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Etiopathogenetic Factors Of Osteoporosis In Women During Menopause

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Abstract. The article presents information related to the pressing problem of our time - the epidemic of osteoporosis of the 21st century, developing in people over 50 years of age, especially women, and its main etiological factors. The table also highlights risk factors and predictors of tubular fractures and osteoporosis in perimenopausal women.
Keywords: osteoporosis, osteoblasts, osteoclast, osteocytes, climacteric syndrome, parathyroid hormone, cytokines, densitometric indicators, hypovitaminosis.

Introduction. Osteoporosis, the silent epidemic of the 21st century, is a very common disease. Today, every 3rd woman and every 4th man over 50 years old suffers from osteoporosis. Osteoporosis can cause fractures of any bone, but the most common fractures are the spine, femoral neck, and radius. The peculiarity of fractures in osteoporosis is that they occur with little or even no trauma.

According to the World Health Organization (WHO) criteria, osteoporosis is defined as "a disease characterized by low bone mass and deterioration of bone microarchitecture, leading to increased bone fragility and, as a result, an increased risk of fractures." Later, WHO clarified: "The criterion for osteoporosis is a decrease in bone mineral density (BMD) T to -2.5 or lower". The US National Institutes of Health and the International Osteoporosis Foundation have updated previous definitions to state that "osteoporosis is a disease of the skeletal system characterized by decreased mechanical endurance of bones, which increases the risk of fractures". A conference dedicated to the problems of diagnosis and treatment of osteoporosis proposed its own definition: "Osteoporosis is a systemic skeletal disease characterized by low bone density and deterioration of the microarchitecture of bone tissue with a subsequent increase in bone fragility and susceptibility to fractures".

Bone tissue is a dynamic system. Normally, bone is constantly remodeled by the cells present in bones: osteoblasts, osteoclasts and osteocytes. Their activities are interdependent. Several stages are constantly observed in the bone remodeling cycle: activation, resorption, formation and quiescence.

When osteoclasts are active, bone is destroyed and calcium and phosphate are released into the extracellular fluid during demineralization. The activity of osteoblasts leads to the formation of new bone. Mineralization promotes the movement of calcium from the extracellular space into the newly formed bone. Osteoclasts do not have receptors for either parathyroid hormone (PTH) or vitamin D, but do have receptors for calcitonin. Osteoblasts have receptors for both

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PTH and vitamin D. The relationship between the activity of osteoblasts and osteoclasts is expressed in the fact that when the osteoblastic activity of PTH is stimulated, the activity of osteoclasts increases. Osteocytes are osteoblast-derived cells that modulate bone remodeling by inhibiting and stimulating the activity of osteoclasts and osteoblasts, respectively. Osteocytes are stimulated by mechanical loads (gravity and exercise).

Direct regulators of bone metabolism are cytokines and growth factors. Osteoblasts are capable of producing cytokines that affect the differentiation and activity of osteoclasts. Cytokines and factors that are involved in osteoclastogenesis include interleukins (IL-1, -6, -11), tumor necrosis factor α, ciliary neurotrophic factor, oncostatin M, macrophage colony-stimulating factor, stem cell factor, etc. On the other hand, IL-4, -10, -13, -18 inhibit the development of osteoclasts .

The strength of bone tissue is a reflection of two main characteristics: density and quality. Bone density is expressed in grams of minerals per unit area or volume, and in each individual is determined by the peak of bone density and the amount of sparse bone tissue. The quality of bone tissue is determined by the structure of bone tissue, its turnover, accumulation of damage and mineralization. A fracture occurs when an osteoporotic bone, with or without trauma, is exposed to a force that exceeds the strength of the bone tissue. Bone density increases during growth during adolescence and reaches a peak in the third decade of life. Later, it is maintained at a peak level for several years and begins to decline in the mid-thirties. Women after menopause experience a period of accelerated bone loss that lasts 6–10 years. After this, bone loss continues, but at a slower rate.

Table for predicting factors and risk levels for osteoporosis and tubular bone fractures among perimenopausal women

№	Indicators	Main characteristics	Points
1	**BMI**	BMI> =18.5<25 kg/m2	**0**
		BMI> =25.1 <30 kg/m2	**5**
		BMI> =30.1<40 kg/m2	**10**
2	**Backache**	Absent	**0**
		Weak	**5**
		Expressed	**10**
3	**Decrease in height**	absent	**0**
		Up to 5 cm	**5**
		Up to 10 cm	**10**
4	**Disturbances in the production of parathyroid hormones**	No violation	**0**
		Minor violation	**5**
		Expressed disorders	**10**
5	**Esteriol content in blood**	No violation	**0**
		Moderate decline	**5**
		Significant reduction	**10**

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6	**Tides**	None	**0**
		Rare	**5**
		Frequent	**10**
7	**Slouch**	Absent	**0**
		Weakly expressed	**5**
		Significantly expressed	**10**
8	**Content of Ca and Vit D in blood**	Fine	**0**
		Decreased slightly	**5**
		Sharply reduced	**10**
9	**Cholesterol concentration indicators (High Density Lipoprotein)**	Not violated	0
		Moderate increase	5
		Sharply increased	10
10	**X-ray examination** (multiple cystic formations)	Absent	0
		There are single	5
		Multiple	10
11	**Densitometric indicators**	Normal bone density	0
		Osteopenia	5
		Osteoporosis is pronounced	10

Wherein:
86 – 100 points - pronounced clinical signs of grade 4 osteoporosis
85 -73 points - not pronounced clinical signs of grade 3
72 -55 points - mild clinical signs of grade 2
55 and below points - no clinical signs of grade 1

The main reason for the development of postmenopausal osteoporosis is a deficiency of estrogen, which is one of the main hormonal regulators of bone tissue metabolism. It is known that estrogens have a direct effect on the function of bone cells through estrogen receptors found in osteoblasts, osteocytes and osteoclasts. The protective role of estrogens in relation to bone resorption occurs through ligand-receptor mechanisms, which increase the functional activity of osteoblasts and osteocytes, as well as suppress osteoclastogenesis and increase osteoclast apoptosis.

Changes in bone metabolism are aggravated as a result of general age-related metabolic changes, against the background of vitamin D and calcium deficiency, secondary hyperparathyroidism and decreased physical activity. In addition, immune factors against the background of estrogen deficiency, which aggravate the course of the disease, are currently considered as another reason for the development of postmenopausal osteoporosis.

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The main risk factors for the development of osteoporosis are:

- female
- postmenopause
- fractures in the past
- cases of fractures with a low level of trauma in close relatives (father, mother, sister), over the age of 50 years
- early (including surgical) menopause (up to 45 years), taking glucocorticoid hormones (more than 3 months), long-term bed rest (more than 2 months). low body mass index and obesity
- Women of white or Asian race, especially those with a family history of osteoporosis.
- Postmenopausal women, including those who have had surgical removal of reproductive organs or menstrual irregularities.
- Eating disorders such as anorexia nervosa or bulimia, low calcium in the diet, alcohol abuse, sedentary lifestyle, taking anticonvulsants.
- There are risk factors associated with deterioration of bone metabolism and risk factors for fracture. However, their use in clinical practice to assess the individual risk of developing osteoporosis is difficult due to the fact that the influence of some factors is very insignificant. The factors that are most important in clinical practice are: family history of the disease, early menopause, constant use of glucocorticoids, prolonged immobility, history of fractures. To a lesser extent, the development of osteoporosis is influenced by: low body mass index (BMI), smoking, alcohol abuse, sedentary lifestyle, low calcium intake, certain diseases (rheumatoid arthritis, chronic liver diseases, hypogonadism, etc.). The risk of developing osteoporosis also depends on genetic predisposition. But these risks can change under the influence of factors such as diet, lifestyle, exercise, and the use of various medications.
- Also, risk factors for the development of osteoporosis include high levels of homocysteine, carriage of the recessive Sp1 allele of the type I collagen gene, and the presence of chronic inflammatory bowel diseases

  The natural process of fading ovarian function and, as a consequence, age-related estrogen deficiency results in every woman having a huge risk of developing those very conditionally preventable diseases from which she ultimately dies. The general preventive direction for every patient in menopause should be exogenous replenishment of hormonal deficiencies. In conditions of age-related decrease in sex hormones, a number of pathological conditions and diseases in postmenopausal women are based on a deficiency of another important hormone - E hormone (more often referred to as vitamin E deficiency), well known for its classical role in the homeostasis of calcium, phosphorus and skeletal health. The global prevalence of vitamin E deficiency and insufficiency affects more than a billion people worldwide. A large international epidemiological study (18 countries) found that 64% of postmenopausal women had decreased vitamin D concentrations. 25(OH)D levels of less than 30 ng/ml were observed in 42% of Brazilian and 92% of South Korean women. Severe vitamin D deficiency, defined as serum 25(OH)D <10 ng/mL, was most common in South Asia and the Middle East. Many authors indicate that the prevalence of hypovitaminosis D is higher in the female population. According to the National Institute of Health, with age, the number of people in the world with vitamin D deficiency increases to 80-90%, especially in the northern latitudes of the earth

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(located above the 42nd parallel), where from November to February there is not enough ultraviolet radiation to produce vitamin D. Modern research supports the role of vitamin D in protection against many common diseases and disorders, such as cancer, cardiovascular disease, autoimmune diseases, musculoskeletal diseases, fractures, infections and depression, diabetes and metabolic syndrome, obesity, mortality. To prevent the above-mentioned diseases, higher dosages of vitamin D are now used than previously. To date, more than 200 candidate genes have been identified that may make a certain contribution to the etiopathogenesis of the disease and influence the rate of BMD loss in postmenopausal women (Yang T.L. et al., 2020). These include genes*VDR* (vitamin D receptor gene–VDR),*MCM6* (minichromosome maintenance complex component 6, regulates lactase gene expression*LCT*),*CALCR*(calcitonin receptor gene)(Tural S. et al., 2013; Maylyan E.A., 2016; Verkhoturova S.V. et al., 2017; Mailyan E.A.,2017; Zimmermann A. et al., 2018; Rudenko E.V. et al., 2019)

Given the significant interest in vitamin D and its biological effects at different ages, many authors have recently emphasized the important role of vitamin D in numerous physiological functions. The presence of vitamin E deficiency is associated with a number of acute and chronic diseases, including calcium metabolism disorders, fractures, insulin resistance and type 2 diabetes mellitus, cardiovascular diseases, metabolic syndrome, Alzheimer's disease, depression, often manifesting and progressing in the postmenopausal period. Particularly alarming is that vitamin E deficiency may remain asymptomatic or manifest itself as vague muscle pain, muscle weakness, decreased physical performance and other nonspecific symptoms, which makes it difficult to diagnose in a timely manner and leads to serious consequences. The importance of determining vitamin D status in patients with neurovegetative and psychoemotional manifestations climacteric syndrome is not sufficiently covered, however, timely replenishment of vitamin D will significantly improve many health indicators and quality of life of early postmenopausal women. The aging of the general population requires a better understanding of age-related metabolic consequences.

In conclusion, older people, notably menopausal women, are more likely to develop osteoporosis. But knowing the etiological and risk factors, it is important to properly approach and prevent the disease. And of course, it is advisable to enrich your daily diet with healthy foods, especially vitamin D.

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