Mathematical model of the bone biological age based on the bone mineral density and quality index and Ukrainian FRAX model


Abstract. Background. It is well-known that with aging there is a loss of bone mass and its strength, which leads to the development of osteoporosis and its complications. The aim of the study was to create a modern mathematical model for determining the biological age of the bone system, taking into account indices of bone mineral density (BMD) and quality and the FRAX questionnaire. Materials and methods. 77 women and 44 men aged 30 to 90 years without any significant somatic pathology were included in the study. Patients were divided into 4 age groups: 30–44 years old — young, 45–59 years — mature, 60–74 years — old age and 75–90 years — senile age. We measured the parameters of BMD in the different areas of the skeleton by means of the dual-photon X-ray absorptiometry (DXA, “Prodigy”). The 10-year probability of major osteoporotic and hip fractures was measured using the Ukrainian version of the FRAX. Statistical analysis was performed in the Statistica 7.0 program (StatSoft Inc., USA). Results. The dependence of the indices of BMD and bone quality, risk of osteoporotic fractures on age and the need for their early determination in young people to predict the risk of osteoporosis and its complications have been proven. The coefficient of determination of the R^2 model was 0.62, which indicates that 62 % of the variance of the “Age” can be explained by the predictors included in the model (DXA and FRAX indices); adjusted R^2 index was 0.59 (p < 0.001), which indicates high significance of the model. Conclusions. The developed model for estimating the bone biological age has high accuracy and can be used to assess the risk of osteoporosis and its complications in young people for the purpose of predicting the disease.

Keywords: biological age; mathematical model; bone mineral density; trabecular bone score; risk of osteoporotic fractures; FRAX

Introduction

During aging, the risk of various diseases increases in a person, as there are age-related changes in various organs and systems. Bone system aging is characterized by the development of degenerative-dystrophic and metabolic changes that lead to the development of osteoporosis and its complications — low-traumatic fractures, which not only reduce the working capacity of the patients and limit their daily capabilities, but also lead to an increase in mortality rates due to low-traumatic fractures [1-3].

Nowadays, the indices of bone mineral density (BMD) and its quality, measured by dual-photon X-ray absorptiometry (DXA), make it possible to assess authentically the bone strength and the risk of osteoporotic fractures. The BMD index determines about 70-75 % of bone strength and, according to the current recommendations of leading world societies (ISCD, IOF), is used for the diagnosis of osteoporosis [1, 2].

The trabecular bone score (TBS) also measured by DXA is currently not used alone for the diagnosis of osteoporosis, but it is highly correlated with 3D parameters of trabecular bone and associated with the risk of osteoporotic fractures in postmenopausal women and men of older age [4, 5].

Another modern method that allows you to assess the risk of osteoporotic fractures without the use of instrumental bone assessment methods is the FRAX (Fracture Risk Assessment Tool) questionnaire. The method of estimating the 10-year probability of major osteoporotic fractures (MOF) and separately of hip fractures (HF) in persons aged 40 years old and older has been used worldwide since 2008. The
Ukrainian version of FRAX appeared in 2016, and in 2019, the criteria for the initiation of antosteoporotic therapy or additional DXA examination for the Ukrainian population appeared [6, 7].

In order to prevent the progression of osteoporosis and the development of low-traumatic fractures, it is important to use comprehensively and in time all indices that assess the strength of bone and the risk of fractures (BMD, TBS, and FRAX), as a result of which there is a need to create a mathematical model of the biological age (BA) of the bone system and to develop a method for estimating the rate of its aging. The results of many studies indicate the lack of complete correspondence between chronological and biological age, and the possibility of predicting osteoporosis and its complications based on the use of formulas for determining BA can increase preventive measures among the persons of risk group.

The purpose of the study was to develop a modern mathematical model for determining the biological age of the bone system, taking into account the bone mineral density and quality parameters and the indices of the Ukrainian FRAX model.

Materials and methods

Population

In a cohort single-center study performed in the D. F. Chebotaiev Institute of Gerontology of the National Academy of Sciences of Ukraine 121 subjects (77 women and 44 men) the aged 30 to 90 years old without any previous diseases of the musculoskeletal system were examined, who went to outpatient doctors for an annual preventive check-up for the period from January 1, 2020 to December 12, 2021.

The research was conducted in accordance with the terms of Helsinki Declaration with the approval of the Commission on Ethics of the D. F. Chebotaiev Institute of Gerontology of the National Academy of Sciences of Ukraine (protocol No. 5 dated the 23-th of April, 2019). All subjects signed a voluntary informed consent for the participation in this study.

The patients were divided into 4 age groups: 30-44 years old — young, 45-59 years old — middle, 60-74 years old — elderly and 75-90 years old — senile age.

Methods

The assessment of BMD and TBS was carried out by the DXA method using the "Prodigy, GEHS Lunar" (Madison, USA, 2005). The quality control of the procedure was carried out in accordance with the manufacturer's recommendations with daily calibration of the device and the use of a phantom.

Bone mineral density (BMD, g/cm²) was determined at the lumbar spine, femoral neck, hip, distal part of the forearm. The indices T (reflects the mean square deviation of bone strength index of the examinee in comparison with that of adults aged 20 years) and Z (reflects the mean square deviation of the subjects index in comparison with the age norm of practically healthy persons) were automatically determined.

To assess the trabecular bone microarchitecture, the TBS index was determined using the program "TBS iNsight® software" (Med-Imaps, Pessac, France) that was installed on the DXA. When evaluating the index, a direct physical measurement of the bone microarchitecture is not carried out, and the calculation is carried out based on the projection of the 3D structure on the 2D plane. The method of assessing the quality of trabecular bone provides an opportunity to analyze the trabecular structure in accordance with various statistical properties of pixels in relation to density, as a result of which an index is calculated that is highly correlated with the 3D parameters of the projected trabecular bone [4, 5].

The assessment of the risk of osteoporotic fractures was carried out using the Ukrainian version of the FRAX (Fracture Risk Assessment Tool®) questionnaire, which measures the 10-year probability (risk) of major osteoporotic fractures (MOF), which includes fractures of the proximal femur and humerus, forearm and clinically significant vertebral fractures, as well as separately the risk of hip fractures (HF) among the persons aged 40 years and older. The calculation was performed on the official FRAX Internet resource (https://www.sheffield.ac.uk/FRAX) without BMD indices [6, 7].

The mean anthropometric indices (height, body weight) were measured using routine methods before conducting DXA.

Statistical data processing was performed in the Statistica 7.0 program (StatSoft Inc., USA). All data were tested for the concordance to normal distribution (according to the Shapiro-Wilk test). Univariate analysis of variance (ANOVA) and the multiple regression method were used for statistical processing of the obtained results. The statistical significance of the indices was determined using univariate analysis of variance (ANOVA) followed by posteriori comparisons of the groups (Tukey HSD post hoc tests). Variational statistics for the data are presented as a mean value ± standard error (M ± m). The differences were considered significant as p < 0.05. The biological age determination model was developed using the multiple regression method. For a qualitative assessment of the model, the coefficient of multiple correlation R and determination R² had been calculated.

Results

The mean values of anthropometric indices, DXA parameters (BMD and TBS), 10-year probability of MOF and HF were calculated in accordance with the age groups, and a significant influence of the "Age" factor on all indices was found, except for body weight and BMD of lumbar spine (p > 0.05) (Table 1).

Basic anthropometric indices, parameters of BMD, and TBS, as well as the 10-year probability of MOF and HF were used in the modeling for a comprehensive assessment of the BA of the bone system. A method of multiple regression analysis was used for the building of the model of determining the biological age of the bone system (Table 2).

As a result of the application of the multiple regression method, we obtained the formula of BA of the bone system:
where \( Y \) (dependent variable) is the biological age of the bone system, years, 

- \( \text{BMD–LS} \) — bone mineral density of the lumbar spine; 
- \( \text{BMD–FN-r} \) and \( \text{BMD–FN-l} \) — bone mineral density of the femoral neck (right and left, respectively); 
- \( \text{BMD–H-r} \) and \( \text{BMD–H-l} \) — bone mineral density of the hip (right and left, respectively); 
- \( \text{BMD–R} \) — bone mineral density of the distal part of radius; 
- \( \text{FRAX–MOF} \) — 10-year probability of major osteoporotic fractures without parameter of bone mineral density; 
- \( \text{FRAX–HF} \) — 10-year probability of hip fractures without parameter of bone mineral density; 
- \( \text{TBS} \) — trabecular bone score.

The coefficient of correlation of the indices with the model \( R \) was 0.79; coefficient of determination of the model \( R^2 \) — 0.62; adjusted index \( R^2 \) (taking into account the number of predictors in the model) — 0.58; Fisher's test \( F \) (11.108) — 15.9; the significance of the model was as high (p < 0.001) with a standard error (SE) of 8.24. The coefficient of multiple correlation \( R \) of predictors with the dependent index "Age" of 0.79 means a high correlation connection between them, while the coefficient of determination of the model \( R^2 = 0.62 \) indicates that 62% of the variance of the "Age" index can be explained using predictors included in the model, which allows to determine the BA of the bone system with an accuracy of 62%. Adjusted \( R^2 \) is a more accurate measure for the assessment of adequacy of the model; it has a quite a high value \( (R^2 = 0.58) \).

Fisher’s criterion \( F \) (11.108) was 15.9 \((p < 0.001)\), which indicates the high significance of the model.

In order to reduce the quantity of the predictors in the calculation of BA, a step-by-step exclusion of uninformative variables was carried out. After excluding low-informative variables from 11 predictors, 8 were remained, the accuracy of the model decreased by 0.5% (Table 3). As a result of the application of the multiple regression method, we obtained the formula of BA of the bone system:

\[
Y = 16.37 \times \text{BMD–LS} – 40.88 \times \text{BMD–FN-r} + 26.83 \times \text{BMD–H-r} – 29.71 \times \text{BMD–FN-l} + 10.40 \times \text{BMD–H-l} – 2.61 \times \text{FRAX–MOF} + 8.65 \times \text{FRAX–HF} – 32.04 \times \text{TBS} + 105.35.
\]

where \( Y \) (dependent variable) is the biological age of the bone system, years, 

- \( \text{BMD–LS} \) — bone mineral density of the lumbar spine; 
- \( \text{BMD–FN-r} \) and \( \text{BMD–FN-l} \) — bone mineral density of the femoral neck (right and left, respectively); 
- \( \text{BMD–H-r} \) and \( \text{BMD–H-l} \) — bone mineral density of the hip (right and left, respectively); 
- \( \text{BMD–R} \) — bone mineral density of the distal part of radius; 
- \( \text{FRAX–MOF} \) — 10-year probability of major osteoporotic fractures without parameter of bone mineral density; 
- \( \text{FRAX–HF} \) — 10-year probability of hip fractures without parameter of bone mineral density; 
- \( \text{TBS} \) — trabecular bone score.

The coefficient of correlation of the indices with the model \( R \) was 0.78; the coefficient of determination of the model \( R^2 = 0.615 \); adjusted \( R^2 \) index (taking into account the number of predictors in the model) — 0.588; Fisher’s test \( F \) (8.111) — 22.2; the significance of the model was as-

Table 1. The influence of the "Age" factor on the dispersion of the index

<table>
<thead>
<tr>
<th>Index</th>
<th>Young age</th>
<th>Middle age</th>
<th>Elderly age</th>
<th>Senile age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height, cm</td>
<td>173.2 ± 1.9</td>
<td>168.2 ± 1.3</td>
<td>165.5 ± 1.4</td>
<td>162.8 ± 3.9</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>83.5 ± 4.6</td>
<td>77.4 ± 2.5</td>
<td>78.7 ± 2.2</td>
<td>71.3 ± 2.9</td>
</tr>
<tr>
<td>BMD–LS, g/cm²</td>
<td>1.13 ± 0.02</td>
<td>1.02 ± 0.03</td>
<td>1.03 ± 0.03</td>
<td>1.03 ± 0.09</td>
</tr>
<tr>
<td>BMD–FN-r, g/cm²</td>
<td>0.93 ± 0.03</td>
<td>0.82 ± 0.02</td>
<td>0.77 ± 0.02</td>
<td>0.68 ± 0.03</td>
</tr>
<tr>
<td>BMD–H-r, g/cm²</td>
<td>1.05 ± 0.03</td>
<td>0.97 ± 0.02</td>
<td>0.98 ± 0.02</td>
<td>0.82 ± 0.04</td>
</tr>
<tr>
<td>BMD–FN-l, g/cm²</td>
<td>0.95 ± 0.03</td>
<td>0.81 ± 0.02</td>
<td>0.77 ± 0.02</td>
<td>0.66 ± 0.03</td>
</tr>
<tr>
<td>MЩКТ– H-l, g/cm²</td>
<td>1.08 ± 0.02</td>
<td>0.96 ± 0.02</td>
<td>0.98 ± 0.02</td>
<td>0.83 ± 0.04</td>
</tr>
<tr>
<td>BMD–R, g/cm²</td>
<td>0.75 ± 0.01</td>
<td>0.70 ± 0.01</td>
<td>0.67 ± 0.02</td>
<td>0.59 ± 0.05</td>
</tr>
<tr>
<td>FRAX–MOF, %</td>
<td>1.44 ± 0.02</td>
<td>1.35 ± 0.01</td>
<td>1.31 ± 0.01</td>
<td>1.31 ± 0.04</td>
</tr>
<tr>
<td>FRAX–HF, %</td>
<td>2.36 ± 0.25</td>
<td>4.02 ± 0.46</td>
<td>4.60 ± 0.36</td>
<td>8.10 ± 1.38</td>
</tr>
<tr>
<td>TBS, units</td>
<td>0.14 ± 0.03</td>
<td>0.61 ± 0.12</td>
<td>1.21 ± 0.15</td>
<td>3.94 ± 0.71</td>
</tr>
</tbody>
</table>

Notes. Here and in the tables 2 and 3: Results are presented as M ± m; the analysis was performed using one-factor ANOVA analysis (F – Fisher's test; p – significance of the influence of the "Age" factor). Here and in the tables 2 and 3: BMD–LS — bone mineral density of the lumbar spine; BMD–FN-r and BMD–FN-l — bone mineral density of the femoral neck (right and left, respectively); BMD–H-r and BMD–H-l — bone mineral density of the hip (right and left, respectively); BMD–R — bone mineral density of the distal part of radius; TBS — trabecular bone score; FRAX–MOF — 10-year probability of major osteoporotic fractures without parameter of bone mineral density; FRAX–HF — 10-year probability of hip fractures without parameter of bone mineral density.
assessed as high (p < 0.001) with a standard error (SE) of 8.16. Further exclusion from the model of indices of BMD — of the proximal part of the femur led to a decrease in the sensitivity of the model by at least 3.5%.

In Figure 1 it is represented the correlation between the calculated (biological) and chronological age of the examined persons. It was established that the dispersion of points around the regression line is small, the coefficient of multiple correlation of predictors with the dependent indicator Y (Age) is high (r = 0.78, p < 0.001), which indicates the high accuracy of the created model.

The coefficient of determination of the R² model of 0.615 indicates that 61.5% of the variance of the Y indicator (Age) can be explained by the predictors that are included in the model. Adjusted R² for the developed model was 0.59; and the F index (8.11) is 22.2 (p < 0.001), which indicates its high significance. The standard error of the estimation (SE of the estimation) was equal to 8.16 years.

Thus, the developed model allows estimating with sufficient accuracy the degree of age-related changes in the bone system by determining the BA of the subject, using the eight most informative indices that had been selected by the exclusion method in the multiple regression procedure.

**Discussions**

In foreign literature, we can find the term "silent disease" when the scientists talk about "osteoporosis" [1, 8, 9]. Elderly and senile ages are critical periods for the development of osteoporosis and its complications — low-energy osteoporotic fractures, the most severe of which is a hip fracture, the occurrence of which leads to prolonged disability and death of the patients [2, 8-10]. Additionally, the presence of other osteoporotic fractures, that are vertebral ones, often leads to back pain and reduced work capacity of the patients. The total risk of osteoporotic fractures at the age of 50 is 39.7% for women and 13.1% for men; the risk of hip fractures is 17.5% and 6%, vertebral ones — 15.6% and 5.0%, distal forearm fractures is 16.0% and 2.5%, respectively [8, 10, 11]. Therefore, early prediction of the risk of fractures can help the patient to maintain health and prevent loss of working capacity.

**Table 2. Results of the calculation of the multiple regression equation in the program Statistica 7.0 for the dependent variable "Chronological age" (Model 1)**

<table>
<thead>
<tr>
<th>Index</th>
<th>b*</th>
<th>SE of b*</th>
<th>b</th>
<th>SE of b</th>
<th>t (108)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>–</td>
<td>–</td>
<td>120.50</td>
<td>20.87</td>
<td>5.78</td>
<td>0.0001</td>
</tr>
<tr>
<td>Height, cm</td>
<td>–0.09</td>
<td>0.11</td>
<td>–0.12</td>
<td>0.14</td>
<td>–0.85</td>
<td>0.395</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>0.05</td>
<td>0.12</td>
<td>0.03</td>
<td>0.09</td>
<td>0.38</td>
<td>0.706</td>
</tr>
<tr>
<td>BMD–LS, g/cm²</td>
<td>0.22</td>
<td>0.10</td>
<td>15.42</td>
<td>7.11</td>
<td>2.17</td>
<td>0.03</td>
</tr>
<tr>
<td>BMD–FN-r, g/cm²</td>
<td>–0.47</td>
<td>0.21</td>
<td>–39.98</td>
<td>17.69</td>
<td>–2.26</td>
<td>0.03</td>
</tr>
<tr>
<td>BMD-H-r, g/cm²</td>
<td>0.29</td>
<td>0.28</td>
<td>24.17</td>
<td>23.42</td>
<td>1.03</td>
<td>0.304</td>
</tr>
<tr>
<td>BMD–FN-l, g/cm²</td>
<td>–0.33</td>
<td>0.20</td>
<td>–28.05</td>
<td>16.53</td>
<td>–1.70</td>
<td>0.092</td>
</tr>
<tr>
<td>МЩКТ- H-l, g/cm²</td>
<td>0.14</td>
<td>0.28</td>
<td>11.41</td>
<td>22.98</td>
<td>0.50</td>
<td>0.620</td>
</tr>
<tr>
<td>BMD-R, g/cm²</td>
<td>0.00</td>
<td>0.11</td>
<td>0.39</td>
<td>13.40</td>
<td>0.03</td>
<td>0.977</td>
</tr>
<tr>
<td>FRAX–MOF, %</td>
<td>–0.62</td>
<td>0.15</td>
<td>–2.73</td>
<td>0.64</td>
<td>–4.23</td>
<td>0.0001</td>
</tr>
<tr>
<td>FRAX–HF, %</td>
<td>0.89</td>
<td>0.14</td>
<td>8.77</td>
<td>1.36</td>
<td>6.43</td>
<td>0.0001</td>
</tr>
<tr>
<td>TBS, units</td>
<td>–0.26</td>
<td>0.10</td>
<td>–29.98</td>
<td>11.08</td>
<td>–2.71</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Notes (for tables 2 and 3). b — regression coefficient; b* — standardized regression coefficient; SE of estimate — standard error of estimation; Intercept — free member of the equation; SE of b* — standardized error of the coefficient; t — Student’s test; p — assessment of the significance of the model.

**Table 3. The results of the multiple regression equation calculations with step-by-step exclusion of low-informative predictors for the dependent variable "Chronological age" (Model 2)**

<table>
<thead>
<tr>
<th>Index</th>
<th>b*</th>
<th>SE of b*</th>
<th>B</th>
<th>SE of b</th>
<th>t (111)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>–</td>
<td>–</td>
<td>105.35</td>
<td>11.32</td>
<td>9.31</td>
<td>0.000001</td>
</tr>
<tr>
<td>BMD–LS, g/cm²</td>
<td>0.23</td>
<td>0.10</td>
<td>16.37</td>
<td>6.79</td>
<td>2.41</td>
<td>0.02</td>
</tr>
<tr>
<td>BMD–FN-r, g/cm²</td>
<td>–0.48</td>
<td>0.21</td>
<td>–40.88</td>
<td>17.38</td>
<td>–2.35</td>
<td>0.02</td>
</tr>
<tr>
<td>BMD-H-r, g/cm²</td>
<td>0.33</td>
<td>0.28</td>
<td>26.83</td>
<td>22.79</td>
<td>1.18</td>
<td>0.24</td>
</tr>
<tr>
<td>BMD–FN-l, g/cm²</td>
<td>–0.35</td>
<td>0.19</td>
<td>–29.71</td>
<td>16.30</td>
<td>–1.82</td>
<td>0.07</td>
</tr>
<tr>
<td>МЩКТ- H-l, g/cm²</td>
<td>0.13</td>
<td>0.27</td>
<td>10.40</td>
<td>22.67</td>
<td>0.46</td>
<td>0.64</td>
</tr>
<tr>
<td>FRAX–MOF, %</td>
<td>–0.59</td>
<td>0.14</td>
<td>–2.61</td>
<td>0.62</td>
<td>–4.24</td>
<td>0.00005</td>
</tr>
<tr>
<td>FRAX–HF, %</td>
<td>0.87</td>
<td>0.13</td>
<td>8.65</td>
<td>1.33</td>
<td>6.52</td>
<td>0.000001</td>
</tr>
<tr>
<td>TBS, units</td>
<td>–0.28</td>
<td>0.07</td>
<td>–32.04</td>
<td>8.33</td>
<td>–3.85</td>
<td>0.0002</td>
</tr>
</tbody>
</table>
A large number of scientific publications testify to the relevance of studying aging processes and the development of osteoporosis [3, 9, 12-16]. In the studies carried out as early as 1935 by D. G. Rokhlin and co-authors, the attempts were made to calculate the "bone age" of a person based on X-ray examinations of bone tissue. Scientists have been studying BA of the bone system for many years, but modern methods of mathematical modeling create new opportunities for obtaining new models of BA and more accurate results of their prediction.

In 1993 at the Institute of Gerontology of Ukraine the bone BA formulas for men and women were described for the first time, taking into account the indices of ultrasound densitometry [8, 15]. The results of these studies demonstrated that the rate of bone system aging in women with hip fractures significantly exceeded the population standard (by 8.5 years in the age group of 60-69 years old and by 10.3 years in the age group of 70-79 years old). Accelerated aging of the bone system led to a probable increase in the proportion of the patients with severe form of osteoporosis among the patients with hip fractures (60-69 years old – 90%; 70-79 years old – 100%) [16].

In 2015, at the D. F. Chebotarev Institute of Gerontology of the National Academy of Sciences of Ukraine, the peculiarities of the BA of the bone system in women of older age groups with vertebral pain syndrome were investigated depending on BMD indices [12]. The examined 257 postmenopausal women at the age of 50-89 years old had been divided into groups: the main group (n=154) with osteoporosis and osteopenia, the comparison group (n=103) with normal BMD. The determination of BA was carried out using an "ambulatory" battery of the tests according to the method of V. P. Voitenko [17]. The authors established significant correlations between the BA index and the body mass index, indices of BMD and its quality. The results of the research showed that in women of older age groups, BA indices reliably worsen both among subjects with normal and low BMD. In women with osteoporosis and without vertebral fractures, the BA index at the age of 60-69 years old was significantly higher compared to the subjects without osteoporosis. This index also significantly increased in subjects at the age of 70-79 years old. The results of the authors [12] have demonstrated that among the women of older age groups with normal BMD, age changes play a significant role in the deterioration of BA, and among the patients with osteoporosis, age-related processes are neutralized by the presence of the disease itself. The results that we have obtained also confirm the reliable influence of age on DXA indices, which are manifested both in the reduction of BMD and indices of bone tissue quality.

Wide implementation of the FRAX questionnaire in the practice of osteoporotic fractures risk assessment, the appearance of its Ukrainian version, thresholds for the initiation of antiosteoporotic treatment, or additional DXA examination made it possible to increase the effectiveness of predicting osteoporotic fractures. The possibility of using three main indices of bone strength and the risk of low-trauma fractures (BMD, TBS, and FRAX) became the basis for the development of new models of BA, which was the goal of this study.

Our results demonstrate the dependence of BMD, TBS and FRAX indices depending on age and determine the need for their early determination in young subjects to predict the development of osteoporosis and its complications. An important finding is that the model with high accuracy included not only the indices of the instrumental assessment of bone tissue (BMD and TBS), but also the FRAX indices, which are a reflection of the clinical risk factors of osteoporosis. Step-by-step modeling of bone BA by the multiple regression method with the inclusion of first 11 and then 8 indices allowed us to propose a model for determining BA that has high accuracy for prediction (R = 0.78; R² = 0.615; p < 0.001).

Thus, practicing physicians can recommend to young subjects with risk factors for osteoporosis a bone assessment using DXA with determination of BMD and TBS indices, as well as an assessment of the 10-year probability of osteoporotic fractures using the FRAX questionnaire, which, according to the results of our studies, are highly informative in predicting the risk of osteoporosis and its complications. This will help to detect the disease in time and to prevent the development of osteoporosis at an older age.

Limitations of the study. The mathematical model of the biological age of the bone system obtained by us has high accuracy, however, to obtain more reliable results, an examination on a larger sample of the patients is required, especially subjects at a young age. In addition, when conducting such studies, it is important to take into account other risk factors for osteoporosis and its complications, which are not included in the FRAX questionnaire. It is important to conduct prospective studies over the course of the decades on large cohorts of individuals to assess the informativeness of this model.

Conclusions

The study had demonstrated the dependence of the indices of bone mineral density and its quality and the risk of osteoporotic fractures depending on age and the need for

![Figure 1. Correlation between the calculated (biological) and chronological age of the subjects](image-url)
their early determination in young subjects to prevent the development of osteoporosis and its complications. 61.5% of the variance of the “Age” index can be explained with the help of predictors included in the model (BMD of the lumbar spine, hip and femoral neck, TBS, and FRAX) with the high significance of the model (p < 0.001).

Thus, the developed method for assessing the bone BA has high accuracy and can be used for the assessment of the risk of osteoporosis and its complications. An implementation of the proposed method allows not only to identify persons at risk of developing osteoporosis in the group of its development, but also to increase the effectiveness of predicting the fractures risk.

References

Received 11.09.2022
Revised 21.09.2022
Accepted 26.09.2022
Математична модель біологічного віку кісткової системи на основі показників її мінеральної щільності та якості й української моделі FRAX

Резюме. Актуальність. Загальновідомо, що зі старінням людини відбувається втрата кісткової маси та міцності кісткової тканини, що призводить до розвитку остеопорозу та його ускладнень. Метою дослідження було створити сучасну математичну модель визначення біологічного віку кісткової системи з урахуванням показників мінеральної щільності та якості кісткової тканини й опитувальника FRAX®. Матеріали та методи. У дослідження були включені 77 жінок та 44 чоловіки віком від 30 до 90 років без будь-якої соматичної патології. Пацієнти були розподілені на 4 вікові групи: 30–44 роки — молодий, 45–59 років — зрілий, 60–74 роки — літній і 75–90 років — старчий вік. Визначали показники мінеральної щільності та якості кісткової тканини за допомогою двофотонної рентгенівської абсорбціотрії (ДРА). Оцінку ризику переломів кісток проводили за допомогою української версії опитувальника FRAX®. Статистичну обробку проводили за допомогою програми Statistica 7.0 (StatSoft Inc., США). Результати. Доведена залежність показників мінеральної щільності та якості кісткової тканини, ризику основних остеопоротичних переломів від віку та необхідність раннього їх визначення у молодих осіб для прогнозування ризику остеопорозу та його ускладнень. Коєфіцієнт детермінації моделі $R^2$ становив 0,62, що вказує на те, що 62 % дисперсії показника «вік» можна пояснити за допомогою предикторів, які увійшли в модель (показники ДРА та FRAX); скоригований показник $R^2$ становив 0,59 ($p < 0,001$), що свідчить про високу значимість моделі. Висновки. Розроблена модель оцінки біологічного віку кісткової системи має високу точність і може бути застосована для оцінки ризику розвитку остеопорозу та його ускладнень у молодих осіб з метою прогнозування захворювання. Ключові слова: біологічний вік; математична модель; мінеральна щільність кісткової тканини; якість кісткової тканини; ризик остеопоротичних переломів; FRAX.