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Original article ■

Bone Mineral Density in Osteoarthritis

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SUMMARY

The literature data suggest an inverse relationship between osteoarthritis (OA) and osteoporosis (OP), implying rare simultaneous existence in the same patient and the fact that OA and OP represent two extremes, i.e. two different patient populations. The data about the association of increased bone mineral density (BMD) and OA, and increased bone loss in long-lasting OA during aging are still controversial. The aim of this paper was to investigate if there was any association between OA of different sites and increased BMD, as well as to investigate the correlation between BMD on one hand, and body mass index (BMI), radiologic grade of OA and duration of postmenopausal status, on the other.

We studied 235 postmenopausal women aged 50-79 years, with 48 of them with hand OA, 28 with hip OA, 39 with knee OA, 55 with GOA, and 65 controls. The studied groups were comparable by the factors of age and duration of postmenopausal period. BMD was measured in the lumbar spine (L1-L4) on DXA densitometer "Lunar" DPX and presented in absolute values in g/cm².

In the groups with hand, hip and knee OA, significantly higher values of BMD were found compared to controls in the age subgroups of 50-59 and 60-69 years, while this difference was not significant in the age subgroup 70-79 years. In the GOA group, significantly higher values of BMD were found in all age subgroups. Between BMD and BMI, a positive corellation was found only in the control group ($p<0.01$) and GOA group ($p<0.05$). There was no correlation of radiologic OA grade and BMD in the studied groups. A negative corellation was found between the duration of postmenopause and BMD in all investigated groups ($p<0,01$).

OA of different anatomic sites is associated with increased BMD, and the association is more conspicuous in younger age groups. The main predictor of the BMD is the duration of postmenopause, with longer postmenopause associated with lower BMD.

Key words: **osteoarthritis, osteoporosis, bone mineral density**

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INTRODUCTION

Osteoarthritis (OA) and osteoporosis (OP) are highly prevalent in more advanced ages, especially in postmenopausal women. There are data in the literature about an inverse relationship between OA and OP, implying rare simultaneous occurrence in the same patient and the fact that OA and OP represent two extremes, i.e. two different patient populations (1, 2).

Clinical experience and epidemiologic data suggest rare simultaneous occurrence of OA and OP, not excluding the possiblity, however, of these diseases in the same person. The data are still controversial about the association of increased bone mineral density (BMD) with OA and about increased bone loss in long-lasting OA in the process of aging.

In the beginning of 1970s, a number of studies appeared, suggesting an inverse relationship of OA and OP based on accumulated surgical experience (absence of OA of the femoral head during the treatment of femoral neck fracture) (3). A possible explanation of rare association of these diseases lies in their pathophysiology. OA has been regarded primarily as a disease of the cartilage, but it is possible, as noted by Radin and Paul, that the primary defect occurs in the subchondral bone and not in the articulatory cartilage (4). The bone in OA is harder and poorly absorbs pressure, transmitting it to the cartilage, while the bone in OP, being softer, is a better impact buffer, sparing and protecting the cartilage from OA.

In view of the fact that patients with OA have higher BMD compared to those with OP, the question is posed whether the patients with OA have higher BMD compared to healthy individuals, too? The answer to this question is still the subject of dispute and controversy.

A part of the controversy is the consequence of study and control group selection (5, 6). Two different study designs have been used: population and patient-based studies. Moreover, BMD can be measured in a number of different places, containing varying amounts of trabecular and cortical bone, and in the last 30 years many different techniques were used to measure BMD. The development of precise measurement of axial BMD, dual-energy x-ray absorptiometry (DXA) above all, made possible the amendment of large epidemiologic studies. There are other aggravating circumstances, since numerous factors affect BMD, such as gender, age, bodily constitution, menopausal status, clinical conditions, some medicaments, diet, alcohol, smoking, physical activity. These factors are not always taken into account.

The aim of the paper was to establish whether there was an association of OA of different sites (hips, knees, hands, generalized OA) and increased BMD, and to assess the correlation between BMD on the one hand, and the duration of menopausal status, body mass index (BMI), and radiological degree of OA on the other.

EXAMINEES AND METHODS

The study was performed on 235 postmenopausal women from the Niš region, aged 50-79 years. Clinical and laboratory examinations were routinely done, as well as radiological assessment of the hands, knees, hips, and lumbosacral spine. Radiograms were classified according to the Kellgren - Lawrence (K - L) scale, with radiologists blinded to the clinical picture and BMD data during the scoring process. The first group of examinees consisted of 170 women aged 50 or more years, divided into four subgroups based on their OA site(s) (clinical symptoms and radiological signs) - those with OA of the hands, knees, hips, and generalized OA (GOA). The study enrolled the examinees with at least second stage radiological changes by the K - L scale. There were 48 women in the group with hand OA, 28 women in the group with hip OA, 39 women in the group with knee OA, and 55 women with GOA. Sixty-five women without clinical and radiological signs of OA comprised our control group. The studied group did not significantly differ by patient age, average year of menopause and duration of postmenopause. According to their age, the patients were divided into 10-year interval subgroups (50-59; 60-69; 70-79). The group aged 50-59 consisted of postmenopausal women who no longer had their menopausal bleeding. Women with chronic diseases interfering with bone metabolism were considered ineligible for the study, as well as those who had described in their history the treatment with drugs with an adverse impact on BMD (glucocorticoids, anticonvulsive agents, tyroxine, propylthiouracil).

BMD assessment was done in all examinees at the Institute for Treatment and Rehabilitation „Niška Banja“, Niš, on „Lunar“ densitometer, based on dual-energy x-ray absorptiometry (DXA). The precision and reproducibility of the machine were reported to be 1%. Anteroposterior scanning of the lumbar vertebrae L1-L4 was utilized. The data obtained were processed with Lunar software. Absolute values of BMD in grams per square centimeter (g/cm^2) for lumbar vertebrae at the level of L1-L4 were obtained. BMI was calculated as the ratio of weight in kilograms and height in meters squared (kg/m^2). Normal body weight implied BMI between 18 and 25 kg/m^2. Those with BMI over 25 and below 30 were regarded as being overweight or preobese, and if BMI was over 30, these individuals were regarded as being obese.

The EXCEL program (Microsoft) was used for statistical data processing. The results were presented as means ± standard deviation. In order to evaluate the differences in BMD, Student's t-test was used. For the purpose of determining the interactions of certain variables, we used the method of correlation with Pearson's „r“ coefficient. Statistically significant were those differences with the common value of $p<0.05$.

RESULTS

Characteristics of the studied groups are presented in Table 1.

The group with hand OA, including 48 women, was similar to control group regarding patient age, mean age at menopause, and BMI. The examinees with hand OA aged 50-59 and 60-69 years had significantly higher average values of BMD compared to controls ($p<0.05$); in the age group 70-79 years with patients with hand OA, BMD was not significantly higher compared to controls of the same age without OA (Table 2).

In the group with hand OA, assessment of the correlation between BMD and BMI values could not find any correlation ($r=0.104$). Assessment of the relationship between BMD and postmenopause duration in hand OA group found a negative correlation ($r=-0.425$; $p<0.01$), meaning that reduced BMD was associated with longer postmenopausal period.

Comparison of BMD and BMI values in controls generated a positive correlation ($r=0.275$; $p<0.05$), meaning that higher BMI was associated with higher BMD. In controls, as well as in the group with hand OA, we were able to establish a highly significant negative correlation of BMD and duration of postmenopause ($r=-0.623$; $p<0.01$).

There were 28 women in the group with OA of the hip. This group was comparable to the control group regarding patient age, mean age of menopause, duration of postmenopause, and mean BMI value. In the group with hip OA we obtained the results similar to those in patients with hand OA. Patients with hip OA aged 50-59 years and 60-69 years had significantly higher average values of BMD compared to age-matched controls ($p<0.05$). In the third age subgroup of 70-79 years, patients with hip OA had higher values of BMD in the lumbar vertebrae L1-L4, but the difference was not statistically significant (Table 3).

In this group, there was no correlation between BMD and BMI. Comparing the BMD values and duration of postmenopause in the group with hip OA, a negative correlation was found ($r=-0.487$; $p<0.01$), meaning that longer menopause was associated with lower BMD.

There were 39 examinees in the group with knee OA. The group was comparable to controls by patient age, duration of postmenopause, and mean age of menopause, but different in patient BMI ($p<0.001$). In the subgroup of women with knee OA aged 50-59 years, BMD was significantly higher compared to controls ($p<0.05$). In the subgroup of patients aged 60-69 years, BMD was significantly higher, too, compared to controls ($p<0.001$). In the sugroup with the eldest women, BMD value was not significantly higher compared to controls (Table 4).

There was no correlation between BMD and BMI ($r=0.145$) in the group with knee OA. A negative value of correlation ($r=-0,433$; $p<0,01$) was found between BMD and duration of postmenopause in the group with knee OA, implying that longer postmenopause was associated with lower BMD.

There were 55 women from the region of Niš in the group with GOA, and the group was comparable to controls in view of patient age, duration of postmenopause, and mean age at menopause, but with significantly higher BMI than that in controls ($p<0.01$). In all subgroups within the GOA group, significantly higher BMD values were found compared to controls, with the statistical significance of $p<0.01$ in the youngest subgroup (50-59 years), and in the subgroups 60-69 and 70-79 years it was $p<0.001$ (Table 5).

Comparing the values of BMD and BMI in the group of examinees with GOA, we established a positive correlation ($r=0.568$; $p<0.01$), meaning that higher BMI was associated with higher BMD. Comparing the values of BMD and duration of menopause we established a negative correlation ($r=-0.449$; $p<0.01$) - longer postmenopause was associated with lower BMI.

Our analysis of the association of the degree of radiological changes by K-L scale and BMD values in all studied groups with OA of different sites (hands, hip, knee, GOA), did not find any correlation in any of the groups. In the group with hand OA the value was r=-0.2; in the group with hip OA, the value was r=-0.15; knee OA value was r=0.138; and in the group with GOA the value was r=-0.069.

Table 1. *Characteristics of studied groups*

	Age	BMI (kg/m²)	Age at menopause	Duration of postmenopause
Hand OA	59,08 ± 7,16	27,68 ± 3,23	49,92 ± 3,53	9,16 ± 7,05
Hip OA	59,96 ± 8,06	27,68 ± 2,83	48,07 ± 4,34	11,89 ± 9,14
Knee OA	63,0 ± 6,88	30,97 ± 3,77	49,56 ± 4,70	13,43 ± 8,27
GOA	64,02 ± 6,94	29,14 ± 4,42	48,87 ± 4,2	15,4 ± 7,75
Control	61,45 ± 8,42	26,68 ± 3,42	48,72 ± 3,99	12,71 ± 9,58

Table 2. *Values of BMD in the examinees with hand OA and in controls*

Age	BMD in examinees with hand OA		BMD in controls		p
	$\bar{X}$ (g/cm²)	±SD	$\bar{X}$(g/cm²)	±SD	
50-59	1,150	0,166	1,066	0,102	< 0,05
60-69	1,052	0,139	0,937	0,108	< 0,05
70-79	0,975	0,115	0,879	0,062	n.s.

Table 3. *Values of BMD in the examinees with hip OA and in controls*

Age	BMD in examinees with hip OA		BMD in controls		p
	$\bar{X}$(g/cm²)	±SD	$\bar{X}$(g/cm²)	±SD	
50-59	1,177	0,161	1,066	0,102	< 0,05
60-69	1,061	0,114	0,937	0,108	< 0,05
70-79	0,925	0,148	0,879	0,062	n.s.

Table 4. *Values of BMD in the examinees with knee OA and in controls*

Age	BMD in examinees with knee OA		BMD in controls		p
	$\bar{X}$(g/cm²)	±SD	$\bar{X}$(g/cm²)	±SD	
50-59	1,182	0,127	1,066	0,102	< 0,05
60-69	1,084	0,153	0,937	0,108	< 0,001
70-79	0,971	0,137	0,879	0,062	n.s.

Table 5. *Values of BMD in the examinees with GOA and in controls*

Age	BMD in examinees with GOA		BMD in controls		p
	$\bar{X}$(g/cm²)	±SD	$\bar{X}$(g/cm²)	±SD	
50-59	1,199	0,129	1,066	0,102	< 0,01
60-69	1,115	0,159	0,937	0,108	< 0,001
70-79	1,011	0,119	0,879	0,062	< 0,001

DISCUSSION

Our results related to OA of the hand, hip, and knee demonstrated significantly higher values of BMD of the spinal column compared to controls, except for the eldest age subgroup (70-79 years). The results agree with most of the literature data describing the association of OA of different sites with increased BMI (7-11).

Dequeker summarized in 1997 all the studies published in the previous 20 years dealing with the interaction and negative correlation between OA and OP and BMD in OA, presenting the information that 37 studies in 16 countries (with 37.774 individuals, 11.137 individuals with OA, and 26.637 controls) had been published. In 28 studies, a significant increase of

BMD had been found compared to gender-, age-, and body weight-matched controls (2).

The Rotterdam study from 1996 was the first longitudinal study investigating the association of radiologic OA of the knee (graded using the K-L scale), femoral BMD, and bone loss. The study enrolled 1.723 patients observed for two years. It was established that hip and knee OA correlated with increased BMD in both genders, and increased bone loss in individuals over 55 years of age, pointing out much larger differences in BMD in younger ages. The authors also noted a tendency of increased BMD with increased number of joints affected by OA and higher K-L scores (7).

Some more recent studies demonstrated significantly higher BMD in the axial and peripheral skeleton in patients with OA compared to controls matched for age, gender, and corrected body weight. In his epidemiologic study, Antoniades measured BMD utilizing the DXA method in 4.855 women aged 65 or more years. It was established that in the group with hip OA, BMD was higher in the proximal femur (9-10%), spine (7%), and appendicular skeleton (3-5%) compared to women without hip OA. Women with bilateral OA of the hip and knee and manifest osteophytosis had generalized higher BMD values (8). The Framingham study demonstrated on 473 women aged 63-91 years that higher BMD increased the risk of more severe radiological forms of knee OA, while those with lower BMD and more rapid bone loss had slower radiologic progression of knee OA (9). The Chingford study confirmed a significant, increased BMD basis in women with subsequent knee OA with osteophytes (10). Most of the above mentioned studies described the association of increased BMD with hip and knee OA, while OA of the hand was not extensively studied. Our results showed that in the group with hand OA the disease was associated with higher BMD values, which agreed with the results of Haugen et al. (11).

Our results demonstrated significantly higher BMD values in the studied groups with OA of the hand, hip, and knee compared to controls, although in the first and second age-subgroups (50-59; 60-69 years). In the eldest subgroups (70-79 years) higher BMD values were observed too, although without statistical significance, so that we can suppose that in the process of OA there occurs increased bone loss with aging and longer disease course, which agrees with the literature data (7). The question remains whether this loss should be attributed to reduced mobility of individuals with OA or to metabolic factors, e.g. cytokines, which can mediate in the association of OA and increased bone loss with aging. In experimental OA, it has been shown that interleukin 6 can be an important mediator in increased bone resorption. Some authors have noted that elevated BMD in OA occurs earlier in life and that the difference in BMD between individuals with and those without OA is probably present before the onset of OA (7,12,13). These remarks support the hypothesis of Radin and Paul that elevated BMD and increased toughness of the subchondral bone initiates the development of OA (4). Elevated BMD in OA is associated with high peak of the bone mass, as shown in a mother-daughter study and a study of twins (13).

Our results also demonstrated a tendency of higher BMD with a growing number of joints affected with OA. In contrast to hand, hip, and knee OA, significantly higher BMD values were found in the group with GOA compared to controls in all age subgroups (even in the eldest examinees, aged 70-79 years). The literature describes not only a positive correlation between the number of involved joints and BMD, but also a positive correlation between the severity of OA, i.e. radiologic grade of OA and BMD values (7,8,14). Our results showed that there was no correlation between the degree of radiologic changes by the K-L scale and BMD, in agreement with the MOST study results (15).

In our paper, in all groups of examinees, both those with OA process and in controls, we found a high negative correlation ($p<0.01$) between BMD and duration of postmenopause, supporting the notion that the duration of menopause is the principal predictor of BMD. Our results did not show that there was a significant positive correlation between BMI and BMD values in the group with hand, knee, and hip OA. A positive correlation between BMI and BMD was found in the group with GOA ($p<0.01$) and in control group ($p<0.05$), meaning that higher BMI was associated with higher BMD in the group with GOA and in controls. There are data in the literature about a positive correlation between BMI and BMD, although our results demonstrated that BMI is not a significant predictor of increased BMD (13).

Most of the above studies have described increased BMD in patients with OA, but the essential questions are whether this „excess of bone“ is beneficial and are the individuals with OA exposed to a lower risk of fractures. Earlier papers have described mostly the data about a diminished risk of fractures in OA (3,16). However, some more recent publications have shown that individuals with radiologic OA, although with increased BMD, are exposed to an even higher risk of vertebral and non-vertebral fractures (17).

In our paper, the groups with hand and hip OA were comparable with control group regarding their BMI. The groups with OA of the knee and with GOA had significantly higher BMI compared to controls ($p<0.001$ in knee OA group; $p<0.01$ in GOA group), supporting perhaps the thesis of obesity as the risk factor for OA of these sites, which agreed with the literature data (18).

The hypothesis that OA and OP are negatively correlated is usually supported in the literature, which can contribute to the elucidation of OA pathogenesis. It is still unknown whether increased BMD is the cause or the result of OA. Though many studies have shown OA and OP to be negatively correlated, this does not mean that the presence of OA excludes the diagnosis of OP in the same patient. Long-lasting patient monitoring within

clinical studies has shown that the association of OA and BMD is a complex one. If our objective is to effectively treat OA and OP, better understanding of the pathogenesis of both diseases and their interactions is mandatory.

CONCLUSION

Our results demonstrated that OA of different sites (hands, knees, hips, and GOA) is associated with increased BMD, with the association being more prominent in younger age groups. With aging and long-lasting disease course, there is increased bone loss in OA. Our results did not confirm the correlation between radiologic grade of OA and BMD value. BMI was not a significant predictor of BMD values. The principal predictor of BMD was the duration of postmenopausal period - longer postmenopausal periods were associated with lower BMD values. Knee OA and generalized OA were characterized by significantly higher BMI compared to controls, so that obesity represented a significant risk factor of OA of these anatomical sites. The results of this study suggested that obesity was not a factor of risk for OA of the hand and hip.

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KOŠTANA GUSTINA U OSTEOARTROZI

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Sažetak

U literaturi postoje podaci o inverznom odnosu između osteoartroze (OA) i osteoporoze (OP), što podrazumeva retku istovremenu pojavu, kao i to da OA i OP predstavljaju dva ekstrema, odnosno dve različite populacije bolesnika. Podaci o udruženosti povećane koštane gustine i OA, kao i o povećanom koštanom gubitku kod OA dugog trajanja tokom starenja još su uvek kontroverzni.

Cilj rada bio je da se utvrdi da li postoji udruženost OA različitih lokalizacija i povećane koštane gustine, kao i da se ispita korelacija između koštane gustine, sa jedne strane i trajanja postmenopauznog statusa, indeksa telesne mase (BMI) i radiološkog stepena osteoartroze, sa druge strane.

Analizirano je 235 žena u postmenopauzi starosti 50-79 godina, 48 sa OA šaka, 28 sa OA kuka, 39 sa OA kolena, 55 sa generalizovanom OA (GOA) i 65 ispitanica činilo je kontrolnu grupu. Ispitivane grupe bile su homogene po godinama starosti i trajanju postmenopauze. Koštana gustina merena je na lumbalnoj kičmi (L1-L4) korišćenjem DXA denzitometra "Lunar" DPX i izražavana u apsolutnim vrednostima g/cm². U grupama sa OA šaka, kuka i kolena dobijene su značajno veće vrednosti koštane gustine u odnosu na kontrolnu grupu u starosnim podgrupama 50-59 i 60-69 godina, dok ta razlika nije bila značajna u podgrupi starosti 70-79 godina. U grupi sa GOA dobijene su značajno veće vrednosti koštane gustine u svim starosnim podgrupama. Ispitivanjem korelacije između koštane gustine i BMI nađena je pozitivna korelacija u kontrolnoj grupi ($p<0,01$) i grupi sa GOA ($p<0,05$). U svim ispitivanim grupama nije nađena korelacija između radiološkog stepena OA i koštane gustine. Nađena je negativna korelacija između trajanja postmenopauze i koštane gustine u svim ispitivanim grupama ($p<0,01$). Osteoartroza različitih lokalizacija udružena je sa povećanom koštanom gustinom, pri čemu je ta udruženost više izražena u mlađim starosnim grupama. Glavni prediktor koštane gustine je dužina trajanja postmenopauze, pri čemu je duže trajanje postmenopauze udruženo sa manjom koštanom gustinom.

Ključne reči: **osteoartroza, osteoporoza, koštana gustina**