ASSESSMENT OF THE USE OF DIFFERENT RISK ALGORITHMS FOR OSTEOPOROTIC FRACTURES IN WOMEN IN THE PRACTICE OF A FAMILY DOCTOR

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1. Introduction

1.1. The object of research

The object of research is women in whom the risk of osteoporotic fractures was assessed using the FRAX, Q-Fracture algorithms, and the risk factors for osteoporosis and their role in the development of osteoporotic fractures were studied.

1.2. Problem statement

Osteoporosis (from the Greek “ostéon” – bone and “póros” – hole, pore) is a systemic disease of the skeleton, characterized by a decrease in bone tissue mass, disruption of bone microarchitectonics, which leads to increased fragility of bones and an increased risk of fractures (WHO, 1993). With the increase in life expectancy, osteoporosis (OP) is becoming one of the main causes of health loss and death, both among women and men. According to the National Osteoporosis Foundation, (2016), 9 million fractures occur annually worldwide due to osteoporosis. From 200, million women worldwide, osteoporosis is diagnosed: up to 60 years in every tenth woman, at 70 years in every fifth woman, in two out of five at the age of 80 and after 90 years it is diagnosed in two out of three [1]. The prevalence of OP in the EU countries was estimated at 27.6 million. In 2013, in men over the age of 50, the prevalence of OP ranges from 5.9 % (Poland) to 7.2 % (Lux-
Innovative technologies in healthcare

embourg). For women, rates vary from 19.1% (Cyprus) to 23.5% (France). The economic burden of these incidents was estimated at 37 billion EUR. Fractures accounted for 66% of this cost, long-term fracture treatment 29%, and pharmacological prophylaxis 5%. Expenditures are expected to increase by 25% until 2025. [2] In Ukraine, osteoporosis is detected in 13.4% of the female population, and with age, the number of sick women increases to 53% [3].

In terms of importance, OP is one of the leading chronic non-infectious diseases, second only to cardiovascular, oncological and endocrine diseases [4]. OP is common in the practice of a family doctor, but doctors perceive OP as a low priority issue and highlight a lack of awareness of the condition. Therefore, there is growing attention to the study of risk factors for osteoporosis, according to their role in the development of osteoporotic fractures. Osteoporosis is a heterogeneous multifactorial disease, in the development of which risk factors and their combinations play an important role. So, the main risk factors for fractures are considered age after 65 years, female sex, family history of fractures, tendency to falls, prolonged use of glucocorticoids, alcohol abuse and the presence of certain somatic diseases, in particular cardiovascular diseases, type II diabetes mellitus, rheumatoid arthritis and others [5, 6].

It is known that osteoporosis is clinically manifested by fractures. But for a long time, the disease is asymptomatic, any manifestations may be absent. The data indicate not only a tendency towards an increase in the incidence of OP, but also a steady increase in the number of osteoporotic fractures (OPF), which is the main clinical outcome of the disease, significantly affecting the economic costs of society, increasing disability and mortality among the population [7].

1.3. Suggested solution to the problem

Ideally, clinical assessment should take into account all determinants of fracture risk, but nowadays, bone mass assessment is the only aspect that can be easily measured in clinical practice, used for diagnosis, treatment, risk prediction and monitoring of patients undergoing treatment. The diagnostic criterion for OP is based on the measurement of BMD – the amount of bone mass per unit volume (bulk density, g/cm³) or per unit area (g/cm²). Both indicators can be measured in vivo using various densitometric methods [8, 9] The reference standard for diagnosing OP is dual-energy X-ray densitometry (DXA), but this technique has significant drawbacks (inability to obtain a three-dimensional image or information about bone microstructure), resulting in insufficient diagnosis of the disease. In addition, total screening for BMD abnormalities is not advisable, since it would exceed 2–10 times the cost of treating all potential OPFs [10].

Ultrasound densitometry has established itself as a screening method for osteoporosis, which makes it possible to early identify persons at risk and promptly direct them for dual-energy X-ray absorptiometry (DXA). This is a safe diagnostic method, because it does not use ionizing radiation, the devices are portable, which makes it easy to implement in primary health care. Thus, recent studies highlight that quantitative ultrasonography of the calcaneus can predict fractures as effectively as dual-energy X-ray absorptiometry in postmenopausal women and men [11, 12].

A family doctor has the ability to assess the risk of osteoporotic fractures using the FRAX and Q-Fracture questionnaires, even without using BMD, which significantly increases the diagnosis of the disease. FRAX® Algorithm - widely used to assess the 10-year likelihood of major osteoporotic and femoral fractures. Today, FRAX algorithms are available for 64 countries, where the epidemiology of fractures is known, in 31 languages, covering more than 80% of the world population, including in 16 of the 27 EU member states [13, 14]. Austria, Belgium, Denmark, Finland, Hungary and the United Kingdom have the highest rates of FRAX use. In many best practice guidelines (e.g. in the UK) the use of FRAX should be ahead of the use of DXA [15].

Based on a mathematical analysis of the existing risk factors for osteoporosis, the algorithm calculates the 10-year probability of a femur fracture (FRAX Hip) and other typical fractures (FRAX Total) associated with OP. FRAX Total includes fractures of the humerus, femur, radius, clinically significant fractures of the vertebral bodies, both with BMD data and without BMD (T-score) in women over 40 years of age [16, 17]. The Q Fracture algorithm calculates the risk of fracture from 1 to 10 years, contains an extended list of questions about the presence of chronic non-communicable diseases, and data on the risk of falling [18] Data obtained using the algorithms are presented in percentages.
The influence of each factor can be very variable and depends not only on the population, but also on the region of the country, prompting a deeper study of this issue.

**The aim of this research** is to identify risk factors for osteoporosis in women of different age groups and to calculate the fracture risk using the Frax and Q Fracture algorithm in women over 40 years of age.

2. Materials and methods of research

The study was carried out on the basis of the Department of General Practice (Family Medicine) of the Bogomolets National Medical University in 2019.

The study was agreed at a meeting of the Commission on Bioethical Expertise and Ethics of Scientific Research at the Bogomolets National Medical University No. 127 dated 12.02.2019. The study does not pose an increased risk to research subjects and is carried out in accordance with existing bioethical norms and scientific standards in accordance with the requirements of Good Clinical Practice (ICH GCP) and the Declaration of Helsinki.

There was a survey of 35 women in the Odessa region of Ukraine, whose average age was 54.1±11.8 years (minimum – 31; median – 55; maximum – 77). All women were divided by age into groups at ten-year intervals.

The structural and functional state of the bone tissue was assessed using a Hitachi AOS-100E EggQus ultrasonic densitometer (Hitachi Medical Systems Singapore, Singapore) on the heel bone. SOS (velocity of ultrasound transmission, in m/s), TI (transmission index), OSI (bone ultrasound index), Z-score indices (comparison with the average norm in a given age group) and T-score (comparison with the norm for a middle-aged adult with “peak” bone mass). Changes in the structure of bone tissue were recorded in accordance with the established WHO criteria (1994) according to the T-score of bone mineral density (BMD) were examined were divided into groups: T score from +2.5 to –1 – normal; from –1.5 to –2.5 osteopenia; from –2.5 and below – osteoporosis [4].

The fracture risk was calculated using online calculators FRAX and Q Fracture in women over 40 years of age [10, 12].

Anthropometric examination included determination of body weight and height. BMI was calculated according to the generally accepted formula.

Inclusion criteria: signed informed consent of the patient to participate in the study, female, age from 30 to 80 years.

Exclusion criteria: type 1 diabetes mellitus; exacerbation of chronic non-communicable diseases and diseases in the stage of decompensation; persons with oncological diseases; taking medications that can affect bone metabolism; pregnancy and lactation.

Statistical processing of the results was carried out using the statistical program “Statistica 10.0”. Descriptive statistics are presented as arithmetic mean and standard deviation. Comparison of parameters in the study groups was carried out using the Student’s test. To study the nature and strength of the relationship between the studied indicators, we used the Pearson or Spearman correlation coefficient, depending on the nature of the data distribution. Differences were considered statistically significant at \( p<0.05 \).

3. Results

We examined 35 women in the Odessa region, whose average age was 54.1±11.8 years. The number of middle-aged and elderly women was 77.1 % . Moreover, most of them were aged 51–70 years. The average indicators of weight, height and BMI of all women included in the study are shown in Table 1.

The structure of concomitant pathology was dominated by diseases of the circulatory system – 16 cases (45.7 %) and of the digestive system – 11 (31.4 %).

The following risk factors for osteoporosis have been identified.

Smoking at the time of the survey was confirmed by 3 women (8.6 %), and one smoked in the past (2.8 %). All surveyed women denied alcohol abuse. Five respondents (14.3 %) suffered fractures of bones of various localization, and 13 respondents (37.1 %) reported fractures of the femur or signs of osteoporosis in their parents; four women noted a decrease in height after 40 years (13.3 % among those surveyed over 40). Periods of amenorrhea were diagnosed in 3 people (8.6 %); the onset of menopause before the age of 45 was confirmed in 4 respondents (11.4 %). Three women (8.6 %) have taken corticosteroids in the past and one (2.8 %) is taking antidepressants. Insufficient
consumption of dairy products was found in 16 women (45.7 %). Reduced physical activity was confirmed by 24 people (68.6 %).

Table 1
Key clinical indicators of all women

| Indicators | Values |
|------------|--------|
| Age (years) | 54.1±11.8 |
| Weight, kg | 75.7±12.8 |
| Height (cm) | 163.4±0.1 |
| BMI (kg/m$^2$) | 27.6±6.6 |
| T-score | −0.96±0.75 |
| Z-score | −0.09±0.75 |

Note: data are presented as M±SD, BMI – body mass index, Z-score, T-score – indicators of ultrasound densitometry

Pre- and postmenopausal women were categorized by age. The lowest BMD indices were found at the age of 70–79 years: −1.96±0.5 ($p<0.004$), and the largest number of women with osteopenic changes was found in the group of 50–59 years.

Osteopenic changes in the bones in women after 40 years were assessed by the T-score, according to the WHO recommendations. A decrease in BMD was diagnosed in 16 women (51.6 %) after 40 years. In young women (n=4), bone density was assessed with a Z-score. Osteopenic changes were found in 2 respondents, the rest had normal BMD.

The 10-year risk of osteoporotic fractures was assessed with and without BMD using the FRAX, Q-fracture algorithms. The data obtained are presented in Table 2.

Table 2
Ratio of BMD and Q-fracture, FRAX algorithms with and without BMD in women after 40 years

| Algorithm metrics/Diseases | Norm (n=15) | Osteopenia (n=15) | Osteoporosis (n=1) | $P$ |
|---------------------------|-------------|-------------------|-------------------|-----|
| FRAX Total, %             | 5.58±4.9    | 6.14±2.5          | 11                | 0.044 |
| FRAX Hip, %               | 0.2±0.1     | 1.56±2.0          | 4.1               | 0.001 |
| FRAX Total without BMD, % | 6.8±5.98    | 7.92±5.3          | 9                 | 0.026 |
| FRAX Hip without BMD, %   | 1.16±1.8    | 2.4±3.5           | 2.7               | 0.087 |
| Q-fracture Total, %       | 3.55±1.4    | 7.76±4.86         | 10.8              | 0.004 |
| Q-fracture Hip, %         | 0.59±0.4    | 2.9±3.31          | 7.8               | 0.004 |
| T-score                   | −0.35±0.4   | −1.52±0.34        | −2.68             | 0.001 |
| Z-score                   | 0.38±0.5    | −0.35±0.6         | −1.36             | 0.003 |

Note: data are presented as M±SD, Z-score, T-score – indicators of ultrasonic densitometry

The risk of fractures according to all algorithms was higher in women in the 70–79 age group: FRAX Total – 8.87±3.2, FRAX Hip – 4.03±3.1, Q fracture total – 12.87±1.5, Q fracture Hip –7.97±2.7, FRAX Total without BMD – 11.9±5.5, FRAX Hip without BMD - 6.3±4.8. Significant differences were found according to the Q-fracture Total, Q-fracture Hip FRAX Hip, FRAX Hip without BMD p <0.01. The data are presented in Table 3.

Table 3
Relationship between algorithms and age in women after 40 years

| Algorithm indicators/Age groups, years | All women (n=31) | 40–49 (n=5) | 50–59 (n=16) | 60–69 (n=6) | 70–79 (n=4) |
|----------------------------------------|------------------|-------------|-------------|-------------|-------------|
| FRAX Total, %                          | 6.02±3.98        | 4.76±1.7    | 6.23±4.6    | 4.65±2.6    | 8.87±3.2    |
| FRAX Hip, %                            | 0.99±1.7         | 0.4±0.6*    | 0.4±0.3#    | 1±0.8 &     | 4.03±3.1*#, & |
| FRAX Total without BMD, %             | 7.41±5.6         | 4.08±1.2    | 6.56±5.3    | 9.48±5.9    | 11.9±5.5    |
| FRAX Hip without BMD, %               | 1.81±2.8         | 0.24±0.1*   | 0.86±0.9#   | 2.68±2.3*   | 6.3±4.8*#, |
| Q-fracture Total, %                   | 5.82±4.1         | 2±0.7*      | 4.33±1.5#   | 8.28±5*#    | 12.87±1.5*# |
| Q-fracture Hip, %                     | 1.94±2.8         | 0.18±0.1*   | 0.72±0.4 #  | 2.63±1.9*#, & | 7.97±2.7*#, & |

Note: * – $p<0.01$ reliability between the age groups 40–49 and 50–59, 60–69 years; # – $p<0.01$ reliability between the age groups 70–79 and 50–59, 60–69 years; & – $p<0.01$ reliability between the age groups 60–69 and 70–79 years
Correlation analysis of BMD and the risk of fractures revealed a negative correlation between T score with FRAX Total with BMD ($r=-0.45$, $p=0.01$), FRAX Hip with BMD ($r=-0.89$, $p=0.008$). Q fracture total ($r=-0.46$, $p=0.007$), Q fracture Hip ($r=-0.51$, $p=0.008$), positive relationship with Z score ($r=0.74$, $p=0.0005$).

It was revealed that FRAX Total without BMD is positively correlated with Q fracture total ($r=0.55$, $p=0.001$), with FRAX Total with BMD ($r=0.66$, $p=0.004$).

Age correlates negatively with the T score ($r=-0.47$, $p=0.007$) and positively with the FRAX Total algorithms without BMD ($r=-0.47$, $p=0.003$), FRAX Hip without BMD ($r=0.78$, $p=0.006$), Q fracture total ($r=0.86$, $p=0.007$), Q fracture Hip ($r=0.92$, $p=0.008$), FRAX Hip with BMD ($r=0.55$, $p=0.009$) ... No statistically significant difference was found with FRAX Total with BMD ($r=0.21$, $p=0.345$).

4. Discussion

Not all countries accept DXA as the only criterion, since BMD has high specificity, but low sensitivity (30–50 %) – most OPFs will occur in individuals with osteopenia or with BMD values above the osteoporosis threshold. Low sensitivity was the main reason not to recommend BMD testing for population screening [14]. Fracture risk assessment is improved by simultaneously considering risk factors that operate independently of BMD [19]. A survey was carried out on a small group of women. But we were able to quickly collect data in a fairly short period of time and clearly demonstrate how osteoporosis screening can be organized in the practice of a family doctor. The results obtained proved that the algorithms are informative and useful even without densitometry data.

The advantages of using algorithms for assessing the 10-year risk of fractures are that they are available (online versions), they are non-value and do not require the experience that is required to perform densitometry. Can be used in rural outpatient clinics to identify individuals at risk of developing OPFs, to determine the need to start osteoporotic therapy or to prescribe DXA. The use of FRAX is more widespread, the advantage of this model is the availability of the Ukrainian version and the possibility of using both with densitometry indicators and without these indicators. The Q fracture algorithm uses English, but it is possible to assess the risk of fracture from one year and contains an extended list of questions about the presence of comorbidities.

It was determined that the question of smoking at the present time, a decrease in growth after 45 years, the presence of fractures in the history of life and in parents, early menopause (up to 45 years), insufficient physical activity is highly informative and helps in the diagnosis of osteoporosis.

*Study limitation.* A thorough history taking is required. The patient, in order to be included in the examination, should not receive anti-osteoporotic therapy. To calculate the risk of fractures, the age must be at least 40 years for the FRAX algorithm, and more than 30 years for the Q fracture. In general, this study is safe, ultrasound densitometry can be used in both children and pregnant women.

*Prospects for further research.* The problem of early identification of persons at high risk of osteoporotic fractures remains open. This issue requires a more detailed study not only in relation to age, but also in relation to the region of the country and the conditions in which the respondents find themselves. Ultrasound densitometry in combination with algorithms for assessing the risk of osteoporotic fractures can be used in epidemiological studies.

5. Conclusions

1. A significant increase in the risk of osteoporotic fractures in women with reduced BMD is found according to all algorithms (except for FRAX Hir without BMD) and the greatest risk was at the age of 70–79 years. Age significantly affects BMD indicators; the greatest decrease in bone density was diagnosed in postmenopausal women. At the same time, only half of women in the age group 30–39 years had normal BMD indices, this fact requires detailed study.

2. At the same time, there is a proportional increase in the number and severity of intercurrent diseases in accordance with age and is the highest in the older age groups of patients.

3. In postmenopausal women, ultrasound densitometry is an informative method for assessing the structural and functional state of bone tissue. And the combination with algorithms for assessing the 10-year risk of osteoporotic fractures significantly increases the early diagnosis of osteoporosis.

4. Algorithms FRAX and Q fracture can be recommended for use by a family doctor to predict the occurrence of osteoporotic fractures and timely identify risk factors associated with osteoporosis.
Innovative technologies in healthcare

even without using the BMD indicator. These are affordable and high-speed methods for assessing the 10-year risk of osteoporotic fractures, which will be useful for planning preventive measures for osteoporosis and its complications, as well as for the next diagnostic steps for early detection of the disease.

Conflict of interest

The authors declare that they have no conflicts of interest.

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