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REVIEW OF MULTIMORBID CONDITIONS IN ATHEROSCLEROSIS.

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Annotation. A review of modern literature on the issues of multimorbidity of atherosclerosis and osteoporosis is presented. There are quite a lot of various scientific studies: experimental, clinical, epidemiological, which have confirmed the mutual coherent relationship between these diseases. It was revealed, that they are based on common risk factors and mechanisms of pathogenesis.

Keywords: atherosclerosis, osteoporosis, cardiovascular diseases, multimorbidity.

Introduction. Modern updating of the issue of the pathogenesis of atherosclerosis is based on the paradigm of the multicausality of this pathological process. Discussions in the scientific world, sometimes quite heated, on this issue have not stopped since the moment scientists defined the very concept of “atherosclerosis.” Despite significant advances, to this day there is no unified theory of origin and development [1, 2, 3, 4, 5].

Apologists of medical science, who have been involved in the development of issues of etiopathogenesis have proposed a number of theories, that have not lost their relevance. These include: infiltrating cholesterol or lipoprotein, inflammatory, endothelial dysfunction, autoimmune, genetic, hormonal, age-related and many others. The emergence of new tools , in the form of the latest developments of an innovative plan, has made it possible to conduct research on this track at a qualitatively new level [6, 7, 8, 9, 10, 11, 12].

As a rule, these expanded capabilities have led scientists to deepen their knowledge of each of the above theories; they have made it possible to make a breakthrough in understanding many subtle and ultra-subtle mechanisms of the development of atherosclerosis.

Why does atherosclerosis continue to attract much attention today? It is not difficult to answer this question. Diseases of the heart and blood vessels associated with atherosclerosis are unrivaled in comparison with other diseases in terms of disability and cause of mortality in the population around the world. Moreover, heart and vascular diseases have remained the leading cause of mortality in the world’s population for 20 years [13, 14, 15].

There is no doubt, that the issues of the pathogenesis of this insidious and

dangerous disease require comprehensive scientific development, because it is well known, that new data on the operating mechanisms of the development of atherosclerosis has one single goal: the search for effective treatment, with the possibility of targeted effects on important links in pathogenesis [16, 17, 18]. Scientific developments are actively underway at this medical site around the world.

Target. As part of this review, I would like to highlight an important, in our opinion, aspect regarding the comorbidity of atherosclerosis. The addition of another pathology, as a combined one, leads to a radical change in the picture of each disease, further complicating the efforts of doctors to achieve good treatment results.

It seemed interesting to consider the issues of comorbidity of two multifactorial diseases - atherosclerosis and osteoporosis. There are quite a lot of multidisciplinary studies: experimental, clinical, epidemiological, which have confirmed the existing connection between these diseases. It has been suggested that they are based on common risk factors and mechanisms of pathogenesis [19, 20].

Material and methods. The material for this review report was the data of numerous scientific studies posted in the open access of Internet resources on scientific platforms, journals, collections, and monographs. An analytical review of publications and literature sources in the PubMed, Medline, Web of Science and Cochrane Library databases starting from 2018 is presented in this article.

Results and discussion. A number of authors to assess the association between cardiovascular diseases caused by atherosclerosis. and osteoporosis used surrogate markers - vascular calcification or parameters of vascular stiffness and bone mineral density [21].

It is a well-known fact that atherosclerosis and osteoporosis are multifactorial diseases, depending on the human genotype, and are caused by the interaction between an unfavorable environment and genetic predisposition, affecting the vascular wall or bone mass and other indicators of bone strength, and possibly simultaneously on some and the same organs and tissues [22].

At the same time, a number of researchers confirm the associations between osteoporosis and cardiovascular diseases caused by atherosclerosis, primarily using surrogate disease markers - calcification of the aorta or coronary arteries or parameters of vascular stiffness and bone mineral density [23]. Recent studies have found that patients with osteoporosis have a higher incidence of aortic calcification than those with normal bone mineral density [24, 25].

It was also found that patients with decreased bone mineral density were more likely to have increased concentrations of lipids (glycerolipids , glycerophospholipids , sphingolipids) in the blood, develop more severe atherosclerosis of the coronary arteries, and significantly increase the risk of stroke and myocardial infarction [26]. These data suggest that an increase in the incidence of osteoporosis, ectopic

calcification and atherosclerosis in the same patients may indicate common pathophysiological mechanisms and, possibly, common genetic determinants in these diseases.

It is instructive that genome-wide association searches association study - GWAS) allows you to successfully determine many genetic markers associated with atherosclerosis and osteoporosis. Using GWAS, it is possible to identify common genetic variants that significantly contribute to the development of common multifactorial diseases. Another alternative method, whole genome sequencing genome sequencing - WGS), allows you to detect unusual and rare genetic variants in osteoporosis and atherosclerosis [27].

According to a number of authors, the identification of genetic factors, responsible for the predisposition to the development of atherosclerosis and osteoporosis, is of fundamental importance for the development of simultaneous prevention of both diseases and the creation of new treatment methods before the occurrence of a cardiovascular accident and bone fracture [28].

Very interesting studies are devoted to the study of various pleiotropic effects used in clinical practice of antihypertensive and lipid-lowering drugs. The mechanisms of action of a wide range of drugs, such as statins, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists and nitrates on bone mineral density and the occurrence of fractures associated with osteoporosis are shown. The data from the study indicated that the effects showed an ambiguous direction, which led the authors to the conclusion that further work in this direction is necessary [29].

There are studies that have studied the effects of anti-osteoporosis drugs on the vascular wall. Both antiresorptive drugs (bisphosphonates , monoclonal antibodies to RANKL, selective estrogen receptor modulators) and bone-anabolic therapy, which includes teriparatide , were studied . The discrepancies in the results of experimental and clinical studies are noteworthy. If in experiments almost all drugs for the treatment of osteoporosis had an atheroprotective effect and suppressed vascular calcification, then in clinical conditions only bisphosphonates confirmed a positive effect on the vascular wall [30].

The report on the connection between biochemical markers of bone tissue metabolism, osteopenic syndrome and coronary atherosclerosis in men with stable coronary heart disease attracted attention. Based on the assessment of the levels of markers of bone tissue metabolism in patients with stable coronary artery disease, a significant relationship between osteopenic syndrome and the severity of coronary atherosclerosis and calcification in men with stable coronary artery disease was revealed. Biochemical markers of bone tissue metabolism were largely associated not with the development of coronary atherosclerosis, but with the calcification of existing vascular lesions [31].

Clinical studies assessing the severity of coronary atherosclerosis in men with coronary artery disease depending on bone mineral density have shown probable common mechanisms for the development of atherosclerosis and osteoporosis, while coronary calcification is considered as a factor potentially increasing the risk of hip fracture [32].

To summarize this review, I would like to present data from studies conducted in a group of multimorbid elderly patients in whom the predictive significance of calcification was assessed. A progressive decrease in bone mineral density in patients with atherosclerosis as a manifestation of osteopenic syndrome not only determines the low quality of life of these patients, but is also associated with the severity of damage to the coronary arteries and non-coronary arteries.

The authors showed in a cohort study that low bone mineral density correlates with a high incidence of fatal complications of coronary artery disease. However, it should be noted that it is necessary to consider a decrease in bone mineral density as an unfavorable factor for patients with coronary artery disease not separately, but in conjunction with studying the influence of bone metabolism disorders on the structural features of a calcified plaque, which determine its stability. An important conclusion was made that expanding the diagnostic spectrum of quantitative assessment of coronary artery calcification with the determination of qualitative characteristics of calcium deposits will allow a non-invasive way to assess the structure of the plaque for risk stratification in cases of suspected coronary artery disease [33].

Conclusion. The proposed literature review does not claim to be complete information on the issues under consideration. The limited volume of the article does not contain even a small fraction of the information that was analyzed. To summarize, it should be said that this topic will continue to attract a large number of scientists. As a result of research, new facets of the pathogenesis of atherosclerosis will be discovered that will help improve the situation with cardiovascular diseases.

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