Frequency and localization of osteoporotic fractures depending on age, bone mineral density and trabecular bone score in postmenopausal women of Ukrainian cohort

Abstract. Background. Low-trauma fractures are the important complications of systemic osteoporosis, which lead to reduced quality of life, increased morbidity, disability and mortality. Nowadays, bone mineral density (BMD) and trabecular bone score (TBS) measured by dual energy X-ray absorptiometry are two major parameters of bone strength. They are widely used when establishing the osteoporosis diagnosis. The purpose was to study the frequency and localization of different osteoporotic fractures in postmenopausal women depending on the age, BMD and TBS. Materials and methods. We have performed cross-sectional study and have examined 1,369 postmenopausal women aged 45–89 years. Patients were divided into groups depending on BMD according to the WHO criteria: normal bone (T-score > –1.0 standard deviation (SD)), osteopenia (≤ –1.0 T-score ≤ –2.5 SD), osteoporosis (T-score ≤ –2.5 SD), and depending on TBS (L₁-L₄) quartiles (groups): QI — the lowest quartile (0.36–1.08); QII — the lower quartile (1.08–1.20); QIII — the upper quartile (1.20–1.32); QIV — the highest quartile (1.32–1.79). BMD and TBS in lumbar spine (L₁-L₄) were measured using Prodigy densitometer (GE Medical systems, Lunar, model 8743, 2005). TBS was determined using the software TBS Insight (Med-Imaps, Bordeaux, France, 2006). Results. Our study found that risk of all types of osteoporotic fractures in females reliably increases with age (for vertebral fractures — by 1.97–4.26 times, non-vertebral — 1.96–5.45 times, combined fractures — 1.54–3.14 times). Additionally, we have revealed that osteoporotic fractures are present in all groups of females with different BMD: osteoporosis (45.5 %), osteopenia (26.9 %) and normal bone (18.1 %). The highest frequency of osteoporotic fractures was detected in osteoporosis (46.5 %), and, predominantly, in women with vertebral and combined fractures. Only 25.5 % of patients with non-vertebral fractures have osteoporosis. Low TBS was observed in 50.8 % of females with vertebral, 43.7 % — non-vertebral and 32.8 % — with combined (vertebral and non-vertebral) osteoporotic fractures. Conclusions. Osteoporotic fractures are partly associated with age, BMD and TBS. However, there are other significant factors, which influence the risk of fractures, and their combination requires further study.

Keywords: osteoporosis; osteoporotic fractures; bone mineral density; trabecular bone score; postmenopausal women

Introduction

Osteoporotic fractures are tremendous medico-social problem in almost all industrialized countries [1–6]. Every year, up to 9 millions of new low-trauma fractures caused by osteoporosis are expected [3]. The rate of mortality associated with fractures of the hip and spine can exceed 20 % [3]. In the United States, about 2 million new fractures are registered each year [7]. Approximately 10 % of 50-year-old women already have at least one osteoporotic fracture [1, 5]. Given the steady increase of life expectancy, these figures will be doubled in the next 40–50 years [8].

Current studies confirm that dual-energy X-ray absorptiometry (DXA) is the gold standard for diagnosing osteoporosis and its indices (bone mineral density (BMD) and trabecular bone score (TBS) are the important parameters of bone density, microarchitecture and strength). However, their relationship with the fractures of different locations (vertebral or non-vertebral) continues to be studied, existing data are limited and depend on age, sex and some national features.

The purpose of this research was to evaluate the frequency and localization of different osteoporotic fractures.
Materials and methods

Participants. We have performed a cross-sectional, case-control research. The study was conducted in Ukrainian Scientific Medical Center of Osteoporosis and department of clinical physiology and pathology of locomotor apparatus of D.F. Chebotarev Institute of Gerontology of the NAMS of Ukraine. It was approved by ethics committee of the Institute (12/10/2013). All patients signed informed consent for participation in the study. 1,369 postmenopausal women aged 45–89 years were examined (mean age — 62.5 [55.0; 73.0] years, mean body mass index — 28.6 ± 6.5 kg/m², the average duration of postmenopausal period — 14.5 ± 9.5 years). We excluded the patients with severe concomitant diseases, high-energy fractures or trauma history, high levels of physical activity, secondary osteoporosis or conditions that could affect the bone, some significant disorders (connective tissue disease, neoplasms in the past medical history, administration of corticosteroids, alcohol abuse and others), clinically manifested vertebral fractures with post-fracture period duration at least 6 months.

For analysis, we divided our patients into groups according to age, BMD and TBS indices. At first, they were divided into three age groups (45–59, 60–74 and 75–89 years). In addition, they were divided depending on BMD parameters according to the World Health Organization criteria and International Society for Clinical Densitometry guidelines. The assessment of BMD indexes was performed according to next DXA criteria: normal bone (T-score > –1.0 standard deviation (SD)), osteopenia (–1.0 T-score > –2.5 SD) and osteoporosis (T-score ≤ –2.5 SD) [5, 9]. The women were divided into next groups: first one (NB) — 563 females with normal BMD parameters, second one (OPEN) — 498 women with osteopenia, third one (OP) — 308 patients with osteoporosis.

Subsequently, patients were divided depending on TBS. Nowadays, TBS has no standard indicators and in various countries, including Ukraine, studies to determine its reference indices are only in process [10]. Standard TBS, as well as BMD, should be specific for definite geographic areas and ethnic groups. Therefore, this section describes a statistical approach that is used in cases of irregular quantitative values, namely quartile distribution groups.

All examined females were divided according to TBS parameters (L₁-L₄) into groups (quartiles): QI — the lowest quartile (0.36–1.08; n = 152); QII — the lower quartile (1.08–1.20; n = 156); QIII — the upper quartile (1.20–1.32; n = 148); QIV — the highest quartile (1.32–1.79; n = 133).

Presence, localization, mechanism and time of fracture were determined using specialized questionnaire developed in Ukrainian Scientific Medical Center of Osteoporosis. All information was gathered from patients by interview. In present study, we evaluated the frequency of vertebral, non-vertebral (non-spine non-hip fractures: humerus, forearm, clavicle, ribs, pelvis, upper and lower extremities) and combined fractures.

Methods. Bone mineral density and TBS were measured at the lumbar spine (L₁–L₄) using dual energy X-ray Prodigy densitometer (GE Medical systems, Lunar, model 8743, 2005). Trabecular bone score was determined using TBS Insight software (Med-Imaps, Bordeaux, France, 2006).

Statistical analysis was performed using Statistica 10.0 software package (StatSoft © Inc., 1984–2011). All variables were distributed using the Kolmogorov-Smirnov test. Intragroup comparisons were made using one-way analysis of variance and Mann-Whitney U test. Differences in the distribution of samples were assessed using χ² test. To evaluate the correlation between variables, we used Spearman’s rank correlation coefficient (R). The critical level of significance was p < 0.05.

Results

The results of our study demonstrated that age is the significant risk factor for osteoporotic fractures in females. Fracture distribution analysis according to the age has shown that frequency of low-trauma osteoporotic fractures (vertebral, non-vertebral and combined) progressively increased from 22.2 % in women aged 45–59 years to 35.8 % in patients aged 75–89 years (Fig. 1). The most significant increase was determined for vertebral fractures.

In addition, it was found that osteoporotic fractures were present in all groups of patients with different BMD: osteo-

<table>
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<th>Figure 1. Proportion of different fractures depending on localization in women of various age groups</th>
<th>Without fractures</th>
<th>Vertebral fractures</th>
<th>Non-vertebral fractures</th>
<th>Combined fractures</th>
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<tr>
<td>45–59 years</td>
<td>6.4 %</td>
<td>10.7 %</td>
<td>51.1 %</td>
<td>77.8 %</td>
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<td>60–74 years</td>
<td>10.1 %</td>
<td>16.2 %</td>
<td>57.5 %</td>
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<tr>
<td>75–89 years</td>
<td>10.1 %</td>
<td>13.7 %</td>
<td>12.0 %</td>
<td>64.2 %</td>
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</table>
Osteoporosis — 45.5 %, osteopenia — 26.9 % and normal bone — 18.1 %. Moreover, the frequency of non-vertebral low-trauma fractures was not significantly different in women with osteoporosis (11.7 %), osteopenia (11.0 %) and normal BMD (9.8 %).

Also, we observed significant differences ($\chi^2 = 95.66, p < 0.0001$) due to vertebral (OP-group — 20.5 %, OPEN-group — 9.6 %, NB-group — 4.3 %) and combined fractures (OP-group — 13.3 %, OPEN-group — 6.2 %, NB-group — 5.0 %). However, the frequency of combined fractures (vertebral and non-vertebral) in OPEN- and NB-group did not differ significantly (Fig. 2).

It was found that frequency of osteoporosis (46.6 %) was significantly higher among patients with vertebral fractures compared to females with normal BMD ($p = 0.02$). Additionally, 53.4 % of women with vertebral fractures had normal BMD (17.8 %) or osteopenic syndrome (35.6 %).

Moreover, patients with osteoporosis accounted for about a quarter (25.5 %) of 141 women with non-vertebral fractures (OPEN-group — 39.0 %, NB-group — 35.5 %). The number of females with osteoporosis who had combine (vertebral and non-vertebral) fractures was 41.0 % and was not significantly different from rates of patients with osteopenia (31.0 %) and normal BMD (28.0 %) (Fig. 3).

Furthermore, we have studied the fractures distribution in postmenopausal women depending on TBS. Our study revealed that despite the lowest TBS (Q1), only 50.8 % of vertebral, 43.7 % of non-vertebral and 32.8 % of combined fractures occurred (Fig. 4).

The results of correlation analysis showed the significant association between the presence of any fracture and age ($R = 0.21$), BMD ($R = -0.28$) and TBS ($R = -0.26$). We also found the significant correlation between TBS and age (highest in NB-group: OP-group — $-0.26$ ($p < 0.05$); OPEN-group — $-0.33$ ($p < 0.05$); NB-group — $-0.43$ ($p < 0.05$)), presence of fractures (highest in OPEN-group: OP-group — $-0.23$ ($p < 0.05$); OPEN-group — $-0.32$ ($p < 0.05$); NB-group — $-0.16$ ($p < 0.05$)), and bone mineral density (only in OPEN-group: 0.23 ($p < 0.05$)).

**Discussion**

It is well known that systemic osteoporosis is an important skeletal disease characterized by low bone mass and microarchitectural deterioration of bone with increased bone fragility and risk of fractures [1, 3, 5]. Low-trauma fractures are the significant complications of systemic osteoporosis, which lead to reduced quality of life, an increase of morbidity, disability and mortality. The frequency of vertebral and non-vertebral fractures (hip, proximal humerus, distal
forearm, etc.) progressively increases in males and females with age, however, it has sex and national features.

Nowadays, the DXA with BMD is gold standard for osteoporosis diagnosis in the absence of detected low-trauma fractures [3]. BMD is one of the main factors that determine bone strength and fracture risk [11], however, there is a significant overlap of BMD indexes among people with and without fractures [12]. There are many other factors that have influence on bone strength and fracture risk, such as macro- and microarchitecture of the bone, presence of microdamages, mineralization of bone matrix and remodeling speed [13, 14]. In recent years, new methods to assess bone microarchitecture were developed. Among non-invasive methods, which significantly improve imaging techniques, there are quantitative (peripheral) computed tomography and magnetic resonance imaging, which allow the direct measurement of bone microarchitecture [5]. However, both methods are impractical for routine screening and monitoring of treatment [15].

According to DXA, the main quantitative characteristic of bone is BMD, the main qualitative parameter — trabecular bone score. It is known that both indices are decreasing with age, worsening the state of bone [12, 16–19]. It depends on the mean thickness and volume fraction of trabecular bone microarchitecture. Significant correlations between TBS and 3D-parameters of bone microarchitecture in corpses were found earlier. The largest correlation was between TBS and the density of connections that explained 67.2 % of variance. Higher TBS reflected better bone strength characteristics, while lower values showed weakness of bone and susceptibility to fractures [12, 19]. TBS may be determined retrospectively based on the DXA images made in advance without the need for any additional studies. Moreover, the rate can be compared to BMD as it determines bone state in the same region. A number of informative studies on simultaneous use of TBS and BMD were conducted [13, 14, 20]. It was proved that in postmenopausal women who had a history of fractures, the index is less than in individuals of corresponding age without fractures [17, 18, 20].

The aim of this study was to evaluate the frequency of osteoporotic fractures in postmenopausal women depending on BMD and TBS.

Our results show that age is the significant risk factor for all osteoporotic fractures. Frequency of low-trauma fractures (vertebral, non-vertebral and combined) progressively increased from 22.2 % in women aged 45–59 years to 35.8 % in patients aged 75–89 years.

In addition, it was found that osteoporotic fractures are present in all examined groups of women with different BMD: osteoporosis — 45.5 %, osteopenia — 26.9 % and normal bone — 18.1 %. Moreover, the frequency of non-vertebral fractures was not significantly different in women with osteoporosis (11.7 %), osteopenia (11.0 %) and normal BMD (9.8 %). Significant differences ($\chi^2 = 95.66$, $p < 0.0001$) were observed due to vertebral (OP-group — 20.5 %, OPEN-group — 9.6 %, NB-group — 4.3 %) and combined fractures (OP-group — 13.3 %, OPEN-group — 6.2 %, NB-group — 5.0 %).

Among patients with vertebral fractures, number of persons with osteoporosis (46.6 %) was significantly higher compared to those with normal BMD (p = 0.02). Additionally, 53.4 % of women with vertebral fractures had normal BMD (17.8 %) or osteopenic syndrome (35.6 %).

It was found that patients with osteoporosis accounted for about a quarter (25.5 %) among women with non-vertebral fractures (OPEN-group — 39.0 %, NB-group — 35.5 %). Moreover, the proportion of patients with osteoporosis who had combine (vertebral and non-vertebral) fractures was 41.0 % and was not significantly different from rates of patients with osteopenia (31.0 %) and normal BMD (28.0 %).

Current literature data confirmed the significantly lower spine TBS and BMD in women aged 50 years or older with major osteoporotic, spine and hip fractures (all $p < 0.0001$). Spine TBS and BMD predicted fractures equally well, and the combination was reliable superior to either measurement alone. Spine TBS predicts osteoporotic fractures and provides information that is independent of spine and hip BMD. Combining TBS with BMD incrementally improved fracture prediction in postmenopausal women. Multiple linear regression and logistic regression (lowest vs highest tertile) was used to define the sensitivity of TBS to other risk factors associated with osteoporosis. Only a small number of the TBS measurement (7–11 %) could be explained by BMD. In multiple linear regression and logistic regression models, reduced lumbar spine TBS was associated with recent major fracture, rheumatoid arthritis, chronic obstructive pulmonary disease, high alcohol intake, and higher body mass index [17].

Our assessment of fracture types (vertebral, non-vertebral or combined) in women depending on TBS showed that despite the lowest TBS (QI), only 50.8 % of vertebral, 43.7 % of non-vertebral and 32.8 % of combined fractures occurred. We also found the significant correlation between TBS and age (highest in NB-group), presence of fractures (highest in OPEN-group) and bone mineral density (only in OPEN-group).
Conclusions

Our study confirmed an increase of low-trauma fractures in postmenopausal women with age and showed the highest frequency of osteoporotic fractures in patients with osteoporosis (45.5%). The proportion of patients with osteoporosis among females with non-vertebral fractures was 25.5%. Moreover, 50.8% of vertebral, 43.7% of non-vertebral and 32.8% of combined fractures occur on a background of poor quality of trabecular bone. The presence of low-trauma fractures is partly associated with age, bone mineral density and trabecular bone score. However, there are other significant factors influencing the risk of fractures. The future studies on BMD and TBS measurement together with other risk factors are needed.

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References

Частота локалізації остеопоротичних переломів залежно від віку, 
мінеральної плотності та якості кісткової тканини в Українських жінок у постменопаузальному періоді

Резюме. Актуальность. Низкотравматичні переломи є важливими осложнениями системного остеопороза, которые приводят к снижению качества жизни, увечению заболеваемости, инвалидности и смертности. В настоящее время минеральная плотность костной ткани (МПКТ) и гребковый костный индекс (ТКИ) являются основными параметрами прогноза повреждений. Они широко используются при диагностики остеопороза. Целью исследования было изучение частоты и локализации различных остеопоротических переломов у женщин в постменопаузальном периоде в зависимости от возраста, МПКТ и ТКИ. Материалы и методы. Проведено однооментное исследование и проанализировано данные 1369 женщин в постменопаузальном периоде (возраст 45–89 лет). Пациентки были разделены на группы в зависимости от МПКТ и ТКИ. Критериями первой группировки были вертебральные и комбинированные переломы. Критериями второй группировки были вертебральные и комбинированные переломы. Третья группа состояла из лиц, у которых были только невертебральные переломы. Результаты. Установлено, что риск всех типов остеопоротических переломов у женщин достоверно увеличивается с возрастом (вертебральных переломов — в 1,97–4,26 раза, невертебральных — в 1,96–5,45, комбинированных — в 1,54–3,14 раза). Кроме того, мы обнаружили, что остеопоротические переломы присутствуют во всех группах женщин с различной МПКТ: при остеопорозе (45,5 %), остеопении (26,9 %) и нормальным состоянием костной ткани (18,1 %). Наиболее частота остеопоротических переломов была при остеопорозе (46,5 %), преимущественно у женщин с вертебральными и комбинированными переломами. Только у 25,5 % пациенток с невертебральными переломами наблюдается остеопороз. Низкий ТКИ отмечался у 50,8 % женщин с вертебральными, 43,7 % — невертебральными и у 32,8 % — с комбинированными (вертебральными и невертебральными) остеопоротическими переломами. Рекомендации. Остеопоротические переломы часто связаны с возрастом, МПКТ и ТКИ. Однако существуют и другие важные факторы, влияющие на риск переломов, и их сочетание требует дальнейшего изучения. Ключевые слова: остеопороз; остеопоротические переломы; минеральная плотность костной ткани; гребковый костный индекс; женщины в постменопаузальном периоде.