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OSTEOPOROSIS: ASSESSMENT OF DIAGNOSTIC TECHNIQUES FOR DRUG THERAPY ADMINISTRATION

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Abstract

Objective. Analysis of the results of various methods of diagnosis of osteoporosis before the appointment of anti-osteoporotic therapy.

Methods. The medical records of patients receiving medical care at the Federal Center for Traumatology, Orthopedics and Endoprosthetics of the Ministry of Health of the Russian Federation (Smolensk), who underwent femoral neck densitometry, as well as an assessment of the 10-year risk of osteoporotic fractures using the FRAX technique, were analyzed. Statistical processing of the material was performed using the Microsoft Office Excel 2016 program using the "Data Analysis" add-ins and AtteStat 12.0.5. These age values are presented as the mean ± standard error of the mean, the T-index – as the mean ± standard deviation (SD), the data in percentages – as the mean ± mean quadratic sample deviation of the fraction.

Results. The methodology of 4 diagnostic schemes of osteoporosis before the appointment of anti-osteoporotic therapy is analyzed. The largest number of people is calculated based on the results based only on the values of densitometry, the smallest – based on the results of the FRAX method according to the recommendations of the RAOP. A group of patients has been identified who are recommended anti-osteoporotic therapy, regardless of the chosen method of diagnosis of osteoporosis. In it, the average age of the patient is 68.0± 1.5 years, the average T-index is -3.3±0.8 SD, the 10–year probability of major osteoporotic fractures without an MPC value is 20.1±9.7%, hip fracture is 5.2±5.4%.

Conclusion. Depending on the method of diagnosis of osteoporosis, the number of patients who are recommended medication has significant differences. It was found that the use of the FRAX method in conjunction with densitometry data increases the accuracy of the prognosis of osteoporosis, which makes it possible to better identify patients who need anti-osteoporotic therapy.

Keywords: osteoporosis, diagnostics, anti-osteoporotic therapy, dual-energy X-ray absorptiometry, bone mineral density, FRAX, risk factors, statistical analysis

ОСТЕОПОРОЗ: ОЦЕНКА МЕТОДОВ ДИАГНОСТИКИ ДЛЯ НАЗНАЧЕНИЯ МЕДИКАМЕНТОЗНОЙ ТЕРАПИИ

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Резюме

Цель. Анализ результатов различных методов диагностики остеопороза перед назначением антиостеопоротической терапии.

Методика. Проанализированы медицинские карты пациентов, получающих медицинскую помощь в ФГБУ «Федеральном центре травматологии, ортопедии и эндопротезирования» Министерства Здравоохранения РФ (г. Смоленск), которым была проведена денситометрия шейки бедренной кости, а также оценка 10-летнего риска остеопоротических переломов по методике FRAX. Статистическая обработка материала произведена с помощью программы Microsoft Office Excel 2016 с использованием надстроек «Анализ данных» и AtteStat 12.0.5. Данные значения возраста представлены в виде среднего±стандартной ошибки среднего, Т-показателя – в виде среднего ±

стандартного отклонение (SD), данные в процентах – в виде среднего значения ± среднее квадратичное выборочное отклонение доли.

Результаты. Проанализирована методология 4 схем диагностики остеопороза перед назначением антиостеопоротической терапии. Наибольшее количество человек рассчитывается по результатам, основанным только на значениях денситометрии, наименьшее – по результатам метода FRAX по рекомендациям РАОП. Выделена группа пациентов, которым рекомендована антиостеопоротическая терапия вне зависимости от выбранного способа диагностики остеопороза. В ней средний возраст пациента составляет 68,0±1,5 лет, средний Т-показатель – -3,3±0,8 SD, 10-летняя вероятность основных остеопоротических переломов без значения МПК – 20,1±9,7%, перелома бедра – 5,2±5,4%.

Заключение. В зависимости от метода диагностики остеопороза, количество пациентов, которым рекомендовано медикаментозное лечение имеет существенные различия. Установлено, что использование метода FRAX совместно с данными денситометрии повышает точность прогноза развития остеопороза, что позволяет лучше идентифицировать пациентов, нуждающихся в назначении антиостеопоротической терапии.

Ключевые слова: остеопороз, диагностика, антиостеопоротическая терапия, двуэнергетическая рентгеновская абсорбциометрия, минеральная плотность кости, FRAX, факторы риска, статистический анали

Introduction

Osteoporosis is known to be responsible for over 8.9 million cases of fractures annually worldwide. The International Osteoporosis Association (IOF) has estimates that by 2010 there were 158 million people at high risk of fractures and this figure is likely to double by 2040 [1]. In Russia, according to a national osteoporosis study in 2020, the expected number of osteoporosis patients in 2035 can be up to 16 million. The disease is a severe problem both because of progressively increasing number of cases, and grave consequences potentially accompanied by high mortality rates, as well as high financial burden.

In most people, the disease can be identified when they seek for medical care because of a bone fracture, resulted from a minor fall accident or certain external impact. Currently, risk factors of the disease are well studied and identified. They are as follows: nutrition disorders, smoking, and lack of physical exercises, as well as taking certain medications (i.g. glucocorticosteroids, antitumor, thyroid hormones, etc.), certain endocrine diseases, and female gender [2]. Moreover, the risks of fall accidents increase with individuals' age and can lead to an increase in the number of injuries, in particular, "low-energy" fractures. The primary indicator for the administration of anti-osteoporotic therapy is a T-score value below - 2.5 standard deviations (SD) in the measurement of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) of the spine or proximal femur [2]. However, rather expensive equipment and diagnostic procedure, respectively, reduce the possibility of widespread application of this efficient diagnostic technique.

Currently, there is a cheaper rather efficient technique FRAX, developed in 2008 by the WHO jointly with the Center of Metabolic Diseases (University of Sheffield, UK). The technique is a test that allows determining risks of fractures within the next 10 years. The results are calculated mathematically and take into account risk factors for each patient and studies in population cohorts of countries. Risks of fracture accidents are specific for each region of the world. This is due to differences in life expectancy and lifestyle [3]. Currently, there are 86 models for 77 countries in 34 languages. Since 2012, the FRAX model for Russia has been developed and registered and is commonly used by physicians both online and in paper versions [4]. The tool can be applicable in individuals from 40 to 90 years of age and integrates the most important clinical risk factors: age, sex, body mass index, previous patient and parental hip fracture, smoking, drinking three units of alcohol per day or more, taking glucocorticosteroids, rheumatoid arthritis and secondary osteoporosis. Calculation is possible with or without the results of femoral BMD measurement [5]. It is worth noting that FRAX does not abolish the diagnosis of osteoporosis when the BMD is below 2.5 SD of the mean values. The technique allows recognizing a group of patients with comorbid conditions who need to start proper treatment [6]. A number of studies have confirmed that FRAX-based indices can identify risks of recurrent fractures higher than individual T-criterion values at densitometry [7-9]. The simplicity and availability of this tool enables earlier diagnosis of osteoporotic changes.

Anti-osteoporotic therapy is a basis of osteoporosis treatment and prescribed if a patient is refereed to a risk group. This therapy can be based on the results of densitometry alone or FRAX, or in combination.

We have analyzed medical records of patients with the corresponding diagnosis in the city of Smolensk in order to clarify the data on morbidity and arrangement of risk groups depending on diagnostic technique.

The aim of the study was to assess the results of different techniques of osteoporosis diagnosis before the administration of anti-osteoporotic therapy.

Methodology

Medical records of patients treated at the Federal Center of Trauma, Orthopedics, and Endoprosthetics under the Ministry of Public Health of the Russian Federation (Smolensk, Russia) in 2012-2021 were studied by a continuous sampling method. The study totally involved 76 patients, including 12 (16%) male patients and 64 (84%) female ones. Eligibility criteria were as follows: patients' age (50-85 years of age); diagnosis of osteoporosis; results of femoral neck densitometry and FRAX to predict 10-year risk of osteoporotic fractures. Treatment efficacy and risk factors that are not included in the FRAX model (falls, biochemical markers, vitamin D deficiency, etc.) were not taken into consideration.

Statistical processing of the material was performed using Microsoft Office Excel 2016 program with the use of "Data Analysis" and AtteStat 12.0.5 add-ons. Age data were presented as mean±standard error of mean, T-score as mean±standard deviation (SD), percentage data as mean±sample mean square deviation of fraction. Reliability of the difference between the studied groups was assessed using the Mann-Whitney test and the Kolmagorov-Smirnov test. Statistical significance was considered at a probability >95% ($p<0.05$).

Results of the study

The WHO and the Clinical Guidelines of the Russian Association for Osteoporosis (RAOP) run that BMD values deviating from the peak bone mass (according to the T-score) by less than 1 SD are considered to be normal. In this case, only a change of diet to calcium-rich foods can be recommended, as well as additional vitamin D supplementation. At values from -1 SD to -2.5 SD osteopenia is diagnosed, and mandatory intake of calcium and vitamin D is required. At T-score less than -2.5 SD the diagnosis is "osteoporosis" and antiestrogenic therapy is mandatory. Thus, the patients were divided into four groups (Table 1).

Table 1. Distribution of patients according to T-criterion value [10]

T-score	Absolute indicator, n	Diagnosis	Risk of fractures	Recommendations
from +2,0 before -1 (total)	0	Normal BMD	Level 1: low	Only dietary recommendations or calcium and vitamin D supplements, exercise
males	0			
females	0			
from -1,0 before -2,5 (total)	11	Osteopenia	Level 2: Moderate	Calcium and vitamin D supplements, possibly other medications
males	1			
females	10			
from -2,5 or less without prior fractures (total)	27	Osteoporosis	Level 3: high	Strong recommendations to treat with anti-osteoporotic drugs, prevention of loss of equilibrium
males	3			
females	24			
from -2,5 or less with prior fractures (total)	38	Severe osteoporosis	Level 4: very high	Same as level 3, but more intense
males	8			
females	30			

Thus, "osteopenia" was diagnosed in 11 patients (14%), including 10 females and one male patient. Anti-osteoporotic therapy was strongly recommended to 65 patients (86%), including 54 women and 11 men. It is worth noting that most of the patients observed (38 patients (50%)) had a history of fractures.

The FRAX technique analyzes risk factors that play their part in osteoporosis development. Based on this, the probability of fractures in the next 10 years can be predicted. The study has found that the number of patients who had no risk factors (including BMI = 18.5 – 24.9) was eight (11%) female, mean age

68.0±0.9 years. Thus, about 90% of patients had at least one risk factor (Table 2). Among them, 45 patients (58%) had a previous fracture history; eight patients (10%) had rheumatoid arthritis; seven patients (9%) had already taken systemic glucocorticosteroids for more than 3 months; five patients (6%) were current smokers; four patients (5%) were with a parental hip fracture; and two patients (3%) had their secondary osteoporosis.

Table 2. Identified risk factors with a questionnaire FRAX

Risk factors	Total		Men		Women	
	Absolute indicator, n=76	Relative indicator, %	Absolute indicator, n=12	Relative indicator, %	Absolute indicator, n=64	Relative indicator, %
Previous fractures	45	59,2	9	75	36	56,3
Rheumatoid arthritis	8	10,5	0	0	8	12,5
Oral glucocorticoids	7	9,2	1	8,3	6	9,4
Smoking	5	6,6	3	25	2	3,1
Family history of fractures	4	5,3	0	0	4	6,3
Secondary osteoporosis	2	2,6	2	1,7	0	0

None of the patients was found with the survey to have more than 3 units of alcohol per day (1 unit of alcohol corresponds to 30 g of spirits (vodka, cognac, whiskey), 120 g of red dry wine or 330 g of beer). International recommendations run that patients at a risk of hip fracture according to the FRAX technique without a BMD value of more than 3% or a total risk of osteoporotic fractures of more than 10% need to be administered anti-osteoporotic therapy [6]. The study identified 52 individuals (68%) meeting the criteria including 48 females and 4 male patients. However, Russian Guidelines recommend to use an age-differentiated threshold of intervention based on determining the 10-year absolute risk of major osteoporotic fractures proposed by the Russian Association on Osteoporosis (RAOP) on the basis of statistical data from Trauma Clinics in Yaroslavl and Pervouralsk in 2012 [4]. When doctors compare patients' age and an individual 10-year probability of major low-traumatic fractures obtained using the FRAX technique, they can make a conclusion that if the results are in the "green zone" the patient does not need any treatment. If they are in the "red zone», proper treatment is recommended. Therefore, in the study performed only 29 patients (38%) can be included into the risk group, among them 24 female and 5 male patients (Table 3).

Table 3. High probability of fractures according to the differential RAOP system [4]

Age	Female patients			Male patients		
	Patients at risk	Total patients	Relative indicator, %	Patients at risk	Total patients	Relative indicator, %
50-54 years	1	1	100	1	1	100
55-59 years	4	6	67	4	5	80
60-64 years	3	7	43	0	2	0
65-69 years	7	12	58	0	3	0
70-74 years	7	17	41	0	0	0
75-79 years	2	13	15	0	0	0
80-84 years	0	7	0	0	1	0
85-89 years	0	1	0	0	0	0
Totally patients:	24	64	38	5	12	42

Following 35-40 years of age a slow decline in bone mass can start. In women, this process is escalating after menopause, and by 60-70 years of age, bone density can become decreased by 30-50%. Man are characterized by less significant losses, from 15 to 30% [11]. The FRAX value has been identified to increase with age due to the accumulation of risk factors, and from 75-79 years of age it decreases, as the probability of death prevails over the probability of fractures [12].

An analysis of FRAX results in patients without BMD calculation was performed. It was found that the mean 10-year probability of possible osteoporotic fractures in the total sample was 15.1±4.1 %, in men 8.9±8.2 %, in women 16.2±4.6 % (Fig. 1). We also assessed FRAX results with BMD results. In this

case, the mean 10-year risk of fracture in the total sample was 25.2±5.0%, in men 30.8±13.3%, and in women 24.2±5.4% (Fig. 2).

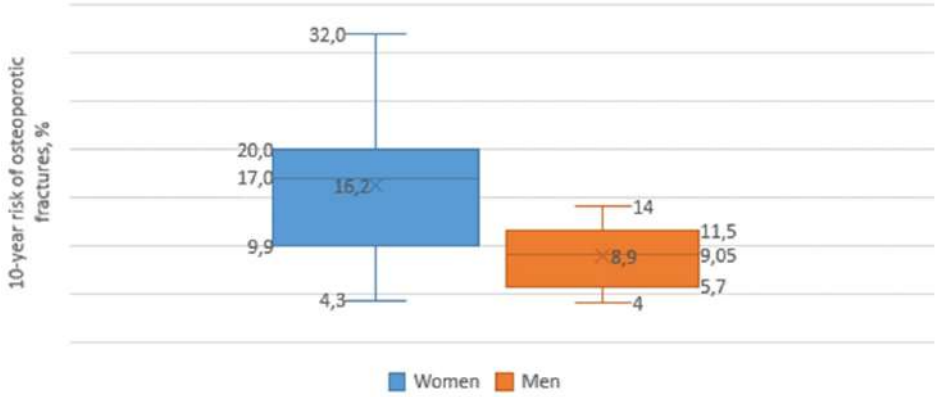

Fig. 1. Scale diagram of the 10-year risk of osteoporotic fractures in the study group according to the FRAX results without BMD

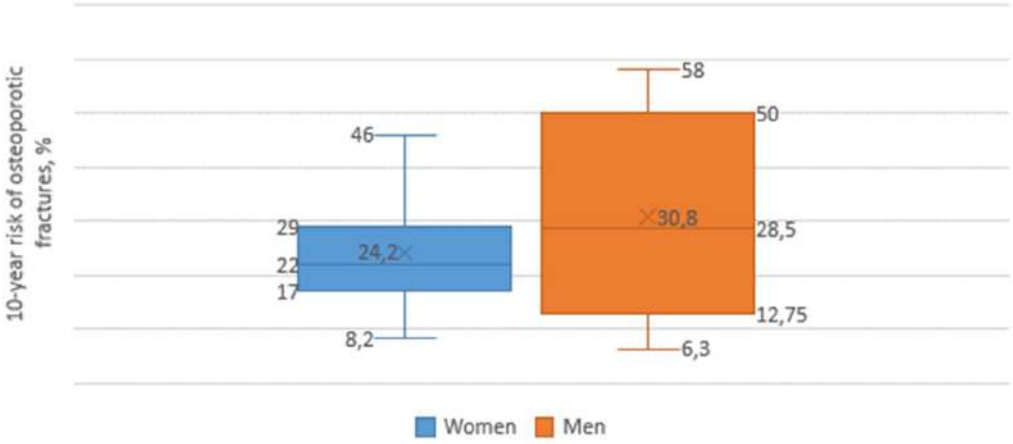

Fig. 2. Scale diagram of the 10-year risk of osteoporotic fractures in the study group according to the FRAX results with BMD

When analyzing the results with BMD values, the probability of fractures in the overall sample increases by 1.7, by 3.5 in males, and by 1.5 in females. It increases diagnostic accuracy and signals the need for earlier treatment.

The study identified a group of patients who require anti-osteoporotic therapy regardless of the chosen diagnostic technique. The group involved 17 patients (22%), including 2 male and 15 female patients. The patients' mean age was 68.0±1.5 years, mean T-score was -3.3±0.8 SD, 10-year probability of major osteoporotic fractures without BMD value was 20.1±9.7 %, and hip fracture was 5.22±5.4 %. Only one patient from the selected group had no previous fracture. The fact indicates the significance of the criterion when taking patient's medical history.

Discussion of the results

Application of four schemes to diagnose osteoporosis before administration of anti-osteoporotic therapy has been analyzed: by the results of densitometry, by the FRAX technique according to International Recommendations and RAOP recommendations as well as data from the combined application of densitometry and FRAX questionnaire. Depending on the method chosen, the number of patients who were recommended medical treatment was found to have significant differences. The greatest number is calculated on the basis of the results based on densitometry values only - 65 patients (86%), the smallest -

on the results of FRAX method according to RAOP recommendations - 30 patients (39%). The group of 17 patients (22%) who were recommended to take anti-osteoporotic therapy regardless of the chosen method of osteoporosis diagnosis was singled out. Their mean age was 68.0±1.5 years, mean T-score was -3.3±0.8 SD, 10-year probability of major osteoporotic fractures without BMD value was 20.1±9.7 %, and hip fracture was 5.22±5.4%.

Conclusion

FRAX technique jointly with densitometry data improves the accuracy of osteoporosis prognosis, and can efficiently identify the patients who require anti-osteoporotic therapy.

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