Bone mineral density and fragility fractures in stroke patients

V. V. Povorozniuk, A. M. Bystrytska, N. V. Hryhor’eva

The aim was to study the parameters of bone mineral density (BMD) and frequency of fragility fractures in males and females with ischemic stroke depending on a side of brain’ injury and duration of post-stroke period.

Materials and methods. We examined 140 patients aged 50–80 years old, divided into 2 groups: I – subjects without any diseases influencing the bone state and II – patients after ischemic stroke. BMD indexes (BMDs) were measured using dual-energy X-ray absorptionometry method.

Results. The males with stroke had significantly lower parameters of total body, upper extremity and trunk BMDs compared to indexes of the control group without any differences in lower extremities BMDs in contrast to women with stroke who had lower BMDs of total body, trunk and upper/lower extremities compared to parameters of the control group. Almost all measured BMDs were significantly lower on a paretic side compared to BMDs on a non-paretic side, except distal radius and total lower extremities BMDs in men with stroke in contrast to women who demonstrated significantly lower femoral neck and total femur BMDs compared to the control group. Most BMDs were decreased in females with post-stroke period duration of more than 1 year in contrast to data in men who did not show any BMD differences, except significantly decreased BMD of upper extremities compared to the control group. Fragility fractures were revealed in 21.4 % of patients after stroke (31.8 % in women and 10.0 % in men, P < 0.05), their frequency was higher only in women compared to the control group patients.

Conclusions. BMDs in stroke patients are lower and frequency of osteoporosis is higher with some sex differences that should be taken into account in their assessment and development of rehabilitation programs for older age subjects.

Mineralna chastynist’ kistkoveoi’ tkannyi’ i nizkoenergeticheskie perelomy

V. V. Povorozniuk, M. A. Bystriits’ka, N. V. Hryhor’eva

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Materials and methods

The study was conducted at Department of Clinical Physiology and Pathology of Locomotor Apparatus with collaboration of Department of Cerebral Vascular pathology of D. F. Chebotarev Institute of Gerontology NAMS of Ukraine and was approved by Ethics Committee of the Institute (19.12.2014, protocol № 5). All patients signed informed consent for participation in the study and treatment in the Institute Clinic.

We have performed a cross-sectional case-control research design and have examined 140 patients aged 50–80 years old, who were divided into 2 groups depending on previous stroke: Group I (control) – subjects without any significant states or diseases influencing bone state and metabolism (n = 70, 30 males and 40 females) and Group II – patients with stroke (n = 70, 30 men and 40 women).

Patients of Group I were examined at the Department of Physiology and Pathology of Locomotor Apparatus for bone mineral density without being admitted to a hospital and signed an informed consent to participate in the study of osteoporosis. All patients of Group II were hospitalized to the Department of Cerebral Vascular pathology of D. F. Chebotarev Institute of Gerontology NAMS of Ukraine for rehabilitation after a stroke. These subjects were advised to participate in a study to examine osteoporosis. Patients who agreed and signed the informed consent to participate in the study were examined in the Department of Physiology and Pathology of Locomotor Apparatus of this institute.

The diagnosis of stroke was confirmed previously by neuroimaging (CT or MRI). Mean duration of post-stroke period did not differ between sex and was 1.7 ± 1.9 years in males and 1.7 ± 1.9 years in females, respectively (t = 0.02, P = 0.98). All patients had unilateral ischemic stroke. The severity of paresis was established according to NIH Stroke Scale [15]. Mild, moderate and severe degree of paresis was observed in 31.1 %, 44.8 %, 24.1 % of men, respectively. The similar data in women constituted 25.0 %, 45.0 % and 30.0 %.

All patients were standardized by age (P > 0.05 for both groups of men and women, Table 1). The parameter of height also did not differ depending on stroke presence in males and females; however, it was higher in men compared to women of both groups. Additionally, we did not find any significant differences in weight and body mass index (BMI) parameter in males and females depending on stroke presence. Characteristics of the patients are presented in Table 1.

Bone mineral density of the femoral neck, total femur, lumbar spine, radius (ultradistal, distal and total) and the total body were measured using dual-energy X-ray absorptiometry (DXA) (Prodigy, GEHC Lunar, Madison, WI, USA). Interpretation of DXA results for men and women aged 50 years and older was conducted according to the International Society for Clinical Densitometry recommendations [15] according to the lowest T-score at lumbar spine, proximal femur or femoral neck (normal bone (T-score > -1.0 SD), osteopenia (-1.0 T-score > -2.5 SD and osteoporosis (T-score ≤ -2.5 SD).

We performed the analysis in women and men separately depending on paretic and non-paretic body side and post-stroke duration. An assessment based on the duration of post-stroke periods was performed by dividing the pa-
Table 1. Characteristic of patients

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>Age, years</td>
<td>65.7 ± 6.0</td>
<td>62.2 ± 5.3</td>
<td>66.2 ± 9.2</td>
<td>66.6 ± 9.6</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.73 ± 0.06</td>
<td>1.62 ± 0.06</td>
<td>1.74 ± 0.06</td>
<td>1.61 ± 0.06</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>81.9 ± 12.7</td>
<td>78.3 ± 9.8</td>
<td>83.3 ± 13.2</td>
<td>75.8 ± 14.6</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.5 ± 4.2</td>
<td>29.9 ± 3.8</td>
<td>27.4 ± 4.3</td>
<td>29.4 ± 5.4</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD. Group I – control group, Group II – stroke patients. \( P_1 \): differences between the indices in men. \( P_2 \): differences between the indices in women.

Analysis of BMD parameters depending on paretic or non-paretic body side revealed more substantial differences in men compared to women after stroke. Almost all measured BMD indexes (Table 3) in males with stroke were significantly lower at paretic side compared to BMD parameters at non-paretic side of body, except distal radius and total lower extremities BMDs. Nevertheless, in females with stroke, only femoral neck and total femur BMD indexes were significantly decreased in comparison with similar BMD parameters in the control group.

Assessment of BMD differences in upper/lower extremities in men depending on side of brain injury showed that differences in paretic upper extremity and control were equal to 11.7 % (0.911 ± 0.149 versus 1.032 ± 0.11 g/cm², \( t = 4.5, P < 0.001 \), respectively), in non-paretic one – 6.7 % (0.974 ± 0.121 versus 1.045 ± 0.118 g/cm², \( t = 2.8, P < 0.05 \), respectively). The same differences in the lower extremities were less pronounced accounting for 4 % at paretic ones (1.359 ± 0.176 versus 1.453 ± 0.112 g/cm², \( t = 2.0, P < 0.05 \), respectively) not significantly different from non-paretic lower extremity.

The similar indexes in women were more expressed in the lower extremities and represented for these fourth specified parameters 9.8 % (∆0.771 ± 0.129 versus 0.356 ± 0.116 g/cm², \( t = 3.4, P < 0.001 \), respectively), 8.8 % (∆0.783 ± 0.134 versus 0.859 ± 0.141 g/cm², \( t = 2.7, P < 0.05 \), respectively), 11.4 % (∆1.122 ± 0.182 versus 1.267 ± 0.122 g/cm², \( t = 4.8, P < 0.001 \), respectively) and 10 % (∆1.130 ± 0.152 versus 1.264 ± 0.111 g/cm², \( t = 5.1, P < 0.001 \), respectively).

The ANOVA-analysis revealed the influence of post-stroke duration on all BMD indexes in females with stroke (lumbar spine: \( F = 5.88, P = 0.002 \); femoral neck: \( F = 6.98, P = 0.0008 \); total femur: \( F = 3.78, P = 0.02 \); upper extremities: \( F = 8.05, P = 0.0003 \); lower extremities: \( F = 3.70, P = 0.02 \); and total body BMDs: \( F = 4.44, P = 0.009 \)). The assessment using Scheffe test did not show any significant differences between first two groups (duration of post-stroke period less than 6 months and 6 months-1 year) for all BMD indexes measured. However, the lumbar spine, femoral neck and upper extremities (Fig. 1A) BMDs in women of the 3rd and 4th groups were significantly lower compared to similar indexes of the 2nd group, whereas BMD parameters in total femur, total body and lower extremities (Fig. 1B) were significantly decreased only in females of the 4th group in comparison with same indexes of the 2nd group.

Fragility fractures were revealed in 14 patients with stroke (20.0 %, 11 females (37.5 % from the all women) and 3 males (10 % from the all men)). Four women with stroke (36.4 % from all fractures in the females) had hip fractures (mean post-stroke duration was 4.3 ± 4.0 years, two of them had moderate paresis and other individuals – severe one), two women (18.2 %, respectively) had vertebral fractures...
(mean post-stroke duration was 3.0 ± 1.4 years, one of them had moderate and the other had severe paresis). The other 5 females with stroke had low-energy distal radius fractures (41 % of all fractures in women, respectively). In the control group, 9 women (13.6 %) had low-energy fracture (four of them had distal forearm fracture, two women had vertebral fractures and three females had other non-vertebral fractures).

Four men with stroke (10 %) had low-energy fractures (three of them had distal radius fractures (75 %) and one had other non-vertebral fracture (25 %)). In the control group men, three had non-vertebral fractures (5 % from all males).

Table 2. Bone mineral density indices in patients depending on stroke presence

<table>
<thead>
<tr>
<th>Index, units</th>
<th>Group I</th>
<th>Group II</th>
<th>( P_1 )</th>
<th>( P_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( L_1-L_4 ) BMD, g/cm²</td>
<td>1.30 ± 0.11</td>
<td>1.19 ± 0.19</td>
<td>1.25 ± 0.21</td>
<td>1.06 ± 0.17</td>
</tr>
<tr>
<td>( L_1-L_4 ) T-score, SD</td>
<td>0.7 ± 0.9</td>
<td>0.1 ± 1.6</td>
<td>0.3 ± 1.8</td>
<td>-1.0 ± 1.4</td>
</tr>
<tr>
<td>( L_1-L_4 ) Z-score, SD</td>
<td>1.0 ± 0.9</td>
<td>1.2 ± 1.5</td>
<td>0.8 ± 1.7</td>
<td>0.1 ± 1.2</td>
</tr>
<tr>
<td>Femoral neck: BMD, g/cm²</td>
<td>0.99 ± 0.04</td>
<td>0.99 ± 0.10</td>
<td>0.97 ± 0.17</td>
<td>0.85 ± 0.13</td>
</tr>
<tr>
<td>Femoral neck: T-score, SD</td>
<td>-0.6 ± 0.3</td>
<td>-0.3 ± 0.7</td>
<td>-0.8 ± 1.3</td>
<td>-1.4 ± 0.9</td>
</tr>
<tr>
<td>Femoral neck: Z-score, SD</td>
<td>0.4 ± 0.4</td>
<td>0.9 ± 0.7</td>
<td>0.2 ± 1.2</td>
<td>-0.1 ± 0.7</td>
</tr>
<tr>
<td>Distal radius: BMD, g/cm²</td>
<td>0.9 ± ± 0.7</td>
<td>0.9 ± 0.12</td>
<td>0.9 ± 0.10</td>
<td>0.72 ± 0.13</td>
</tr>
<tr>
<td>Distal radius: T-score, SD</td>
<td>-1.1 ± 0.8</td>
<td>-0.8 ± 1.4</td>
<td>-0.5 ± 1.0</td>
<td>-1.9 ± 1.4</td>
</tr>
<tr>
<td>Distal radius: Z-score, SD</td>
<td>0.6 ± 0.8</td>
<td>0.6 ± 1.3</td>
<td>0.2 ± 1.0</td>
<td>-0.3 ± 1.0</td>
</tr>
<tr>
<td>Total body: BMD, g/cm²</td>
<td>1.27 ± 0.07</td>
<td>1.17 ± 0.09</td>
<td>1.22 ± 0.12</td>
<td>1.06 ± 0.11</td>
</tr>
<tr>
<td>Total body: T-score, SD</td>
<td>0.6 ± 0.8</td>
<td>0.5 ± 1.1</td>
<td>0.1 ± 1.5</td>
<td>-0.8 ± 1.3</td>
</tr>
<tr>
<td>Total body: Z-score, SD</td>
<td>0.8 ± 1.0</td>
<td>1.2 ± 1.0</td>
<td>0.3 ± 1.3</td>
<td>-0.1 ± 1.0</td>
</tr>
</tbody>
</table>

Table 3. Differences in bone mineral density indices between paretic and non-paretic side of body in males and females with stroke, g/cm²

<table>
<thead>
<tr>
<th>Index</th>
<th>Males</th>
<th></th>
<th></th>
<th>Females</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M ± SD</td>
<td>t</td>
<td>P</td>
<td>M ± SD</td>
<td>t</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>0.05 ± 0.07</td>
<td>4.02</td>
<td>&lt; 0.001</td>
<td>0.03 ± 0.05</td>
<td>3.84</td>
</tr>
<tr>
<td>Ward’s triangle</td>
<td>0.06 ± 0.13</td>
<td>2.49</td>
<td>0.02</td>
<td>0.01 ± 0.07</td>
<td>0.50</td>
</tr>
<tr>
<td>Trochanter</td>
<td>0.06 ± 0.11</td>
<td>3.45</td>
<td>0.001</td>
<td>0.01 ± 0.05</td>
<td>1.33</td>
</tr>
<tr>
<td>Total femur</td>
<td>0.05 ± 0.07</td>
<td>4.38</td>
<td>0.0001</td>
<td>0.02 ± 0.05</td>
<td>2.37</td>
</tr>
<tr>
<td>Upper extremities</td>
<td>0.06 ± 0.13</td>
<td>3.04</td>
<td>0.004</td>
<td>0.01 ± 0.09</td>
<td>0.53</td>
</tr>
<tr>
<td>Lower extremities</td>
<td>0.02 ± 0.08</td>
<td>1.84</td>
<td>0.07</td>
<td>0.00 ± 0.06</td>
<td>0.28</td>
</tr>
<tr>
<td>Ultradistal radius</td>
<td>0.05 ± 0.07</td>
<td>3.03</td>
<td>0.007</td>
<td>0.02 ± 0.04</td>
<td>1.71</td>
</tr>
<tr>
<td>Distal radius</td>
<td>0.04 ± 0.08</td>
<td>1.87</td>
<td>0.08</td>
<td>0.01 ± 0.06</td>
<td>0.63</td>
</tr>
<tr>
<td>Total radius</td>
<td>0.03 ± 0.07</td>
<td>2.20</td>
<td>0.04</td>
<td>0.02 ± 0.05</td>
<td>1.72</td>
</tr>
<tr>
<td>Total body</td>
<td>0.02 ± 0.05</td>
<td>2.62</td>
<td>0.01</td>
<td>0.01 ± 0.05</td>
<td>1.76</td>
</tr>
</tbody>
</table>

Fig. 1. Bone mineral density of upper (A) and lower (B) extremities in women depending on the stroke duration.
1: duration of post-stroke period less than 6 months; 2: form 6 months to 1 year; 3: from 1 to 2 years; 4: post-stroke period more than 2 years; *: \( P < 0.05 \) compared to Group 2.

Men and women with stroke and low-energy fractures did not differ significantly by age (in males and females, 66.9 ± 7.3 vs 64.7 ± 7.3 years, \( t = 0.54, P = 0.05 \), respectively), duration of post-stroke period (1.69 ± 2.3 and 1.7 ± 1.7, \( t = 1.6, P > 0.05 \) and severity of paresis (2.0 ± 0.78 and 2.1 ± 0.65, Mann–Whitney U Test = 1.05, \( P > 0.05 \)). However, comparative analysis demonstrated that frequency of fragility fractures was higher in women with stroke compared to the control group patients (\( P < 0.05 \)) without significant difference in men. Furthermore, the frequency of low-energy fractures in males with stroke was significantly lower compared to similar parameters in females (\( P < 0.01 \)).
Discussion

Stroke and systemic osteoporosis, which are associated with a high risk of disability, are both crucial age-related diseases with own prevalence, risk factors and clinical features [1,3,7]. Sex is one of the common risk factor for both pathologies [5,6]. Since the mid 1990s, various cross-sectional and longitudinal studies have been performed in patients after stroke. These studies have confirmed that osteoporosis and its complication (low-trauma fractures) are major challenges for these patients, significant bone loss is detected mainly on the paretic side, depends on the severity of functional deficits, post-stroke duration etc. and more evident in the upper extremities. However, all these studies were performed in various European, American and Asian populations therefore may have some ethnic differences, but studies among the Ukrainian population have not yet been conducted.

Our study is the first one in Ukraine aimed at identifying the features of BMDs and frequency of fragility fractures in a Ukrainian cohort with stroke depending on the side of brain injury and duration of post-stroke period. Our previous studies focused on some particularities of risk factors in stroke patients [17,18], however, they analyzed the parameters of body composition, and did not studied the frequency of osteoporotic fractures.

This research has demonstrated that all measured BMD parameters (lumbar spine, femoral neck, total hip, radius and total body) in women with stroke were significantly lower compared to similar indexes in the control group in contrast to men with stroke who had only significant lower only distal radius and total body BMDs in comparison with the control group confirming sex differences in bone loss in stroke patients and coinciding with the results of other authors [7,9].

Furthermore, the assessment of peripheral body BMD indexes in men with stroke has shown that parameters of upper extremity and particularly in radius were significantly lower than similar indexes in the control group. In addition, males with stroke had significantly lower parameters of trunk, total hip BMD and total body BMDs compared to control indexes without any significant differences in lower extremities BMDs. In contrast, stroke women had lower BMD indexes in trunk and upper / lower extremities in comparison with control parameters.

According to the existing literature data, more pronounced process of bone loss in patients with stroke is present on the paretic side [10]. In stroke patients, BMD rapidly decreased in the paretic upper limb, whereas in the nonparetic one could be increased due to more widely habitual use of it. In addition, BMD of the paretic lower limb could be decreased up to 10 % within 1 year while a relatively smaller decrease was typical for the nonparetic limb [10].

Analysis of BMD parameters depending on paretic and non-paretic body side in our patients with stroke has revealed more substantial differences in men compared to women after stroke. Almost all measured BMD indexes were significantly lower on the paretic side compared to BMD parameters on the non-paretic side of body, except distal radius and total lower extremities BMD. In contrast, in women with stroke, only femoral neck and total femur BMD indexes were significantly lower than similar ones in the control group.

Additionally, we have confirmed more pronounced bone loss in the upper extremities compared to the lower ones in men (11.7 % and 4.0 % in paretic side, respectively), which is consistent with the results of other authors without any differences in the rate of bone loss depending on upper/lower limbs in women that require further longitudinal studies to assess gender features of osteoporosis development.

According to some literature data, the length of the post-stroke period is another important factor for bone loss [1,7]. Bone loss starts immediately following brain injury and progressively increases during 3–4 months. Then bone loss progresses slowly until the end of the first year after stroke. After that, the rate of bone loss decreases and reaches some stable condition of permanent bone loss with subsequent high risk of fractures.

Furthermore, our research has demonstrated that most BMD indexes were decreased in females with post-stroke period duration of 1 year and more (L₁₋₃, femoral neck, total femur, total body and upper/lower extremities and trunk) in contrast to the data in men who did not show any significant differences in BMD indexes, except the upper extremities BMDs, which were significantly lower compared to the control group.

Fragility fractures are the dangerous complication of systemic osteoporosis. The risk of osteoporotic fracture increases with post-stroke duration, age of patients (old age), female sex, stroke severity, a positive history of previous fractures or falls, preexisting osteoporosis and concomitant diseases (rheumatoid arthritis, hyperparathyroidism, etc.) [11,13,19]. Despite the prevalent bone loss in the upper extremities in patients with stroke, literature review has demonstrated that hip fracture is the most common osteoporotic fracture [12,13,19].

The retrospective analysis of Swedish register [13] that analyzed the data of patients from 1987 to 1996 years (273 000 individuals were hospitalized with stroke) showed that the risks of low-trauma fractures were higher in women than in men. This risk decreased with the age of the patient and time since stroke; however it was always higher than age- and sex-matched controls, except for patients over the age of 80 years. The relative risk of any osteoporotic fracture requiring hospitalization immediately with stroke was 3.72 in women aged 50 to 54 years, and the risk for hip fracture was 11.75.

Analysis of Ontario Stroke Registry (23751 patients were hospitalized with stroke in 2003–2012) [13] also showed that 2-years risk for any low-trauma fracture was lower (HR = 1.32, 95 % CI 1.19–1.46), than for hip fracture (HR = 1.57, 95 % CI 1.35–1.83). In addition, females had greater risk of low-trauma fracture than males (HR = 1.72, 95 % CI 1.53–1.94).

Given the wide range of osteoporotic fracture incidence in patients with stroke (from 7 per 1000 person-years in Dennis’ et al. study [20] to 32 per 1000 person-years in Andersson’ et al. study [19], it is essential to analyze rate of low-energy osteoporotic fractures in the Ukrainian cohort.

Our study has found that that frequency of osteoporotic fractures in the Ukrainian population was higher in women with stroke compared to patients of the control group (P < 0.05) without significant difference in men. Furthermore, the frequency of low-energy fractures was
significantly lower in males compared to similar parameters in females with stroke. Fragility fractures were revealed in 20.0 % of patients with stroke (37.5 % of all the women and 10 % of all the men). Hip fracture was about 36.4 % of all fractures in women. Among females, 18.2 % of all fractures were vertebral fractures and 45.4 % -- distal radius fractures. These fractures are the main osteoporotic complications which have great negative consequences on the quality of life and average mortality even in patients without stroke.

The limitations of our study are cross-sectional design and sample size that did not allow determining the effect of some other stroke-related parameters on bone tissue state. Further large-scale longitudinal studies in men and women are required to find the association between the rate of bone loss, frequency of osteoporotic fractures to better define the bone-preserving strategy for patients with stroke.

Conclusions

1. The parameters of BMD in the lumbar spine, femoral neck, total hip, radius and total body in stroke women are significantly lower compared to similar indexes in the control group in contrast to stroke men who only have significantly lower parameters of the distal radius and total body BMDs in comparison with the control group.

2. The stroke males have significantly lower parameters of the upper extremity and trunk BMDs compared to indexes in the control group without any significant differences in the lower extremities BMDs in contrast to stroke women who have lower BMD indexes in the trunk and upper/lower extremities in comparison with these parameters in the control group.

3. Almost all measured BMD indexes are significantly lower on the paretic side compared to BMD parameters on the non-paretic side of body, except the distal radius and total lower extremities BMDs in stroke men, in contrast to women who only demonstrate significantly lower parameters of the femoral neck and total femur BMDs compared to the control group.

4. Most of the BMD indexes were decreased in females with post-stroke duration of 1 year and more in contrast to the data in men who did not show any significant differences in the BMD indexes, except significantly lower upper extremities BMDs.

5. The frequency of fragility fractures in stroke patients is 21.4 % (31.8 % in women and 10 % in men, P < 0.05); it is higher only in women compared to patients of the control group without any differences in males.

Prospects for further research. Further cross-sectional and longitudinal researches devoted to the study of sex-specific bone loss and other risk factors of fragility fractures will allow developing more sophisticated individual approaches to the rehabilitation of stroke patients with concomitant disturbances of bone mineral state.

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Conflicts of interest: authors have no conflict of interest to declare.

References


