CHARACTERISTICS OF BONE MINERAL DENSITY AND DENSITOMETRY DATA IN PATIENTS WITH OSTEOARTHRITIS, NON-ALCOHOLIC STEATOHEPATITIS AND OBESITY

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ABSTRACT

The objective of the study was to determine the characteristics of bone mineral density in patients with osteoarthritis (OA), non-alcoholic steatohepatitis (NASH) and obesity.

Material and methods. 90 patients were examined and distributed into three groups: group 1 (n = 30) consisted of patients suffering from OA of knee joints, grade 2-3 according to Kellgren and Lawrence classification, with normal body weight (mean BMI 22.88±0.39 Kg/m²); group 2 (n = 30) – patients with OA with NASH and obesity (mean BMI 34.38±0.69 Kg/m²). The control group consisted of 30 healthy subjects of the corresponding age. The average age of patients was 62.3±5.7 years. The bone mineral density (BMD) at the level of the proximal femoral bone was evaluated on a dual-energy X-ray densitometer using the STRATOS apparatus DMS-APELEM (France) under a densitometry cabinet based on the Swedish-Ukrainian Medical Center «Angelholm», Chernivtsi, Ukraine. The diagnosis of osteoporosis

Résumé

Les caractéristiques des données de densité et de densitométrie minérale osseuse chez des patients atteints d’ostéoarthrite, combinées d’une stéatose hépatique non-alcoolique et d’obésité.

L’objectif de l’étude était de déterminer les caractéristiques de la densité minérale osseuse chez les patients souffrant d’arthrose, associées à une stéatose hépatique non-alcoolique et à l’obésité.

Matériel et méthodes. 90 patients ont été examinés et répartis en trois groupes: 1 groupe (n = 30) était composé de patients souffrant d’arthrose du genou arthrosique, grade 2-3 selon la classification de Kellgren et Lawrense avec un poids corporel normal (IMC moyen 22.88±0.39); Groupe 2 (n = 30) – patients atteints d’arthrose avec stéatose hépatique non-alcoolique et obésité (IMC moyen 34.38±0.69). Le groupe témoin était composé de 30 sujets en bonne santé de l’âge correspondant. L’âge moyen des patients était de 62,3±5,7 ans. La densité minérale osseuse au niveau

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and low BMD was done according to the criteria of
the ISCD Official Positions, 2007 (revised in 2015).
Statistical analysis was performed using SPSS Statistics
20 Multilingual.

**Results.** Osteoporosis and low BMD were found to
be significantly higher in patients with osteoarthritis
compared with those from the group with osteoarthritis,
NASH and obesity.

**Conclusions.** In patients with isolated osteoarthritis,
a significant decrease of bone mineral density was
found, especially in the intertrochanteric region of the
femur. In individuals suffering from OA, the risk of
fractures was higher than in those with concomitant
NASH and obesity. The difference was significant only
in the case of osteoporotic and femur fracture, without
considering only the case of osteoporotic and femur fracture, without considering
BMD.

**Keywords:** non-alcoholic steatohepatitis, osteopo-
rosis, mineral density of bone tissue, obesity.

**List of abbreviations:**
NAFLD = non-alcoholic fatty liver disease
NASH = non-alcoholic steatohepatitis
OA = osteoarthritis
OB = obesity
BMI = body mass index
PHP = practically healthy persons
OP = osteoporosis
BMD = bone mineral density
SD = standard deviation
DXA = dual-energy X-ray absorptiometry

**INTRODUCTION**

Osteoarthritis (OA) and osteoporosis (OP) are
common diseases of the musculoskeletal system, affect-
ing millions of people with significant comorbidity.
These are one of the most common causes of disabil-
ity in the elderly, especially in postmenopausal women.

In a recent review of male osteoporosis, Willson
et al argued that osteoporosis is a common pathol-
ogy of the musculoskeletal system, which occurs as a
result of micro-architectural deterioration of bone tis-
sue and low bone mineral density, under conditions
of an imbalance between the formation of bone tis-
sue and its resorption. Therefore, in this situation,
the significance of resorption may increase the risk
of bone fragility.

It is worth noting that non-alcoholic fatty liver
disease (NAFLD) is not an isolated disease; in recent
years, a link between NAFLD and many extrahepatic
diseases has been identified. In particular, patients
with NAFLD have a higher risk of cardiovascular dis-
ease. NAFLD is more common in diabetes mellitus.

Currently, an association between NAFLD and hor-
monal anomalies of the thyroid gland and chronic
kidney disease has been established.

The liver is the source of many proteins and is
the regulator of several metabolic pathways, includ-
ing bone metabolism; one of the most famous of
all is the pathway for the metabolism of vitamin D.
Considering the role of the liver in bone metabolism,
the relationship between NAFLD and bone anoma-
lies is not unexpected, especially due to the signifi-
cant achievements of recent times.

Since the conversion of testosterone to estradiol,
androstenediol to estrone occurs in the adipose tissue,
the activity of bone osteoblasts, which have receptors
to them, increases, and osteoblastic osteoporosis ac-
activates, then obesity may have a protective effect on
bone tissue. Some authors also pointed to the positive
effects of obesity on the bone mineral density (BMD).
Other authors argue that increased body weight
does not always have a protective effect on the de-
velopment of low BMD. Thus, in particular, a decrease
in the positive effect of body mass on bone tissue
occurs in the period of menopause, when the decrease in the secretion of sex steroids leads to stimulation of secretion and increase the activity of osteoclasts.

The T-score is an indicator that characterizes the number of standard deviations in comparison with the peak of bone mass, that is, with the mean value for the age at which the BMD in this section of the skeleton reaches a maximum. The decrease of this criterion is associated with a decrease in bone mass with age.

The Z-score is a comparison with the age norm, that is, with an average value for a given age. The comparison result is presented as the standard deviation (SD) of the relevant norm. According to World Health Organization’ recommendations, women and men aged 50 years and older use the T-score, and the age of 50 is the Z-score. The use of the T-score is also possible in women during premenopausal period. Within the limits of the norm there are values that do not exceed +2.5 SD and not less than –1 SD, but more than –2.5 SD correspond to osteopenia. Indices below –2.5 SD are defined as osteoporosis; the value of less than –2.5 SD in the presence of at least one fracture of the vertebra or low-energy fracture of the neck of the thigh is classified as a severe OP. In accordance with accepted standards, BMD is calculated with an accuracy of 0.001 g/cm², and the T-score is up to 0.1. The deviation in determining BMDs on bone densimeters (Explorer, Discovery and other similar devices) constitutes 1%. According to the recommendations of the ISSD for the diagnosis of OP, it is necessary to measure BMD in two sections of the skeleton (lumbar spine and proximal femur)⁴. When diagnosis of OP can be guided by a decrease in bone mineral density even in one of the studied sites – the segment of lumbar vertebrae (LI-LIV), femoral neck, or in all structures of the proximal femur.

**The objective of the study** was to compare the mineral density of the proximal part of femur bone according to densitometry data in patients with osteoarthritis and the comorbidity of osteoarthritis with non-alcoholic steatohepatitis on the background of obesity.

**Material and methods**

The study was carried out in the Higher State Educational Institution of Ukraine “Bukovinian State Medical University”, Ukraine, and is a fragment of the research of the Department of Internal Medicine, Clinical Pharmacology and Occupational Diseases “Features of the Comorbidity of Diseases of Internal Organs: Risk Factors, Mechanisms of Development and Interaction, Pharmacotherapy” (State registration number: 0114U002475).

90 patients were examined and distributed into three groups: group 1 (n = 30) consisted of patients suffering from OA knee joints, grade 2-3 according to Kellgren and Lawrense classification, with normal body weight (mean BMI 22.8±0.39 Kg/m²); group 2 (n = 30) – patients with OA with NASH and obesity (mean BMI 34.3±0.69 Kg/m²); the control group consisted of 30 healthy subjects of the corresponding age. The average age of patients was 62.3±5.7 years.

The diagnosis of NASH was established on the background of anamnestic, clinical, laboratory data, identification of serological markers for hepatitis B and C viruses, the results of ultrasonography according to the unified clinical protocol, approved by the Order of the Ministry of Health of Ukraine No 826 from 06.11.2014, in the presence of criteria for the exclusion of chronic diffuse liver disease of the viral, hereditary, autoimmune or drug etiology, as causes of cholestatic or cytolitic syndromes, taking into account the 10th revision of ICE. The OA diagnosis was made on the basis of the EULAR recommendations (2010) and the Order of the Ministry of Health of Ukraine No 676 dated October 12, 2006, “Clinical Protocol for the Provision of Medical Aid to Patients with Osteoarthritis” in accordance with section 13 “Rheumatology” and the Protocol of the Ministry of Health of Ukraine No 263 from section “Rheumatology” April 11, 2014. The presence of abdominal obesity in patients was established on the basis of the Order of the Ministry of Health of Ukraine No 16 dated January 14, 2013 “Methodical Recommendations for General Practitioners – Family Medicine on Counseling Patients on the Basic Principles of Healthy Eating”.

BMD was determined using dual-energy x-ray absorptiometry (DXA) on the STRATOS device DMS-APELEM (France) under the densitometry cabinet based on the Swedish-Ukrainian Medical Center “Angelholm”, Chernivtsi. The projective mineral density of the bone (g/cm²), T and Z-scores were measured. We analyzed the results of the DXA of the neck of the femur, trochanter, interfemoral space, and femur. The T-score below –1.0 standard deviation (SD) was considered as low BMD (an indicator of –1.0 to –2.5 SD testified to the presence of osteopenia, less than –2.5 SD – osteoporosis) according to the ISCD Official Position⁴. In addition, we were scheduled to establish a 10-year prediction of the risk of fracture: an osteoporotic fracture of the femur.

The protocol for the examination of patients was approved at the meeting on biomedical ethics at HSEI of Ukraine „Bukovinian State Medical University”. The document has been compiled in accordance with
The statistical processing of the research outcomes was carried out with the help of the standard applications Microsoft Excel and SPSS Statistics 20 Multilingual. The mean values (M), the arithmetic mean (t), and the validity of the differences p according to Student’s t-distribution were evaluated. The difference in indices for various periods of the study was considered probable at p <0.05. To determine the relationship between the indices, Kendall’s tau-b correlation coefficient was used.

**RESULTS AND DISCUSSION**

Among the 30 patients with OA and normal BMI, there were 8 men and 22 women. Among the men in 4, the T-score was within the normal range, and in 4 patients, according to the T-score, osteopenia was diagnosed. Among women of this group, according to the T-score, 12 patients had a normal mineral density, 8 had a diagnosis of osteopenia, 2 – OP. The BMI of this group was 22.8±0.39 Kg/m². The average age was 56.46±2.97 years.

Among 30 patients with OA, NASH and obesity, there were 10 men and 20 women. Among 10 men, in 8 of them the T-score was normal, and in 2 patients, according to the T-score, osteopenia was diagnosed. Among women of this group, according to the T-score, 14 patients have normal mineral density, 5 were diagnosed with osteopenia, 1 – OP. The BMI of this group was 34.38±0.69 Kg/m². The average age was 63.88±1.21 years.

Table 1 shows the results of a study of the state of BMD in the groups of surveyed patients. It was found that at all investigated levels, the mineral density of bone tissue was lower in persons of groups 1 and 2, compared with healthy subjects; however, not all levels of change were probable (Table 1).

|                        | Practically healthy persons (n=30) | OA with normal body weight (n = 30) | NASH + OB+ OA (n = 30) |
|------------------------|----------------------------------|----------------------------------|---------------------|
|                        | BMD, g/cm² neck of the femur      | BMD, g/cm² trochanter major      | BMD, g/cm² intertrochanteric region |
|                        | 1.030±0.020                      | 0.977±0.056                     | 1.013±0.037         |
|                        | BMD, g/cm² trochanter major       | 0.864±0.011                     | 0.751±0.031*        | 0.844±0.037         |
|                        | BMD, g/cm² intertrochanteric region | 1.241±0.018             | 1.005±0.045*        | 1.092±0.039**      |
|                        | BMD, g/cm² femur                  | 1.066±0.013                     | 0.946±0.040*        | 1.029±0.036°        |
|                        | T-score neck of the femur         | 0.01±0.0012                     | 0.10±0.0042*        | 0.45±0.0030/**      |
|                        | T-score trochanter major          | 0.13±0.02                        | -0.40±0.025*        | 0.39±0.032*        |
|                        | T-score intertrochanteric region  | -0.35±0.14                      | -1.29±0.25*         | -0.82±0.22*        |
|                        | T-score femur                     | -0.15±0.009                     | -0.88±0.027*        | -0.31±0.0147/**    |

Notes: * – the difference in rates is probable (p <0.05) with a group of practically healthy individuals. ** – the difference is probable (p <0.05) between groups 1 and 2.
intergroup difference, with a decrease in the indicators relative to the PHP group by 13% and 4%, respectively.

Assessing the T-criterion at the level of the intervertebral space, it was found that in group 1 the rates were lower by 3.69 times, and in group 2 it was 2.34 times compared with the group of PHPs, with the presence of a probability between the group difference. The T-score of the femur was significantly lower in the 1 group of comparison in 5.87 times. At other levels of the proximal femur, no reliable changes in mineral density were found.

By establishing a 10-year prediction of fracture risk (osteoporotic and femur fracture), we found the following significant differences: in patients with NASH + OB + OA the risk of osteoporotic fracture was 27% lower without considering BMD, and 2.09 times lower in femur fracture risk without considering BMD (Table 2).

The results we obtained confirmed that the risk of fractures in patients suffering from OA was higher than in those with concomitant NASH and obesity. The difference was significant only in case of osteoporotic and femur fracture without considering BMD.

The prospects for further research in this direction are the search for and study of the effectiveness of drugs that normalize the bone tissue mineral density in patients suffering from osteoarthritis with osteoporosis.

Compliance with Ethics Requirements:
“The authors declare no conflict of interest regarding this article”
“The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study”
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Osteoarthritis of the knee joint in patients aged 50-60 years is more often associated with decrease in mineral density of the bone tissue, especially in the presence of pronounced inflammatory changes (synovitis, bursitis).

In patients with isolated osteoarthritis a significant decrease of bone mineral density was found, and in the intertrochanteric region of the femur in particular. In individuals suffering from OA the risk of fractures was higher than in those with concomitant NASH and obesity. The difference was significant only in case of osteoporotic and femur fracture without considering BMD.

Conclusions
In patients with osteoarthritis, in addition to traditional X-ray studies, it is necessary to conduct a densitometric study to detect changes in the mineral density of the bones of the skeleton.
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