INTRODUCTION: Osteoporosis is defined as a quantitative and qualitative deterioration of bone tissue leading to increased risk of fracture. In women, loss of mineral bone density is connected to menopause.

AIM: To establish effect of menopause onset and duration to the level of mineral bone density.

MATERIAL AND METHODS: Prospective study encompassed 130 postmenopausal women referred for osteodensitometric test at the Special hospital for rheumatic diseases in Novi Sad. Test results were interpreted according to valid definition of osteoporosis. All patients were asked about the onset of their menopause and accordingly the menopause duration was calculated for the moment of mineral bone density test. In order to establish connection between mineral bone density and onset of menopause, as well as menopause duration, Pearson’s correlation coefficient has been used.

RESULTS: Average age of patients was 63.92±8.12 years. Patient’s age at the time of menopause onset was 48.69±4.86 years, and duration of menopause at the time of BMD test was 15.12±7.93 years. Average value for spinal and hip T score was -1.99±1.58 and -1.54±1.45, respectively. There is statistically significant connection of mineral bone density to the onset of menopause and its duration, at the p <0.01 level.

CONCLUSION: Menopause is a significant risk factor for development of decreased mineral bone density and it would be crucial to refer all postmenopausal women to osteodensitometric test of bone mineral density in order to prevent osteoporotic fractures by timely diagnosis and treatment.
estrogen on bone health is decreasing after menopause onset. Progressive changes in the bone structure lead to pathological fractures and cause increased morbidity and mortality among menopausal women (5).

In accordance to recommendation by World Health Organization (WHO) we used method of dual energy X-ray absorptiometry for Caucasian, postmenopausal women. When measuring bone mineral density, a bone quantity is assessed at the lumbar spine and the hip. Obtained values of bone mineral density (BMD) are compared to those of a healthy adult, age 20-40, and expressed as a T score in standard deviations (SD) (6).

**AIM**

To establish effect of menopause onset and duration to the level of mineral bone density.

**MATERIAL AND METHODS**

Prospective study encompassed 130 postmenopausal women referred for osteodensitometric test at the Special hospital for rheumatic diseases in Novi Sad. All patients were subjected to measurements of mineral bone density at the lumbar spine (L1-L4) and at the hip, using osteodensitometer type Lunar, and values were expressed as absolute values (g/cm²), and as a T score. T score values were analyzed according to valid definition of osteoporosis, so that values ≤ -2,5 SD correspond to osteoporosis, between -2,5 and -1 SD correspond to osteopenia, and >-1 SD is a normal result. All patients were asked identical questions about the onset of their menopause and accordingly the menopause duration in years was calculated for the moment of mineral bone density test. Premenopausal patients and those with comorbidity or a risk factor that may trigger lowered bone mineral density were excluded from the study. In the statistical analysis, arithmetic mean was used as a measure of central tendency, and standard deviation as a measure of the variability. In order to determine the relation between two continuous variables, the Pearson correlation coefficient was used.

**RESULTS**

The sample encompassed 130 healthy postmenopausal women, with average age of 63.92±8.12 years. Distribution of patient’s age is shown in Table 1.

**Table 1. Age of patients**

<table>
<thead>
<tr>
<th>Intervals of age</th>
<th>Frequency (f)</th>
<th>Percentage (%)</th>
<th>Min</th>
<th>Max</th>
<th>X</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>44 - 55</td>
<td>19</td>
<td>14.6</td>
<td></td>
<td></td>
<td>44</td>
<td>85</td>
</tr>
<tr>
<td>56 - 65</td>
<td>59</td>
<td>45.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>66 -75</td>
<td>41</td>
<td>31.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>76 - 85</td>
<td>11</td>
<td>8.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (Σ)</td>
<td>130</td>
<td>100.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Average age of menopause onset was 48.69±4.86 years, and its average duration was 15.12±7.93 years, as shown in Table 2.

**Table 2. Onset and duration of menopause**

<table>
<thead>
<tr>
<th>MENOPAUSE</th>
<th>Min</th>
<th>Max</th>
<th>X</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of menopause</td>
<td>30</td>
<td>56</td>
<td>48.69</td>
<td>4.86</td>
</tr>
<tr>
<td>Duration of menopause</td>
<td>1</td>
<td>39</td>
<td>15.12</td>
<td>7.93</td>
</tr>
</tbody>
</table>

Average T score value at the lumbar spine and at the hip was -1.99±1.58 and -1.54±1.45 respectively, as shown in Table 3.

**Table 3. T score of lumbar spine and hip**

<table>
<thead>
<tr>
<th>T score</th>
<th>Min</th>
<th>Max</th>
<th>X</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>T score of spine</td>
<td>-5,30</td>
<td>2,20</td>
<td>-1,99</td>
<td>1,58</td>
</tr>
<tr>
<td>T score of hip</td>
<td>-4,70</td>
<td>3,10</td>
<td>-1,54</td>
<td>1,45</td>
</tr>
</tbody>
</table>

**Table 4. BMD of lumbar spine and hip**

<table>
<thead>
<tr>
<th>BMD</th>
<th>Min</th>
<th>Max</th>
<th>X</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMD of spine</td>
<td>0,55</td>
<td>1,45</td>
<td>0,94</td>
<td>0,18</td>
</tr>
<tr>
<td>BMD of hip</td>
<td>0,43</td>
<td>1,37</td>
<td>0,91</td>
<td>0,17</td>
</tr>
</tbody>
</table>

**Table 5. Correlation between T score and duration of menopause**

<table>
<thead>
<tr>
<th>Duration of menopause</th>
<th>T score of spine</th>
<th>T score of hip</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>-0.546</td>
<td>-0.453</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>p</td>
<td>0.000</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

**Table 6. Correlation between T score and onset of menopause**

<table>
<thead>
<tr>
<th>Onset of menopause</th>
<th>T score of spine</th>
<th>T score of hip</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>0.566</td>
<td>0.475</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>p</td>
<td>0.000</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

Graph 1. Correlation between T score of lumbar spine and duration of menopause

Originalni članci/ Original articles
Duration of menopause was in statistically significant negative correlation to T score for both hip and spine. This correlation was of medium intensity. Hence, the longer a woman is in menopause, the lower T score she has. (Graph 1; Graph 2).

There was a statistically significant positive correlation between the menopause onset and the T score. This correlation was of medium intensity. Hence, the earlier a woman enters menopause, the lower T score she has. (Graph 3; Graph 4).

**DISCUSSION**

According to the definition, osteoporosis is a skeletal disease characterized by altered bone density causing increased risk of fracture. WHO experts believe that clinical risk factors for osteoporotic fracture are sometimes more significant than osteodensitometric results for bone mineral density and that they should be actively sought after, especially in postmenopausal women who are a target group for early osteoporosis diagnose (6, 7, 8, 9).

In our study, all subjects were menopausal with menopause onset at the average age of 48.69±4.86 years and menopause duration of 15.12±7.93 years; these values have proven to be connected to the level of bone mineral density.

Recker et al. 2004 published a study where bone remodeling rates were measured by transiliac biopsy in 50 healthy women before menopause, one year after menopause and 13 years after menopause, as well as in 89 women with osteoporosis. Bone remodeling rates were almost doubled one year after menopause onset, tripled 13 years after and remained increased in women with osteoporosis, leading to conclusion that osteoporosis has the major role in bone loss (10).

Shuster et al. in 2010 had analyzed women in premature menopause, i.e. onset before 40 years of age, and early menopause, onset between 40 and 50 years of age. Both ranges were below the median age of natural menopause (age 51 years), regardless of cause of premature or early menopause. Women with lack of estrogen in years before the median age of natural menopause have increased risk for early morbidity and mortality (11).

A study by Akdeniz et al. encompassed 540 healthy postmenopausal women with average age 59.3±8.4 years. All patients were subjected to osteodensitometric test and results were correlated to height, weight, body mass index (BMI) and menopause duration in years. It was concluded that body weight and duration of menopause are major risk factors for development of osteoporosis (12).

Denir et al. in 2008 studied effect of different menopause duration on bone mineral density. Their study included 2769 postmenopausal women who did not take any preventive therapy for osteoporosis, divided into three groups, depending on duration of menopause at the time of BMD measurements. They were also divided into 4 age groups according to their age at the onset of menopause. A multinomial logistic regression has been done; 16.2% of patients had osteoporosis, 39.2% had osteopenia and 44.6% had normal BMD. Osteoporosis had been found in 10.6% of women who had menopause for 0-3 years, 16.2% of those with menopause duration of 4-7 years and 31.9% in those with menopause longer than 7 years. Osteopenia percent were unchanged between 3 intervals: 37.2% for menopause duration 0-3 years, 42.1% for 4-7 years and 40.9% for menopause longer than 7 years. 30% women with menopause onset before 40 years of age had osteoporosis. Duration of menopause at the time of BMD measurement was in positive correlation to osteoporosis and osteopenia. Age of menopause was negatively correlated only for osteoporosis (13).

In Sweden in 2012, results were presented of a prospective observation study that lasted 34 years. It included 390
women who were 48 at the onset of a study; early menopause as a risk factor for development of osteoporosis, fractures and mortality was observed. Menopause was established in accordance to the criteria of World Health Organization (WHO) as at least 12 months of continuous amenorrhea. Subjects were divided into two groups, those with early menopause (onset before 47 years of age) and with late one (after 47 years of age). Women with early menopause had risk of 1.83 (95% Cl 1.22-2.74) for osteoporosis, risk of 1.68 (95% Cl 1.05-2.57) for fractures and risk of 1.59 (95% Cl 1.04-2.36) of mortality. Based on results obtained, it was concluded that menopause onset before 47 years of age is connected to the increased risk of osteoporosis, fractures and mortality (14).

In 2012 another prospective study was published, encompassing 1245 patients of both genders who were submitted for osteodensitometric test of lumbar spine and at the hip at the Special Hospital for Rheumatic Diseases in Novi Sad, between January and July of 2011. Premenopausal women and men younger than 50 years were excluded from the study. Clinical risk factors that may be responsible for lowered bone mineral density and osteoporotic fractures were studied. The most frequent risk factor was early menopause with 28.27%, followed by previous fractures with 23.29% and family history of fractures with 13.73%. Effects of treatments by glucocorticoids, smoking, autoimmune diseases, rheumatoid arthritis, low body mass index and alcohol consumption were present in significantly lower percentage (15).

Sioka et al. in 2010 analyzed relation of osteopenia and osteoporosis in healthy postmenopausal women with age of menarche, menopause onset and fertility duration. Study included 124 healthy postmenopausal women who were subjected to osteodensitometric test. According to results obtained, there were no statistically significant differences regarding age of menarche. On the other hand, lower level of bone mineral density (BMD) was found in patients whose fertility duration does not exceed 30 years and age at menopause is less than 45 years. The study concluded that total exposure to endogenous estrogens, measured in menstruation years, is a significant protection factor regarding development of postmenopausal osteoporosis. Also, the early menopause, but not early menarche, is in correlation to lowered BMD in postmenopausal women (16).

Recent cross-sectional study, conducted in China between June 2011 and January 2012 and published in 2013, analyzed 6242 women aged between 21 and 92 years, with the aim to estimate connections between age, menarche and menopause on one side and development of cardiovascular diseases, diabetes mellitus and osteoporosis on the other. It was concluded that menarche and menopause are not connected to diabetes mellitus, and late menarche and menopause are connected to lower risk of development of cardiovascular diseases, while early onset of menopause is connected to high risk of development of osteoporosis, odds ratio 1.59 (95% Cl 1.07-2.36) (17).

CONCLUSION

There is statistically high connection between menopause onset and bone mineral density, as well as between menopause duration and bone mineral density. Therefore all menopausal women should be referred to osteodensitometric tests in order to diagnose osteoporosis early, so that timely and adequate therapy could prevent osteoporotic fractures.
Sažetak

UVOD: Osteoporoza se definiše kao kvantitativno i kvalitativno oštećenje koštanog tkiva što dovodi do povećanog rizika za nastanak preloma kosti. Kod žena je gubitak mineralne koštane gustine povezan sa menopauzom.

CILJ: Utvrditi povezanost početka i trajanja menopauze sa nivoom mineralne koštane gustine.

MATERIJAL I METOD: Prospektivna studija je obuhvatila 130 postmenopauzalnih žena kojima je u Specijalnoj bolnici za reumatske bolesti u Novom Sadu rađen osteodenzitometrijski pregled. Dobijene vrednosti su interpretirane prema važećoj definiciji osteoporoze. Takođe su sve ispitanice bile ispitivane o vremenu nastanka menopauze i prema tome je računato trajanje menopauze u trenutku merenja mineralne koštane gustine. Za utvrđivanje povezanosti mineralne koštane gustine i početka nastanka menopauze, kao i trajanja menopauze korišćen je Pearsonov koeficijent korelacije.

REZULTATI: Prosječna starosna dob ispitanica je bila 63,92±18,12 god. Starosna dob ispitivanih u vreme nastanka menopauze je bila 48,69±18,86 god, a trajanje menopauze u vreme merenja BMD je bila 15,12±7,93 god. Prosječna vrednost T skora kičme je bila -1,99±1,58, a T skor kuka -1,54±1,45. Postoji statistički značajna povezanost mineralne koštane gustine sa početkom menopauze i trajanjem menopauze na nivou p <0,01.

ZAKLJUČAK: Menopauza je značajan riziko faktor za nastanak snižene mineralne koštane gustine, te je stoga potrebno sve postmenopauzalne žene uputiti na osteodenzitometrijsko merenje mineralne koštane gustine kako bi se pravovremenom dijagnostikom i terapijom prevenirali osteoporotični prelomi.

References


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