EFFECT OF ATHEROSCLEROSIS ON BONE TISSUE

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Atherosclerosis and osteoporosis are not only age-related, but also have common pathogenetic mechanisms. Blood vessels and bone tissue have similar morphological characteristics, and vascular calcifications are composed of the same components as bone tissue.

Modern medicine emphasizes the need to identify specific relationships between these diseases and their common pathogenetic mechanisms in order to develop a complex and individual approach to diagnosis, treatment and prevention.

Key words: *cardiovascular diseases, atherosclerosis, osteoporosis.*

The 20th century saw an increase in non-communicable diseases. Cardiovascular diseases and osteoporosis stand out among them. These diseases not only significantly reduce the quality of life, but also take the leading place among the causes of death in developed countries. According to epidemiological studies, the prevalence of cardiovascular disease in women is slightly higher than in men, which is partly explained by the frequent false positive results in women. In studies conducted in Leningrad in 1997, heart disease was found in 8.9% of men aged 40-49 and 10.1% of women, in the age group 50-59 - in 18% of men and 20.5%. women [32; 2].Osteoporosis, which is initially asymptomatic, often leads to bone fractures, which are associated with disability and high mortality, especially in the elderly. The increase in the prevalence of these diseases is mainly explained by the increase in the average life expectancy and the accumulation of various pathologies in old age. [9]. Research on the problem of osteoporosis began to develop actively only in the last 10 years with the advent of special diagnostic equipment. According to densitometric tests, osteoporosis was found in 30.5-33.1% of women and 22.8-24.1% of men over 50 years of age [10]. A similar prevalence of osteoporosis among women has been reported in the white population of North America and some Western European countries [7]. The social importance of osteoporosis is determined by its consequences, for example, fractures of the bones of the peripheral parts of the vertebrae and segments of the musculoskeletal system.The most serious medical and social consequences are associated with fractures of the proximal femur. Mortality during the first year after such a fracture varies from 30.8% to 35.1%, with 78% of survivors requiring ongoing care at one year and 65.5% at 2 years [4; 1].The role of various factors in the mechanism of the occurrence and development of atherosclerosis has been identified and confirmed. Local factors contributing to the

development of atherosclerosis were studied, and the leading role of dyslipidemia in this process was determined. Risk factors and their impact on the incidence of cardiovascular diseases have been determined [5].Vascular calcification, the final stage of atherosclerotic plaque development, or ectopic mineralization of vessel walls is an independent risk factor for cardiovascular complications. Over the past 20 years, numerous epidemiologic, experimental, and clinical studies have identified an association between bone loss and cardiovascular disease, independent of age and traditional risk factors [26; 8].

There is a growing body of evidence linking bone mass to cardiovascular health.

New scientific research points to an interesting relationship between osteoporosis and atherosclerosis, which is more common, especially in older people.These diseases share a number of common risk factors, such as older age, smoking, a sedentary lifestyle, and postmenopausal estrogen deficiency. Epidemiological studies have found an association between the decrease in bone mineral density characteristic of osteoporosis and an increased incidence of atherosclerotic disease, which may indicate common pathophysiological mechanisms [12]. Several hypotheses have been proposed that chronic systemic inflammation, excessive oxidative stress, and impaired mineral metabolism are common mechanisms contributing to the development of both osteoporosis and atherosclerosis [29].Common risk factors such as age, smoking, lack of physical activity, alcohol abuse, and hormonal imbalances (such as those associated with menopause) play an important role. Decreased physical activity increases bone loss in patients with cardiovascular disease. There is also a mechanical and rheological approach, according to which atherosclerotic changes in arteries lead to disruption of bone microcirculation, which leads to changes in bone metabolism and, as a result, to the development of osteoporosis. On the other hand, these conditions may be associated with more complex regulatory mechanisms, which opens up prospects for the development of general therapies aimed at correcting disorders of bone metabolism and cardiovascular diseases. Calcification of the vascular wall is not only a passive process of phosphate and calcium accumulation, but also a complex active mechanism similar to the system that regulates the mineralization of bone tissue. It significantly reduces the elasticity of arteries, which contributes to the development of arterial hypertension, aortic stenosis, myocardial hypertrophy and stroke. It increases the risk of developing cardiovascular diseases by 3-4 times and can lead to myocardial infarction and acute heart failure [16; 31]. The non-collagenous bone protein osteonectin also plays a role in the development of atherosclerosis. With the development of atherosclerosis, especially with the calcification of atherosclerotic plaque, its expression in the cells of the vascular wall increases significantly.

In addition, many studies show a positive correlation between cardiovascular diseases and pathologies of the bone system [15].

Calcification of blood vessels is often associated with atherosclerosis, which is the basis of many cardiovascular diseases. Pathophysiological vascular calcifications are divided into four types depending on the localization of the process: atherosclerotic calcification of the intima, calcification of the media (Mönkeberg arteriosclerosis), calcification of heart valves and calcific uremic arteriopathy [24; 20].Estrogen is known to have a cardioprotective effect, which is weakened by its decline after menopause. One of these effects is the improvement of lipid metabolism. Estrogen stimulates the production of high-density lipoprotein cholesterol (HDL-C), which is involved in reverse cholesterol transport, reducing the risk of atherosclerotic plaque formation. At the same time, estrogen helps reduce low-density lipoprotein cholesterol (LDL-C) and triglycerides, which are associated with the development of AS. Estrogen deficiency in postmenopausal women may lead to a worsening of the lipid profile, which increases the risk of atherosclerosis [28;3].Estrogen also plays a critical role in maintaining endothelial health by promoting the production of nitric oxide, a potent vasodilator, and by having anti-inflammatory properties that reduce vascular inflammation, a major factor in the development of atherosclerosis [30] .With a decrease in estrogen levels, these protective mechanisms are weakened, which increases susceptibility to vascular inflammation and endothelial dysfunction, which precedes the development of atherosclerosis [27].Although some parallels have been described in the mechanisms of vascular calcification and bone formation, a clear relationship between osteopenia and physiological markers of risk for the development or development of calcification in atherosclerosis has not yet been established.A promising concept is that cardiovascular disease and osteoporosis are linked through markers that simultaneously affect vascular and bone cells [23].Despite the fact that vascular calcification occurs in the majority of people over 70 years of age and often leads to serious heart problems, strategies for its prevention have not been developed to date, because the pathogenesis of this process remains unclear. The relationship between atherosclerosis and osteoporosis is supported by observations showing that asymmetric atherosclerotic peripheral vascular disease is accompanied by an asymmetric decrease in bone mineral density in the studied skeletal regions [21]. In addition, histological studies of bone tissue in the ilium and femur in elderly women with hip fractures revealed atheromatous lesions of the large and small vessels of the ligaments and para-articular structures in the area of the fracture [25].Some proteins involved in bone turnover may be involved in the pathogenesis of AS. Bone tissue proteins such as osteocalcin, bone morphogenic proteins, sialoprotein, osteonectin and osteopontin are found in the vessel wall. During the formation of atherosclerotic plaque, the concentration of a number of these proteins can be significantly increased [11].

Originally studied as a key factor involved in bone matrix remodeling, osteoprotegerin (OPG) is now gaining research attention as a protein that affects

vascular calcification and the development of atherosclerosis [33]. Osteoprotegerin (osteoclast inhibitory factor) or osteoclast binding factor inhibits the differentiation and activation of osteoclasts, making it an important component of the bone resorption process. This glycoprotein belongs to the tumor necrosis factor receptor (TNF-α) family and consists of 401 amino acids divided into 7 domains. It functions in two main forms: mono- and homodimer [19].

A number of experimental studies have provided evidence that osteoprotegerin is involved in calcification of arterial walls and heart valves, formation of endothelial dysfunction, remodeling of heart muscle, as well as in the development of atherosclerosis and arteriothrombosis. The degree of calcification of the vascular wall of arteries was directly related to the level of osteoprotegerin expression. In addition, some researchers found an increase in osteoprotegerin in the media of the walls of the aorta and its branches in patients with early and severe osteoporosis [14].

The main factors stimulating the synthesis of osteoprotegerin are anti-inflammatory cytokines, for example, interleukins (IL-1, IL-2, IL-6, IL-11), monocyte chemoattractant protein-1, as well as regulatory peptides, including o sish changer factor-β (TGF-β) and fibroblast growth factor (FGF) [17; 18; 22]. Osteoprotegerin synthesis is also influenced by hormones (estrogens, glucocorticoids, parathyroid hormones) [35] and vitamins such as vitamin D3, which are usually tissue type-independent. Thus, IL-1α, IL-18, TNF-α, vitamin D3 and estradiol promote the increase of osteoprotegerin on the surface of endothelial cells, smooth muscle cells [34], osteoblasts and stromal cells of bone tissue.

IL-1ß, IL-6, IL-11, IL-17, glucocorticosteroids and prostaglandin E2, on the contrary, suppress this process. Osteoprotegerin interacts not only with the RANKL molecule, but also with TRAIL (tumor necrosis factor-related apoptosis-inducing ligand - TNF-α-related ligand-inducing cell apoptosis).The assumption that there is a common pathogenetic basis of osteoporosis and atherosclerosis, as well as the similarity between the mechanisms of their development and the calcification of blood vessels, is confirmed by many experimental and clinical observations [13].

Today, there is a lot of evidence in the scientific literature about the existence of common pathogenetic mechanisms in the development of osteoporosis and cardiovascular diseases. However, there is still insufficient reliable data to allow the development of new practical recommendations for the combined treatment of these conditions. Certainly, further research in this area is appropriate and relevant.

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