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Diagnosics of Osteoporosis and Osteopenics On the Data of Screening Research of Ryazan Region Residents (Russian Federation).

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ABSTRACT

The article presents the results of the study of bone mineral density and fracture risk assessment using the FRAX tool in 358 residents of the Ryazan region, and also examines the effect of rheumatoid arthritis on the development of osteoporosis. According to the results of densitometry of the distal forearm in 29% of cases, osteopenia was revealed, and in 17% - osteoporosis. The risk of fractures calculated by the FRAX method correlates with the results of densitometry, which indicates the possibility of using the FRAX tool for the diagnosis of osteoporosis.

Keywords: osteoporosis, relative fracture risk, bone mineral density, FRAX, rheumatoid arthritis.

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INTRODUCTION

In recent years, there has been a trend towards an increase in the prevalence of diseases of the musculoskeletal system, among which a special place is occupied by osteoporosis [1, 2].

Osteoporosis is a systemic metabolic disease of the skeleton, characterized by a decrease in bone mass and a disturbance of the micro architectonics of bone tissue, leading to increased brittleness and bone fractures [3].

Osteoporosis in Russia, like the rest of the world, is one of the most important health problems, despite the fact that its frequency has been steadily increasing in recent decades. In Russia, densitometric examination reveals osteoporosis in 30.5-33.1% of women and 22.8-24.1% of men aged 50 years and older [4]. Thus, in Russia more than 10 million people suffer from osteoporosis. In recent years, the prevalence of osteoporosis is continuously increasing around the world, which is partly due to the wider introduction of modern diagnostic methods (dual-energy x-ray absorptiometry) into practice. Over the past 10 years, the number of reported cases of osteoporosis among adults in Russia has increased more than 3-fold, according to a screening study of persons over 50 years old who performed a densitometric study of the axial skeleton.

The high social significance of osteoporosis is determined by its consequences - fractures of the vertebrae and bones of the peripheral skeleton, leading to an increase in morbidity, disability and mortality among the elderly, and hence to large material costs in the field of health. The incidence of fractures associated with osteoporosis increases with age. The most severe medical and social consequences are caused by fractures of the proximal femur: about a third of patients die within the first year after this fracture, and among the survivors more than half need constant care.

In recent years, modern principles of diagnosis and treatment of osteoporosis based on measurement of bone mineral density (BMD) using X-ray dual energy absorptiometry - densitometry and risk assessment of osteoporotic fractures have been developed and implemented. For the timely conduct of preventive measures, the risk factors for osteoporosis and fractures are well defined. Risk factors with a level of evidence of A include:

- age over 65;
- female;
- previous fractures with minor trauma;
- family history of osteoporosis, in particular, hip fracture);
- hypogonadism in men and women;
- smoking;
- insufficient intake of calcium;
- vitamin D deficiency;
- alcohol abuse;
- lowBMD.

The lower level of evidence (B) has such risk factors as: belonging to the European race, low physical activity, prolonged immobilization, body mass index <20 kg/m² and/or weight less than 57 kg, decrease in creatinine clearance and/or glomerular filtration, period time to 5 years from the time of the previous fracture.

In addition to risk factors, modern studies have identified a number of diseases associated with the development of secondary osteoporosis [5]. Among them are the following:

- endocrine system diseases (Cushing's disease and syndrome, thyrotoxicosis, hyperparathyroidism, hypogonadism, diabetes mellitus);
- rheumatoid arthritis;
- celiac disease;
- chronic inflammatory bowel disease (ulcerative colitis, Crohn's disease);
- transplantation of ungainly organs (liver, lungs, heart, kidneys, bone marrow);
- rheumatic diseases (systemic lupus erythematosus, ankylosing spondylitis);
- diseases of the digestive system (condition after gastrectomy, malabsorption, chronic liver disease);

- kidney disease (chronic renal failure, renal tubular acidosis, Fanconi syndrome);
- blood diseases (myeloma, thalassemia, systemic mastocytosis, leukemia and lymphoma);
- genetic disorders (imperfect osteogenesis, Marfan syndrome, Ehlers-Danlo syndrome (imperfect desmogenesis), homocystinuria and lysinuria);
- chronic obstructive pulmonary disease.

Rheumatoid arthritis takes a special place among various diseases that can cause secondary osteoporosis. The clinical importance of osteoporosis is primarily determined by the high risk of skeletal bone fractures, which significantly reduces the quality of life and worsens the prognosis in RA patients. The development of osteoporosis and joint destruction in chronic rheumatoid inflammation has common pathogenetic mechanisms of development and is associated with activation of the immunity system, hyperproduction of "pro-inflammatory" and insufficient synthesis of "anti-inflammatory" cytokines, imbalance in the RANKL/RANK/OPG system, leading to activation of osteoclastogenesis and increased bone resorption.

Loss of bone mass in rheumatoid arthritis can be either local (epiphyseal) or systemic (generalized). Epiphyseal osteoporosis is one of the earliest diagnostic criteria for rheumatoid arthritis

For the diagnosis of osteoporosis, in addition to the densitometric examination of the IPC, the FRAX tool is proposed, a method developed on the website developed by a specialized center located at the University of Sheffield, UK and collaborating with the World Health Organization (WHO). The Center studies metabolic diseases of the skeleton using a technique based on models for estimating the probability of fracture in men and women. These models, based on studies in population cohorts in Europe, North America, Asia and Australia, have been carefully tested in additional population cohorts with a data volume of more than 1 million patients per year [6].

The FRAX algorithms integrate well-tested clinical risk factors, such as age, body mass index, and some dichotomous variables (for example, fracture history, smoking, treatment with corticosteroids, rheumatoid arthritis), as with regard BMD, and without it.

The main applications of FRAX include the identification of patients in need of defining the MDB and medical treatment (in some cases, sufficient data on clinical risk factors) [7].

As for the FRAX methodology, it is worth noting that she, unlike densitometry, requires almost no financial cost and specialized medical equipment, which greatly expands the horizons of its application. However, at the same time, the technique has its disadvantages, in particular: FRAX should not be used in women in premenopausal women, men younger than 50 years and children; currently not installed error methods FRAX; FRAX cannot be used in patients receiving antiosteoporotic treatment. Work on FRAX continues, and new data on many clinical risk factors will help to enrich it with algorithms that will only lead to increased reliability, accuracy and significance of prognostic score [8].

The aim of the study was to assess the prevalence of osteoporosis and osteopenia in persons over 40 years old by osteo screening with BMD study of the distal third of the forearm using X-ray dual energy absorptiometry and an estimate of the relative fracture risk with the FRAX tool, and a comparison of the capabilities of these methods.

The frequency of development of osteoporosis and osteopenia in patients with rheumatoid arthritis was assessed separately, as well as the presence of possible predisposing factors. For this purpose, 80 patients with diagnosed RA (10 men and 70 women) - residents of the city of Ryazan and the Ryazan region at the age of 52 to 80 years were selected from the total number of examined patients. Rheumatoid arthritis at the same time acted only as one of the factors in the development of osteoporosis. The mean age was 59.6 ± 3.1 for women and 62.0 ± 2.3 years for men. The distribution by sex was 1/7.

MATERIALS AND METHODS

The study was conducted from January 2014 to December 2015 within the framework of program «Osteo screening of Russia» on the basis of the Department of Faculty Therapy of the Ryazan State Medical University and was carried out in accordance with the requirements of good clinical practice and the Helsinki

Declaration of the World Medical Association "Ethical Principles of Medical Research with Participation people as subjects of research" as amended in 2008. The study included 358 subjects - residents of the city of Ryazan and the Ryazan region aged 40 to 80 years who applied for the purpose of screening osteoporosis and assessing the risk of osteoporotic fractures, including 52 men and 306 women. The average age of the examined women was 56.3 ± 8.4 years, for men - 60 ± 3.8 years. The distribution by sex was 1/6.

In the course of the study, patients were questioned in order to identify risk factors, namely: the presence of previous fractures, hip fractures in parents, smoking, taking glucocorticoids, history of rheumatoid arthritis, alcohol use, history of diseases contributing to the development of secondary osteoporosis (type 1 diabetes mellitus, imperfect osteogenesis in an adult, long-term untreated hyperthyroidism, hypogonadism or early menopause (<45 years), chronic malnutrition or malabsorption and chronic liver disease).

Measurement BMD in the distal third of the forearm was carried out by dual-energy X-ray absorptiometry (Densitometry) with determination of the T-test using a DTX-200 DEXA Care densitometer from Osteometer Mediatech (USA). For the diagnosis of osteoporosis, WHO criteria were used: MIC values deviating from the bone mass peak (T-test) by less than 1 standard deviation were regarded as the norm; values from -1 standard deviation to -2.5 standard deviations - as osteopenia; less than -2.5 standard deviations - like osteoporosis. To calculate the 10-year probability of osteoporotic fractures, including fractures of the neck of the femur, the FRAX tool was used.

Statistical processing of data was carried out in the Statsoft Statistica 8.0 program using descriptive statistics methods, including calculation of the mean, standard error of the mean and confidence interval. The normality of the distribution was verified by the Kolmogorov-Smirnov test. Correlation analysis using the Pearson correlation coefficient was used to evaluate the correlation of phenomena.

RESULTS AND DISCUSSION

Risk factors for osteoporosis were detected in 79% of the subjects. Among the risk factors identified:

- low-fracture fractures - 23%,
- hip fracture in parents - 5%,
- smoking at the time of the study - 12%,
- taking systemic glucocorticosteroids for more than 3 months - 32%,
- rheumatoid arthritis - 30%,
- endocrine system diseases - 20%,
- menopause at the age of 45 years - 16%,
- chronic liver disease - 10%.

For one person revealed from 1 to 5 risk factors, an average of 1.5 ± 1.1 . None of the examinees, according to the questionnaire, established the fact of drinking alcohol at a dose of more than 3 units per day, which is probably due to the concealment of this information by the test subjects (1 unit of alcohol corresponds to a standard glass of beer (285 ml), one standard portion of strong alcohol (30 ml), a glass of medium-sized wine (120 ml) or one serving of an aperitif (60 ml).

Evaluation of the 10-year risk of osteoporotic fractures using the FRAX method has established that the average risk of major osteoporotic fractures is $11.9 \pm 8.0\%$, including the risk of a hip fracture of $1.9 \pm 3.8\%$. According to international recommendations, patients with a risk of fracture of the femur by the FRAX method of more than 3% or a common risk of osteoporotic fractures of more than 10% are at risk and require the appointment of anti-osteoporotic therapy [6]. In our study, 46% of patients who meet these criteria were identified. However, the Russian recommendations suggest using age-differentiated threshold of intervention based on the definition of a 10-year absolute risk of major osteoporotic fractures, according to which only 25% of patients fall into the risk group [3].

According to the results of densitometry of the distal forearm in 29% of cases, osteopenia was revealed, and in 17% - osteoporosis. The results obtained are somewhat lower than the information on the prevalence of osteoporosis according to x-ray densitometry data reported in the literature. So in a similar study conducted in the city of Cheboksary in 2012, osteoporosis was detected in 16% of cases, and osteopenia

in 37% of cases [9]. The results of the screening in Volgograd testify to an even higher prevalence of osteoporosis (21%) and osteopenia (42%) [10]. However, the result obtained by us can be explained by differences in the sample of patients used in other studies. While the patients screened in our study were between the ages of 40 and 80, in Cheboksary, the sample represented patients older than 50 years, which explains the higher prevalence of osteoporosis. In Volgograd, the same data on the epidemiology of osteoporosis were obtained on the basis of an analysis of the appeal to a specialized center for the diagnosis and treatment of osteoporosis, which can hardly adequately reflect the prevalence of osteoporosis in the population, since it does not include healthy individuals without risk factors. Such discrepancies testify to the need to conduct extensive all-Russian screening studies to assess the actual prevalence of osteoporosis in the population.

During the analysis of the obtained material, a significant moderate negative correlation between the risk of osteoporotic fractures calculated by the FRAX instrument and BMD of the distal forearm was revealed; between the risk of fractures and the T-test of the distal forearm. A reliable, moderate positive correlation was also established between the number of identified risk factors and the overall risk of osteoporotic fractures. The obtained correlations indicate the possibility of using the FRAX technique for the diagnosis of osteoporosis along with two-energy absorption spectrometry, especially in cases where the application of the latter is impossible for technical reasons.

It should be noted that not always the values of high fracture risk are associated with a low BMD, since the FRAX tool also takes into account the influence of risk factors that has not yet led to a decrease in the MIC. Thus, even at normal or threshold values of the T-test, the patient may have a sufficiently high risk of osteoporotic fractures, which makes it possible to identify a group of patients in whom the appointment of anti-osteoporotic therapy is able to prevent not only the development of fractures, but also the expected decrease in BMD. This indicates that, when deciding whether to prescribe medications for the prevention and treatment of osteoporosis, one should rely not only on the densitometric examination carried out, but also on the use of the FRAX tool.

In a sample of patients with rheumatoid arthritis, osteoporosis was diagnosed in 26 (32.5%) cases, osteopenia in 36 (42.5%), and only 20 patients (22.5%) had normal bone density. Comparing the results with the data of the main study, we will get a nearly twofold increase in the indices (32.5% versus 17% of diagnosed osteoporosis and 42.5% against 29% of diagnosed osteopenia).

In the study of risk factors, the following patterns were revealed. Risk factors for osteoporosis have been detected in the vast majority (95%) of patients. The average number of risk factors in patients with rheumatoid arthritis was 9 versus 7 in standard studies. This, according to existing international recommendations, already requires the prevention of osteoporosis (namely, the appointment of combined calcium and vitamin D3 preparations in conjunction with a certain physical activity, diet).

The distribution of patients with revealed osteoporosis and / or osteopenia according to BMI showed that the norm is only 40%, 2.5% body weight deficit, 37.5% excess body weight and 20% obesity. Smoking, as a risk factor, was detected in 30% of the subjects and was second after an increased BMI for frequency of occurrence.

Patients who took glucocorticoids for more than 3 months in a dose of prednisolone 5 mg or higher were assigned to a high-risk group. The detection of osteoporosis according to densitometry was 53.8% in this group against 32.5% of the total number of patients. Estimation of calcium intake with food showed an expected greater number of detected cases of osteoporosis and / or osteopenia in patients consuming less than 1000 mg calcium per day for people over 50 years old and was 67.3% versus 42.6% for patients consuming sufficient calcium.

Evaluation of the 10-year risk of osteoporotic fractures by the FRAX method established that the average risk value is $22.7 \pm 9.7\%$ without taking into account BMD.

Most of the risk values of osteoporotic fractures in the FRAX - 77.5% - in accordance with the recommendations for diagnosis and management of osteoporosis - were in the area of prescription of medicines, because it corresponds to a high risk of OP fractures. During the analysis of the obtained material,

we established reliable risk correlations without taking into account the BMD of the forearm ($p = 0.03$) and the risk with the number of risk factors ($p = 0.01$).

In accordance with the risk assessment and the subsequent decision to prescribe medications according to the FRAX method without taking into account the IPC, we found that 77.5% of the examined patients need medicines, compared to 75%, detected by standard criteria. This once again shows that when deciding on the need for medical appointments for the prevention and treatment of OP, we must rely not only on the densitometric study performed, but also on the risk assessment of OP fractures using the FRAX technique.

CONCLUSIONS

Based on this study, we can draw the following conclusions:

1. Osteoporosis remains a global problem, and it needs to be addressed globally, for example, by increasing the number of centers for osteoporosis, and by promoting healthy lifestyles.
2. In the examined persons with densitometry in 10% of cases, osteoporosis was diagnosed, in 20% - osteopenia. When calculating the risk of osteoporotic fractures, the average risk is $11.9 \pm 8.0\%$.
3. With the introduction of the FRAX method into day-to-day practice, primary care physicians can calculate the risk of osteoporotic fractures in patients based on an integrated assessment of clinical risk factors.
4. Rheumatoid arthritis is not only a risk factor for the development of osteoporosis, but also a disease with a similar autoimmune nature, and patients with rheumatoid arthritis in addition to basic and anti-inflammatory therapy should receive a comprehensive medication for osteoporosis.
5. The FRAX tool, currently included in therapeutic recommendations in many countries around the world, is an updated tool for dividing patients into categories, depending on the need for measuring BMD, and the prescription of drug treatment. However, the FRAX tool does not replace a thorough clinical examination, and if necessary, the physician should also consider other clinical risk factors that are not currently included in the FRAX model. In this respect, FRAX is an actively developed method which, as new epidemiological data and clinical fracture risk factors appear, will be updated to increase diagnostic reliability.

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