTEOPOROSIS

The global burden of osteoporosis can be quantified by DALYs (Disability Adjusted Life Years) and QALY (Quality Adjusted Life Years).

DALY is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death. It was developed in the 1990s as a way of comparing the overall health and life expectancy of different countries [19]. In the year 2000 there were an estimated 9 million osteoporotic fractures world-wide of which 1.6 million were at the hip, 1.7 million at the forearm and 1.4 million were clinical vertebral fractures. The total DALYs lost was 5.8 million accounting for 0.83 % of the global burden of non-communicable disease. In Eu-rope osteoporotic fractures account for 2 million DALYs annually, somewhat more than accounted for by hypertensive heart disease and rheumatoid arthritis, but less than chronic obstructive pulmonary disease [20]

The QALY is a multi-dimensional outcome measure frequently employed in health economic analysis that incorporates both the quality (health related) and quantity (length) of life. QALYs are derived by multiplying the duration of life (years) with a health utility between 0 (death) and 1 (perfect health) [21]. The value of a QALY may differ between and within countries due to a number of factors including degree of pros-perity, cultural attitudes and the opportunity costs of resources devoted to obtain a marginal QALY. Approximately 1,165,000 QALYs were lost due to oste-oporosis in the EU27 in 2010. Women and men suffered approximately 781,000 and 384,000 QALYs lost, respectively. Prior fractures were the main driver of QALYs lost, accounting for approximately 58 % and 50 % of the loss in women and men respectively [22].

TYPES OF FRACTURES

Osteoporotic fractures are one of the most common causes of disability and a major contributor to medical care costs in many regions of the world. Fragility fractures are particularly common in the spine, hip and forearm, but may also affect other sites [23].

1. Hip fracture

Hip fracture may be classified as intracapsular or extra-capsular. According to Garden scale categorizing intracapsular hip fractures of the femoral neck, 4 types of fractures can be distinguished: Type 1 – incomplete, stable fracture with impaction in valgus; Type 2 – complete without displacement; Type 3 – complete with partial displacement and Type 4 – complete with full displacement [24]. Intracapsular proximal femoral fracture may be also classified using the Pauwels classification, which relates to the shearing angle of the fracture surface. Pauwels observed that the obliquity of the fracture line with the horizontal plane significantly affected the prognosis of the fracture. The angle formed by extending the fracture line upwards to meet an imaginary horizontal line drawn through the transtubercular (iliac crest) plane on AP film is described as "Pauwels' angle". The higher the value of this angle, the greater is the instability of the fracture [25]. However, a literature review showed that Pauwels angle nor the classification had any predictive value for the incidence of non-union [26]. The Pipkin classification, consisting of four grades is a system of categorizing femoral head hip fractures based on the fracture pattern. Type I –Fracture below the fovea, not involving weight-bearing surface of the head; Type II – Fracture above the fovea, involving weight-bearing surface of the head; Type III – Type I or II fracture with associated femoral neck fracture and Type IV – Type I or II fracture with associated acetabulum fracture [27]. The Evans-Jensen classification is a system of categorizing intertrochanteric hip fractures based on the fracture pattern of the proximal femur. Type IA –2-part non-displaced; Type IB – 2-part displaced; Type IIA - 3-part fracture with separate greater trochanter fragment; Type IIB – 3-part fracture with separate lesser trochanter fragment; Type III - 4-part fracture [28].

2. Distal forearm fracture

The most common distal forearm fracture is Colles' fracture, that occur as the result of a fall onto an outstretched hand. They consist of a fracture of the distal radial metaphyseal region with dorsal angulation and impaction, but without involvement of the articular surface. The reverse injury is known as Smith's fracture (also known as a Goyrand fracture in the French literature). This is a fractures of the distal radius with associated palmar angulation of the distal fracture fragment. Barton fractures are also fractures of the distal radius, extend through the dorsal aspect to the articular surface, but not to the volar aspect. Therefore, it is similar to a Colles fracture. There is usually associated carpal subluxation/dislocation [29-33]. Frykman classification of distal radial fractures describes eight types. It is based on the involvement of the radiocarpal and the distal radioulnar joints. Even types are based on odd types with additional fracture of the ulnar styloid process. However, this traditional classification has little impact on treatment decision or outcome, because it does not consider the extent or direction of displacement or shortening. Eight type of fractures were as follows: Type I - transverse metaphyseal fracture, this type include Colles' and Smith's fracture; Type II - type I + fracture of the ulnar styloid process; Type III - fracture involving the radiocarpal joint, this type includes Barton and reverse Barton fracture; Type IV - type III + fracture of the ulnar styloid process; Type V - transverse fracture involving the distal radioulnar joint; Type VI - type V + fracture of the ulnar styloid process; Type VII - comminuted fracture involving both the radiocarpal and the distal radioulnar joint; Type VIII - type V + fracture of the ulnar styloid process [34-35].

3. Vertebral fracture

Vertebral fractures are the most common consequence of osteoporosis, occurring in a substantial proportion of post-menopausal women and elderly men. However, there is strong evidence of widespread under-diagnosis of vertebral fracture [36,37]. The Vertebral Compression Fractures (VCFs) that result from osteoporosis are usually classified into three categories: wedge, biconcave, and crush. Wedge fractures are the most common, accounting for more than 50% of all VCFs. These fractures occur in the midthoracic region and are characterized by compression of the anterior segment of the vertebral body. Biconcave compression fractures are the second-most common, accounting for approximately 17% of all VCFs. In these fractures, only the middle portion of the vertebral body is collapsed, whereas the anterior and posterior walls remain intact. The least common VCFs are crush compression fractures. They account for only 13% of VCFs. In these fractures, the entire anterior column, including anterior and posterior margins, is collapsed. Complex fractures account for the remaining 20% of VCFs. [38].

TREATMENT OF OSTEOPOROSIS

Although osteoporosis cannot be reversed, it can be prevented and treated in a variety of ways. Osteoporosis treatments include the "rule of CDEF " - calcium(C), vitamin D (D), weight-bearing exercise (E), and prevention of Falls (F). A number of effective medications are approved for the prevention and treatment of osteoporosis. Different studies have consistently shown that, depending on the drug and the patient population, treatment reduces the risk of vertebral fracture by between 30-65% and of nonvertebral fractures by between 16-70% [39].

Studies of the benefits of supplementation with calcium and vitamin D are conflicting. Retrospective, cross-sectional, and prospective studies suggest that increasing calcium intake during the premenopausal period would allow women to enter menopause with greater bone density. Increasing calcium intake in the immediate postmenopausal period does not appear to affect the rapid bone loss that occurs during early menopause [40]. Recent study has shown that supplementation of 800 mg of calcium daily may prevent bone loss in post-menopausal

women, and the results of clinical trials also suggest that such supplementation may prevent hip and vertebral fractures in the elderly [41]. Some but not all studies have shown that low-dose 1,25(OH)2D3 (the two most potent vitamin D analogues) increase bone mass and/or reduce fracture frequency in patients with established osteoporosis [42]. However, a 2013 review by the USPSTF found insufficient evidence to determine if supplementation with calcium and vitamin D results in greater harm or benefit in men and premenopausal women [43]. In turn, Daniel found that combination of calcium (1.2 g/day) with vitamin D3 (800 IU/day) prevent fractures in elderly women. Author reported that the number of hip fractures was 43% lower and the total number of nonvertebral fractures was 32% lower among women treated with vitamin D3 and calcium than among those who received placebo [44]. From the other side, some meta-analyses have found a benefit of vitamin D supplements combined with calcium for fractures, they did not find a benefit of vitamin D supplements alone [45,46].

Estrogen replacement therapy (ERT) is the most effective HRT and a treatment of choice for prevention and treatment of osteoporosis by decreasing fracture rates in women immediately after menopause. Estrogen reduces bone turnover and thus conserves bone mass. Numerous studies also have shown that women treated with estrogen within 3 years of natural or induced menopause have a reduced rate of bone loss and significantly lower rates of fractures of vertebrae, wrists, and hips [47,48]. Large epidemiologic studies have indicated that the risk of hip and Colles' fractures may be reduced by as much as 50%, with an even greater reduction in the risk for vertebral fracture [42].

REHABILITATION

The main objective of rehabilitation in osteoporosis is to prevent fractures rather than to treat the complications of fractures. According to ROPE (Rehabilitation of Osteoporosis Program Exercise), physiotherapy should include: sedative physical therapy, exercise for prevention and management of osteoporosis, and application of proper orthotics. Moreover rehabilitation should improve the individual's quality of life despite osteoporosis and fragility [49]. In the design of an exercise program 5 principles should be taken in mind: 1. Specificity: The program must be designed to load specific bones or body regions, 2. Overload: To induce stimulation for increasing bone density according to mechanostat theory exercise must overload the bone, 3. Reversibility: In adults, any gains in bone density during an exercise program will be lost if the program stops, 4. Initial Values: The response of bone to increased loading is greater when bone mass is below average. Patients with bone mass below normal will experience greater gains in bone density with exercise programmes, compared with people who have a good bone density, 5. Diminishing Returns: The greatest gains in bone density will be seen early in an exercise program. After the initial increase, the benefits continue, but at a slower pace [50].

Regular physical activity and exercise plays an important role in maintaining or improving bone density. the American College of Sports Medicine recommends that exercise programs for elderly people should include weight-bearing endurance and resistance activities aimed at preserving bone mass, and also activities designed to improve balance and prevent falls [51]. A review on the osteogenic effects of walking, showed that the impact promoted by this activity could improve femoral BMD in postmenopausal women, with no positive effects on spine BMD [52]. Another study confirmed that walking as a singular exercise therapy has no significant effects on BMD at the lumbar spine, at the radius, or for the whole body in perimenopausal and postmenopausal women, although significant and positive effects on femoral neck BMD are evident with interventions with more than 6 months in duration [53]. The resistance training program of moderate to high intensity (70 to 90% of one maximum repetition-1RM), including 3 to 4 bouts of 8 to 12 repetitions of each exercise, performed 2 or 3 times a week, is able to maintain or improve the BMD of hip and femur in postmenopausal

women when performed over one year duration [54]. Sinaki et al., observed that by improving the back extensors muscle force in postmenopausal women a significant reduction in vertebral fracture occurred, as well as the enhancement of body balance and fall reduction [55]. Other study showed that the increase in the back extensors strength reduced the incidence of new vertebral fractures in patients that underwent vertebroplasty surgery [56].

Studies of fall prevention have shown varying results. Data from three studies with a total of 566 community-dwelling women ≥80 years using the same individually tailored program of progressive muscle strengthening, balance retraining, and a walking plan indicated that this intervention reduced the number of individuals sustaining a fall over a 1-year period [57-59]. Among elderly people, participants who practiced tai chi had a lower rate of falling than controls [60]. Another study showed that six months of practicing tai chi could reduce the risk of falling by 70% in people 70 years and older [61]. A study performed by Teixeira et al., demonstrated in 100 women over 55 years that 18 weeks of resistance, proprioception and balance training can reduce the number of falls, improve functional capacity, dynamic balance and quality of life when compared to the control group [62].

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