Clinical and instrumental characteristics of subsequent osteoporotic fractures in patients of Gomel area and therapeutic strategy

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Abstract
The dual–energy X-ray densitometry and surveys were conducted in 2 356 women aged over 50. The osteoporotic fractures of the forearm, spine and proximal femur were found in 523 (22.2%) of women. More than one fracture was revealed in 106 patients (20.3%) of the total number of patients with fractures. The average age of first fracture in patients with multiple fractures was 59.9 years, second – 63.3 years and third – 66.6 years. Most subsequent fractures (67%) have been occurred within the first three years from the time of the first fracture and were not associated with the densitometry data. Despite the presence of multiple osteoporotic fractures, the adequate specific therapy of severe osteoporosis was appointed only to every third patient out of the needed in treatment.

Key words: osteoporotic fracture, osteoporosis, bisphosphonates

Introduction
Low-trauma fractures are a major complication of osteoporosis resulting in significant social and economic losses, as well as in mortality increase of the elderly. The international project GLOW is the most large-scale study on incidence and risk of recurrent fractures where the analysis of fractures was conducted in more than 50000 women aged over 55 [1]. The study revealed that 17.6% of the patients had a history of a single fracture, 4.0% – subsequent and 1.6% were reported to have three or more fractures. Compared with the females without fractures, the women with previous single fracture have had a doubled risk of re-fracture, up to 1.81 (95% CI 1.66–1.97). The females with two previous fractures have had a doubled risk of next fracture development, up to 2.98 (95% CI 2.63–3.38).

According to GLOW study results it was found that after earlier primary osteoporotic fracture of the proximal femur and spine there is a credible risk of re-fracture of the femur (3.50; 95% CI 2.30–5.32) and vertebral re-fractures (7.34; 95% CI 5.42–9.92). Thus, after a single forearm fracture the probability of occurrence of a second more
severe fracture is lower, up to 1.04 – for a hip (95% CI 0.71–1.51) and up to 1.37 – for a spine (95% CI 1.01–1.85).

The main purpose of this study was to examine the medical history, clinical and instrumental data of patients with previous single and subsequent osteoporotic fractures of the forearm, proximal femur and spine, as well as to evaluate the existing therapeutic treatment strategy for patients with low-trauma fractures.

**Material and Methods**

The research has been organized and carried out in the Republican Research Centre for Radiation Medicine and Human Ecology and approved at a meeting of the local Ethics committee. The survey among patients was performed by the unified protocol developed in the Republican Research Centre for Radiation Medicine and Human Ecology. The questionnaire includes passport information, gender, age, previous fractures data (forearm, proximal femur and vertebrae), the year of fracture, information about medical history (diabetes, ulcers of the gastrointestinal tract, chronic obstructive pulmonary disease, acute cerebrovascular circulation, acute myocardial infarction, chronic heart failure, cirrhosis, chronic renal failure, cancers, rheumatoid arthritis, myocardial infarction). The Comorbidity index was evaluated by Charlson scale [2]. The scale is based on the points summation. 1 point is assigned for patient aged 50–59 years, 2 points – aged 60–69, 3 points – aged 70–79 and 4 points – aged 80–89. Further the points are added concerning concomitant diseases, depending on the severity and prognosis: up to 1 point – for acute myocardial infarction in the anamnesis, earlier stroke with no or minimal impact, chronic nonspecific lung diseases, peptic ulcer disease, mild liver disease without cirrhosis and diabetes mellitus and up to 6 points – for metastatic malignant tumours.

The dual-energy X-ray absorptiometry method (DXA) was applied to quantify bone mineral density (BMD) by the first four lumbar vertebrae and proximal femur (LUNAR Prodigy, GE-USA, with CORE software v 8.5). The diagnosis ‘Osteoporosis’ was defined based on the calculation of the standard deviation of ≤−2.5 from average BMD values of population of healthy young subjects (T-score) of densitometer database for maximum available amount of lumbar vertebrae (L₁–L₄), but not less than two, and by the minimum value of T-score of the proximal femur intact limb [3].

The collection of clinical, anamnestic and instrumental indicators was performed within the program on calculating the risk development of osteoporotic fractures (certificate of registration No. 116 in the register of the registered computer programs in the National Centre of Intellectual Properties, the authors are H. Ramanau, L. Starastenka and E. Rudenka). The statistical processing has been done with the use of the application package Statistica 8.0 and SPSS 17.0. The methods of parametric statistics were applied for a analysis with the presentation of data in the format of ‘mean ± standard deviation’ (M ± σ). The Student’s t-test is used to determine the statistical significance for independent samples, the frequency of occurrence of indicator was evaluated by the criterion χ². If the expected frequency was 5 and lower, the exact Fisher-Irvin criterion was used to obtain the achieved level of significance p. The method of multivariate analysis of variance was applied taking into account the effects of covariates. The statistically significant differences were considered for values of p < 0.05.

**Results and Discussion**

According to the elaborated schedule the study included 2356 female patients aged over 50. The measurement of anthropometric indicators was provided for all participants including an axial densitometry of the lumbar spine (L₁–L₄) and proximal femur, as well as a survey on typical localization of low-trauma fractures. The standardized evaluation of bone mineral density (BMD) was performed by calculating the T-score of lumbar spine L₁–L₄ (LS) and T-score of the femoral neck (FN). The general characteristics of the study cohort are presented in the Table 1.

According to the obtained data, the patients participating in densitometric study showed a BMD reduction mostly in the lumbar spine than in femoral neck. As a result of the survey the study cohort included 523 patients with low-trauma fracture aged over 50, and out of them, 106 patients had more than 1 osteoporotic fracture in anamnesis. Law-trauma fractures were classified as fractures of typical localization (forearm, spine and proximal femur), resulting from a minor injury and/or falling from its own height.

The current treatment strategy involves the administration of a specific anti-osteoporotic therapy in patients with instrumentally verified diagnosis ‘osteoporosis’ according to densitometric study. However, a significant proportion of patients after densitometry, according to WHO definition, is classified into the group ‘osteopenic’ or “low BMD” with a T-score between −1.0 and −2.5. This category of patients is the most difficult in terms of indications for a
possible purpose of treatment. Within the performed study it was revealed that 73 patients (14%) with fractures in anamnesis had the minimum value of T-score according to densitometry, within –1.0 to –2.5. A comparative analysis was provided on frequency of occurrence of possible fractures risk factors in patients with low BMD depending on the history of fractures (Table 2).

As can be seen from Table 2, there were not revealed statistically significant differences on incidence of occurrence of the analysed risk factors in patients with low BMD depending on earlier low-trauma fracture in anamnesis. The obtained results require further research to identify predictors of fracture development in patients without DXA verified osteoporosis.

The Charlson comorbidity index (CCI) was calculated to examine the interconnection of fractures development of typical localization taking into account the patient’s age and the type of somatic pathology. The patients aged over 50 with osteoporosis were included into the comparison group without previously observed fractures. The results of the comparison are shown in the Figure 1.

![Figure 1. The indicators of Charlson Comorbidity Index in patients aged over 50 depending on fractures (FRX) presence in anamnesis](image)

According to the data obtained CCI was higher in the group of patients with earlier low-trauma fractures than in patients with osteoporosis, but without reference to the anamnesis of fractures. All previous low-trauma frac-

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**Table 1.** General characteristics of the cohort study

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Study cohort (n = 2 356)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>64.7 ± 8.2</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>71.0 ± 13.3</td>
</tr>
<tr>
<td>Height, cm</td>
<td>158.2 ± 6.2</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.4 ± 5.1</td>
</tr>
<tr>
<td>T-score FN</td>
<td>–1.8 ± 1.0</td>
</tr>
<tr>
<td>T-score LS</td>
<td>–2.9 ± 1.0</td>
</tr>
</tbody>
</table>

The number of patients with fractures:
- with single fracture: 417
- with multiple fractures: 106

Total number of fractures in a study cohort:
- Forearm: 491
- Vertebral: 116
- Proximal femur: 44

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**Table 2.** The frequency of occurrence of risk factors for osteoporotic fractures development in group of patients with low BMD aged over 50

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Patients without fractures, n = 434</th>
<th>Patients with fractures, n = 58</th>
<th>Significance, p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burdened family anamnesis of fractures</td>
<td>9.0%</td>
<td>11.5%</td>
<td>0.556</td>
</tr>
<tr>
<td>Somatic diseases associated with osteoporosis</td>
<td>2.8%</td>
<td>3.4%</td>
<td>0.805</td>
</tr>
<tr>
<td>Smoking</td>
<td>5.5%</td>
<td>3.4%</td>
<td>0.467</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>4.1%</td>
<td>3.4%</td>
<td>0.792</td>
</tr>
</tbody>
</table>
Clinical and instrumental characteristics of subsequent osteoporotic fractures in patients of Gomel area and therapeutic strategy

Tures were taken into account during the questioning of patients aged over 50, with location and the year of fracture occurrence. After statistical data processing there were identified 106 patients who had more than one fracture. The patients were divided into 3 groups by the number of fractures. One group was consisted of patients with only one previous fracture, the second – 2 fractures and the third group included patients with 3 previous fractures. In addition the question from the questionnaire was included into analysis concerning the administered treatment after fracture in relation to medicine reducing the risk of the subsequent fracture and increasing BMD (bisphosphonates). The overall comparative characteristics of the patients are presented in the Table 3.

According to the data obtained, the patients had no statistically significant differences by age, BMI, and densitometric parameters. However, despite the multiple osteoporotic fractures, an adequate specific therapy of osteoporosis was administered only to every third patient out of the needed in treatment.

Taken into account that no significant differences were obtained by T-score level in patients with multiple fractures in anamnesis, it was supposed the impact of patient’s age as a well-known factor in the development of osteoporosis and fractures. In order to test this hypothesis there was performed a multivariate analysis of variance (ANOVA) with the covariates. A quantitative value of T-score of spine and femoral neck was chosen as a dependent variable, the fixed factors involved the presence of fractures in anamnesis and their number, and the patient’s age at the time of examination was used as a covariate. The graphical results of the statistical analysis are presented in the Figure 2.

According to the obtained data, the patients, regardless the number of fractures, have significantly lower values of T-score of femoral neck and spine than the patients without previous fractures. With the increasing number of fractures there is a tendency to T-score reduction, but the differences significance threshold was not reached. Thus, the occurrence of subsequent fractures is

<table>
<thead>
<tr>
<th>Indicator</th>
<th>1 fracture, n = 417</th>
<th>2 fractures, n = 84</th>
<th>3 fractures, n = 22</th>
<th>Significance of differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at the moment of examination, years</td>
<td>68.2 ± 8.0</td>
<td>68.6 ± 7.7</td>
<td>69.4 ± 7.8</td>
<td>p = 0.705</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.9 ± 4.8</td>
<td>28.2 ± 4.2</td>
<td>26.6 ± 4.6</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>T-score FN</td>
<td>-2.2 ± 0.8</td>
<td>-2.3 ± 0.8</td>
<td>-2.5 ± 0.9</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>T-score LS</td>
<td>-3.2 ± 0.9</td>
<td>-3.3 ± 1.0</td>
<td>-3.5 ± 1.3</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>23.7%</td>
<td>25.0%</td>
<td>31.8%</td>
<td>p &gt; 0.05</td>
</tr>
</tbody>
</table>

Fig. 2. The covariance analysis of differences of T-score of femoral neck and spine in patients depending on the presence and the number of previous fractures (FRX) in anamnesis at a fixed age effect
not associated with the values of densitometric studies. In view of the mentioned above, the application of the densitometry method is not mandatory under determining of indications for specific antiresorptive therapy in patients with previous fractures.

Under the planning of this study there was defined the task on calculation of the average age of low-trauma fracture, as well as the assessment of the probable period of subsequent fractures. A questioning of patients was conducted concerning previous fractures and the information was collected on the date of fracture. The age of low-trauma fracture development was calculated according to the patient’s date of birth and date of fracture occurrence. These average age data of the primary fracture and subsequent fractures are shown in the Figure 3.

Thus, the average age of first fracture in patients with multiple fractures was 59.9 years, re – 63.3 years and subsequent – 66.6 years. The detailed structure of occurrence of the subsequent fracture is shown in the Figure 4.

According to the data obtained, the majority of subsequent fractures (67%) occur during the first three years from the date of the first fracture. In view of the mentioned above, it is necessary to carry out the immediate prevention of subsequent fractures immediately after the initial fracture. The main directions of the secondary prevention are the following:

- An adequate intake of calcium and vitamin D
- Anti-osteoporotic treatment
- Exercising
- Reducing of falls risk

The most effective medication way at present is the administration of a specific anti-osteoporotic therapy with proven efficacy to prevent subsequent low-trauma fractures (Table 4).

Thus, the use of specific therapy for severe osteoporosis with fractures will significantly reduce the risk of recurrent osteoporotic fractures and prevent significant social and economic losses.

Table 4. Efficiency of anti-osteoporotic drugs in patients with postmenopausal osteoporosis to prevent repeated fractures [4]

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effect on vertebral fractures</th>
<th>Effect on out-of-vertebral fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Zoledronate</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Strontium ranelate</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Conclusions

1. The average value of T-score of spine and femoral neck in patients with previous fracture was significantly lower than in patients without fractures in anamnesis ($p = 0.001$).

2. The Charlson Index of comorbidity in patients with fractures was significantly ($p < 0.05$) higher than in the group of patients with osteoporosis and without reference to fractures in anamnesis.

3. Of the total number of patients with fractures, 106 patients (20.3%) had more than one fracture. The average age of first fracture in the group of patients with multiple fractures was 59.9 years, repeated – 63.3 years and subsequent – 66.6 years.

4. Most subsequent fractures (67%) occur during the first three years from the date of the first fracture and are not associated with the values of densitometric parameters.

References


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