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CONNECTION OF MENOPAUSE ONSET AND DURATION ON THE LEVEL OF MINERAL BONE DENSITY

POVEZANOST POČETKA I TRAJANJA MENOPAUZE SA NIVOOM MINERALNE KOŠTANE GUSTINE

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menopause onset, menopause duration, mineral bone density

Ključne reči
početak menopauze, trajanje menopauze, mineralna koštana gustina

Abstract

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.

INTRODUCTION

Osteoporosis is defined as a quantitative and qualitative deterioration of bone tissue leading to increased risk of fracture (1). Skeletal bone mass depends on coordinated activities of osteoblasts that form the bone, and osteoclasts that resorb it. Remodeling is important not only for keeping bone mass, but also for microdamage repair, to prevent accumulation of too much old bone and for mineral homeostasis. Osteoblasts and osteoclasts are regulated by cytokines and hormones, as well as by mechanical load (2). Beneficial effect of estrogen is to suppress osteoclastogenetic cytokine production in T cell. It is also proven that estrogen induces osteoclastic apoptosis (3). In women, rapid loss of bone density is connected to menopause onset that increases bone brittleness, which is explained by decreased efficiency of estrogen alpha receptors (4). Osteoporosis is most common in women over 50 years of age, since hormonal effect of

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/cm^2), 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*

Intervals of age	Frequency (f)	Percentage (%)	Min	Max	$\bar{X}$	SD
44 - 55	19	14,6	44	85	63,92	8,12
56 - 65	59	45,4				
66 -75	41	31,5				
76 - 85	11	8,5				
Total (Σ)	130	100,0				

Min - minimum, Max -maximum, $\bar{X}$ - arithmetic mean, SD - standard deviation

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*

MENOPAUSE	Min	Max	$\bar{X}$	SD
Onset of menopause	30	56	48,69	4,86
Duration of menopause	1	39	15,12	7,93

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*

T score	Min	Max	$\bar{X}$	SD
T score of spine	-5,30	2,20	-1,99	1,58
T score of hip	-4,70	3,10	-1,54	1,45

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

BMD	Min	Max	$\bar{X}$	SD
BMD of spine	0,55	1,45	0,94	0,18
BMD of hip	0,43	1,37	0,91	0,17

BMD- Bone Mineral Density

Average bone mineral density at the lumbar spine and at the hip was 0,94±0,18 and 0,81±0,17 respectively, as shown in Table 4

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

Duration of menopause	T score of spine	T score of hip	Statistical significance
r	-0,546	-0,453	p<0,01
p	0,000	0,000	

r – Pearson correlation coefficient, p – statistical significance

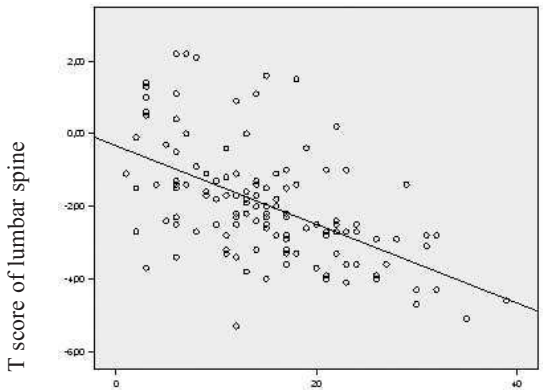
Correlation between T-score and duration of menopause is present at the statistical significance level od p <0,001 wich is 99% reliability interval, as shown in table 5.

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

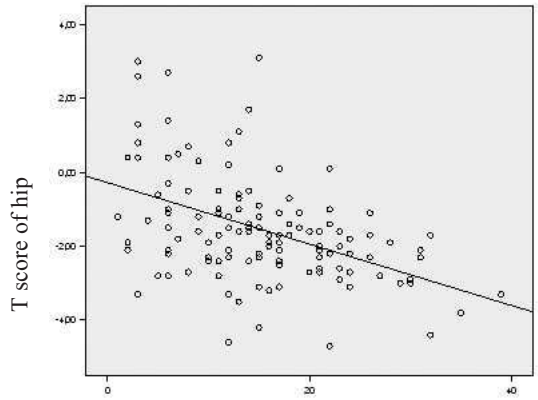
Onset of menopause	T score of spine	T score of hip	Statistical significance
r	0,566	0,475	p<0,01
p	0,000	0,000	

r – Pearson correlation coefficient, p – statistical significance

Correlation between T-score and onset of menopause is present at the statistical significance level od p <0,001 wich is 99% reliability interval, as shown in table 6.

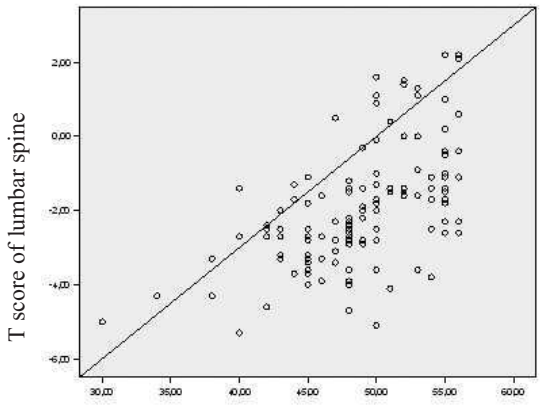


***Graph 1**. Correlation between T score of lumbar spine and duration of menopause*

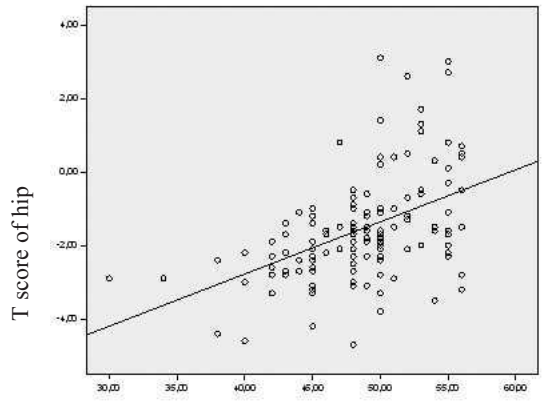


***Graph 2**. Correlation between T score of hip and duration of menopause*

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).



***Graph 3.** Correlation between T score of lumbar spine and onset of menopause*



***Graph 4**. Correlation between T score of hip and onset of menopause*

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 and vice versa. (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 percents 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 Pirsonov koeficijent korelacije.

REZULTATI:Prosečna starosna dob ispitanica je bila 63,92±8,12 god. Starosna dob ispitanica u vreme nastanka menopauze je bila 48,69±4,86 god, a trajanje menopauze u vreme merenja BMD je bila 15,12±7,93 god. Prosečna 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 uputi na osteodenzitometrijsko merenje mineralne koštane gustine kako bi se pravovremenom dijagnostikom i terapijom prevenirali osteoporotični prelomi.

REFERENCES

1. Adami S, Bertoldo F, Brandi ML, Cepollaro C, Filipponi P, Fiore E et al. Guidelnes for the diagnosis, prevention and treatment of osteoporosis. Reumatismo 2009;61(4):260-284.
2. Lemer UH. Bone remodeling in post-menopausal osteoporosis. J.Dent Res 2006;85(7):584-95.
3. Krum SA, Brown M. Unraveling estrogen action in osteoporosis. Cel Cycle 2008;7(10):1348-52.
4. Lanyon L, Armstrong V, Ong D, Zaman G, Price J. Is estrogen receptor alpha key to controlling bones' resistance fracture?.J Endocrinol 2004;182(2):183-91.
5. Christenson ES, Jiang X, Kagan R, Schnatz P. Osteoporosis management in post-menopausal women. Minerva Ginecol 2012;64(3):181-94.
6. WHO Study Group. Assessment of fracture risk and its application to screening for postmenopusal osteoporosis. WHO Technical Report Series,No843. Geneva,World health Organisation,1994.
7. Pilipović N. Dijagnoza osteoporoze. Acta rheum Belgrad 2011,41(1):18-22.
8. Klimo A. T skor i klinički faktori rizika u nastanku osteoporotskih preloma. MD-Medical Data 2011;3(4):361-365.
9. Janković T, Zvekić-Svorcan J, Subin-Teodosijević S, Gojkov-Žigić O. Povezanost snižene koncentracije serumskog 25(OH)D vitamina u nastanku osteoporotičnih preloma. Zdravstvena zaštita 2013; 42(2): 67-71.
10. Recker R, Lappe J, Davies KM, Heaney R. Bone remodeling increases substantially in the years after menopause and remains increased in older osteoporosis patients. J Bone Miner Res 2004;19:1628-1633.
11. Shuster LT, Rhodes DJ, Gostout BS, Grossardtt BR, Rocca WA. Premature menopause or early menopause: long term health consequences. Maturitas 2010;65(2):161.
12. Akdeniz N, Akpolat V, Kale A, Erdemoglu M, Kuyumcuoglu U, Celik Y. Risk factors for postmenopausal osteoporosis; anthropometric measurements, age, age at menopause and the time elapsed after menopause onset. Ginecol Endocrinol 2009;25(2):125-9.
13. Denir B, Haberal A, Geyik P, Baskan B, Ozturkoglu E, Karaccy O, Deveci S. Identification of the risk factors for osteoporosis among postmenopausal women. Maturitas 2008;60(3): 253-256.
14. Svejme O, Ahlborg HG, Nilsson JA, Karlsson MK. Early menopuse and risk of psteoporosis, fracture and mortality: a 34-year propective observational study in 390 women. BJOG:An International Journal of Obstetrics & Gynaecology 2012;119(7):810-816.
15. Zvekic-Svorcan J, Jankovic T, Filipovic K, Subin-Teodosijevic S, Lazarevic M, Erdeljan B, Boskovic K. The importance of risk factors for occurrence of the osteoporotic fractures in patients with low bone denity. Osteoporosis International 2012;23(2):158.
16. Sioka C, Fotopoulos A, Gergiou A, Xourgia X, Papadopoulos A, Kalef-Ezra JA. Age at menarche, age at menopause and duration of fertility as risk factors for osteoporosis. Climacteris 2010;13(1):63-71.
17. Qui C, Chen H, Wen J, Zhu P, Lin F, Huang B et al. Associations between age at menarche and menopause with cardiovascular disease, diabetes, and osteoporosis in Chinese women. J Clin Endocrinol Metab 2013:98(4):1612-21.

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