



## Osteoporosis – risk factors, prophylaxis, diagnostic tests and pharmacotherapy

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### ABSTRACT

Progressing osteoporosis is a pathological process, which leads to increased bone brittleness and the risk of spontaneous fractures. The prophylaxis of osteoporosis is aimed at preventing its development. It is important to adjust prophylactic measures to each patient's needs and capabilities. In the case of osteoporosis, the procedure involves taking the medical history, physical examination, densitometry, radiological examination and analytical tests. The following drugs are used in the treatment of osteoporosis: bisphosphonates, calcitonin, estrogens, tibolone, drugs from the SERM group (raloxifen), fluoride, parathormone, strontium. Furthermore, osteoporosis treatment is supplemented with calcium, vitamin D and phosphorus.

**Keywords:** osteoporosis fractures, risk factors, prophylaxis, diagnostic tests, pharmacotherapy

### OSTEOPOROSIS FRACTURES

Women who have fractured one vertebra, experience further fractures 2.6-3 times more often compared to women without a history of fractures, regardless of the bone mass. In turn, women with low bone mass who have experienced spinal or paraspinal fractures are 16 times more likely to have further spinal fractures. Among the most dangerous are femoral neck fractures since mortality among patients with this type of fractures is very high. Among patients of over 60 years of age, 25% of cases end in death, and after reaching the age of 90 over half of patients die [5,11,13]. When it comes to fractures of the distal part of the radial bone, the procedure involves setting the bone and stabilising displaced fractures. Closed resetting under local anaesthetic is applied together with immobilisation in plaster. Displaced, unstable fractures are qualified for surgical treatment. Analgesics are used

when needed. In turn, fractures of the proximal humerus are usually treated using non-surgical methods. Both non-displaced fractures and successfully reset ones are put in Dessault or Velpeau plaster for 2-3 weeks, followed by two weeks in abduction orthosis, starting the gradual rehabilitation of the elbow joint and shoulder. Proximal femur fractures are treated surgically. Osteoporotic spinal fractures are of a stable nature, are classified as compression fractures and practically do not require surgical intervention. Due to the acute pain accompanying such fractures, sometimes opiate analgesics are used [23]. Rehabilitation following any type of osteoporotic fracture is applied in order to improve the patient's quality of life and facilitate the return to self-sufficiency. Kinesiotherapy is aimed at increasing the mineral density of bones, to preserve its structure, improve the patient's muscular and motor coordination, as well as enhance the functioning of the cardiovascular and respiratory system and the general fitness. By using physiotherapy pain intensity can be reduced and muscular tension can be controlled, while orthopaedic appliances enhance the patient's functioning, reduce the risk of falling and mitigate pain [13].

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## OSTEOPOROSIS RISK FACTORS

Factors contributing to the risk of and influencing the course of osteoporosis can be divided into unmodifiable, i.e. the ones depending on genetic determinants and comorbidities and modifiable, i.e. the ones which can be influenced through a change in lifestyle. Genetic factors – an increased risk of the disease was identified in families with a history of osteoporosis. Age is also considered a risk factor because the bone tissue degenerates with age and thus the risk of osteoporosis rises [4]. Another factor is sex – men in their young age reach a higher peak value of bone mass than women; also, their bones are larger. In turn, women at menopause lose more bone mineral mass than men [25]. The factors which can be influenced include, *inter alia*, nutrition. Too low amount of calcium in diet increases the risk of osteoporosis and fractures. Similarly, vitamin D and protein deficiencies considerably increase the risk of osteoporosis [4,25]. Hormones constitute another modifiable risk factor. Estrogen deficits intensify osteoclastic activity and bone resorption. A 1% annual decrease in BMD in an untreated women after menopause translates into a 40-50% loss of the peak bone mass after reaching the age of 90 [3,4,11,27]. Reduced physical activity is also a natural way to relieve bones, although in the long run it may increase the rate of bone mass loss due to a decreased mechanical stimulation of osteoblasts. However, during a prolonged period of intensive physical activity women may experience eating disorders, the lack of menstruation or osteoporosis. These symptoms are called the female athlete triad syndrome [4,22]. Pharmaceuticals such as corticosteroids, anticonvulsant medicines, ciclosporin and heparin decrease bone density. Corticosteroid therapy constitutes an important cause of secondary osteoporosis [4,11,18,28]. Tobacco smoking leads to decreased bone density, which is probably due to the reduced synthesis of estrogens and their intensified deactivation. It has been proven that tobacco smoking has an impact on women's bone mineral density. In order to stop bone mass deterioration, smoking women must receive higher doses of estradiol than non-smoking women [4,11,21]. Disorders such as diabetes, hyperparathyroidism and hyperthyroidism cause an increased bone turnover, which leads to general bone mass deterioration. Intestinal inflammatory diseases, gastrectomy, coeliac disease, Crohn's disease, and pancreatic endocrine disorders are accompanied by disorders in the intestinal absorption of calcium, phosphorus and vitamin D. Cushing's disease and depression involve an increased concentration of endogenous cortisol in blood serum, which entails a loss in bone mass similar to the one observed in corticotherapy [4]. Bone metabolism in diabetes may be influenced by insulin-like growth factors and other cytokines. Retinopathy and diabetogenic neuropathy are the risk factors contributing to frequent falling, as

they cause vision, balance or gait disorders [6]. Rheumatoid joint inflammation is a comorbidity of osteoporosis. A prolonged rheumatoid process leads to generalised osteoporosis related to joint damage and, in consequence, to the impairment of physical fitness [16].

## PROPHYLACTIC MEASURES

Osteoporotic fractures can be prevented by avoiding injuries, because one fracture leads to another. Prophylaxis is also an important element of combatting osteoporosis at all stages of a person's life. Children and adolescents should be educated about the proper supply of calcium and vitamin D3 as well as an active lifestyle. In the case of adults, it is important to avoid smoking and drinking excessive amounts of alcohol. Women in menopause are recommended a hormone replacement therapy unless there are serious contraindications. Moderate physical activity is also recommended. Elderly people are advised to maintain the proper body weight and the required calcium and vitamin D3 consumption, take advantage of sunbathing, preserve a possibly high level of physical fitness and suitable amount of exercise [24]. People aged 25-30 until reaching the peak bone mass are advised to exercise because the lack of physical activity is a major risk factor of osteoporosis. However, it should be borne in mind that too intensive physical exercise in young women can induce the temporary lack of menstruation and consequently a reduction in estrogen activity stimulating the development of bone tissue. Maintaining physical activity after the age of 50 is the most important factor preventing bone mass deterioration. Strolling is a good prophylactic measure, because patients can enjoy sunlight which stimulates the production of vitamin D. Elderly people due to the weakened skeletal system should choose less strenuous exercises, such as walking, and supplement them with resistance exercises of the upper and lower part of the body. Excessive strain on a failing skeletal system may lead to fatigue-induced damage and stress fractures [4,20,22]. According to general practice, daily diet supplementation with on average 1000 mg calcium, 800 IU of vitamin D and proteins in the amount of 1 g/kg of body weight can be recommended to osteoporosis patients as a supplementary treatment.

## DIAGNOSTIC TESTS IN OSTEOPOROSIS

Apart from the traditional taking of the medical history, physicians may use questions from the osteoporosis risk test recommended by the International Osteoporosis Foundation (IOF).

Physical examination starts with the measurement of the patient's height, body weight and the calculation of the BMI (Body Mass Index). The signs of faulty posture typical for this disease are also evaluated, including the

increase of thoracic kyphosis with a secondary increase of lumbar and cervical lordosis, deformation of the thorax (dowager's hump). The physician also performs a standard examination of the spine and limbs [8].

Densitometry is a specialist examination performed to measure the mineral density of bones. Densitometric methods are based on measuring gamma radiation absorption sent by a radioactive isotope or an x-ray tube. By measuring the radiation density from the x-ray tube before and after going through the object, it is possible to calculate the object's mass [17]. Bone density measurements are also made with the use of radiological absorptiometry based on the traditional radiological examination [8]. Another method is the single x-ray absorptiometry – SXA, where radiation measurement is carried out with densitometers constructed specifically for this purpose. However, performing examinations remains problematic, especially in the area of limb bones. It also does not allow the distinction between the cortical and trabecular structure [8,17]. Dual energy x-ray absorptiometry (DEXA, DXA) is another densitometric method. New generation apparatus is used here, in which the source of radiations is an x-ray lamp which, employing a special filter, emits a beam with double energy. Owing to this method, the bone mineral density can be measured in the lumbar section of the spine in the anteroposterior and lateral projection in the proximal part of the femur, forearm and in the entire spine. The available software also allows the measurement of BMD around the hip joint prosthesis. The test is absolutely safe, as the measurement takes from 5 to 12 minutes, the applied radiation dose is low, and sensitivity is high [1,8,15,17]. For patients and physicians Z and T scores are the most important in the interpretation of a densitometric test. The Z score shows standard deviations between the patient's bone density and statistical data for a healthy person of the same sex, race and age. The T-score defines standard deviations between the patient's bone density and the peak, ideal bone mass, which the patient could have achieved in adolescence. The World Health Organisation (WHO) suggests densitometric testing of osteoporosis progression [8].

Bone density measurements are also performed through quantitative computerised tomography – QCT. Acoustic parameters of bones are made with the use of quantitative ultrasonography – QUS. Differential diagnosis and documentation of fractures is prepared on the basis of a radiological examination, typically of the dorsal and lumbar section of the spine [1,8].

Each person with suspected osteoporosis should undergo analytical examinations such as complete blood count, erythrocyte sedimentation rate and general urine test, calcium and alkaline phosphatase ratio in blood serum, and calcium and creatinine ratio in urine. Bone markers based on the analysis of bone metabolism prod-

ucts in serum or urine make it possible to determine bone metabolism. They are divided into bone formation markers (the bone fraction of alkaline phosphatase, osteocalcin, N-terminal propeptide of procollagen type I) and resorption markers (pyridinoline, deoxypyridinoline) [1,8].

## PHARMACOTHERAPY IN OSTEOPOROSIS

For prophylaxis it is recommended to take 600-1500 mg of elemental **calcium** daily [2]. **Vitamin D** also participates in calcium absorption from the gastrointestinal tract and its reabsorption in kidney tubules. For prophylaxis men and women who have turned 50 are recommended to supplement vitamin D with daily doses of 400-800 units [2,10]. Phosphorus constitutes an important element affecting calcium balance. Body **phosphorus** in 90% is located in bones and teeth in the form of calcium phosphates; its absorption is also dependent on vitamin D. Its sources include meat, poultry, fish, milk and dairy products, especially fermented cheese, cottage cheese and yoghurts, and cereal products – dark bread, and pearl barley [12]. **Fluoride** increases the number of osteoblasts, i.e. active bone-forming cells, so it contributes to bone creation. According to the experts from the National Food and Nutrition Institute in Warsaw, the application of fluoride in osteoporosis therapy can be effective and safe under the condition that the daily dose does not exceed 15-30 milligrams [10].

Among osteoporosis medicines there are the following: **bisphosphonates**, which effectively prevent the deterioration of bone mass, permanently bonding with hydroxyapatite crystals on the bone surface. They also inhibit the activity of osteoclasts. Among bisphosphonates there are **etidronate**, **alendronate**, and **risedronate** [2,10]. **Ibandronate** is a bisphosphonate of the newest, third generation. Its anti-resorptive effect is at least ten times stronger than that of alendronate. It is used in the treatment and prophylaxis of post-menopause osteoporosis. In this case, however, adverse reactions such as influenza-like syndrome have been observed. Similarly as other bisphosphonates, ibandronate has an anti-neoplastic effect and reduces the risk of bone metastases [9,14]. **Calcitonin** is a hormone regulating calcium balance. It is secreted as a result of a high concentration of calcium in blood. Calcitonin has an effect opposite to parathormone. It lowers the concentration of calcium and decreases bone resorption by directly blocking osteoclastic activity. Osteoporosis can be treated with salmon calcitonin because it has a stronger effect than human calcitonin. The effects of calcitonin also include the reduction of pain, which contributes to the improvement of the general condition and physical fitness of osteoporosis patients [2,10,19]. **Estrogens** have a direct impact on osteoblasts, increasing their activity and extending their lifetime, while stimulat-

ing natural cell decay [2,10,19,27]. **Tibolone** is a synthetic analogue of sex hormones with estrogen, androgen and progestagen effects. It prevents the deterioration of bone mass and, due to the androgen component, lowers bone turnover by 30 - 50%, leading to a 2-5% increase in bone mass in the first two years of use [10]. **SERM** (Selective Estrogen Receptor Modulator) inhibits the formation of osteocytic lacunae by osteoclasts. In women in the postmenopausal age **raloxifen** causes a decrease in the concentration of bone turnover markers, an increase in bone mass in vertebral bodies, and considerably reduces the risk of vertebral fractures during three years of therapy [2,10,19,26]. **Parathormone**, secreted by parathyroid glands, together with calcitonin, is responsible for regulating calcium balance. It has been found that parathormone treatment decreases the risk of vertebral and paravertebral fractures, increases the average mineral density of bones and is well tolerated by patients [2,10,13]. **Strontium ranelate** is a medicine with a double effect – it inhibits resorption and stimulates the formation of bone tissue by limiting the differentiation and activity of osteoclasts and increasing the synthesis of collagen by osteoblasts [7,10,14].

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