Archives of the Balkan Medical Union
vol. 54, no. 3, pp. 467-472
September 2019

ORIGINAL PAPER

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

Oksana S. KHUKHLINA[1], Oksana D. LIAKHOVYCH[1]✉, Ludmila V. KANIOVSKA[1], Vera O. SHUPER[1], Iryna B. HORBATIUK[1], Olha Ye. HRYNIUK[1]

[1] Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsi, Ukraine

Received 06 June 2019, Accepted 28 July 2019
https://doi.org/10.31688/ABMU.2019.54.3.10

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 Lawrense classification, with normal body weight (mean BMI 22.88±0.39 Kg/m^2); group 2 (n = 30) – patients with OA with NASH and obesity (mean BMI 34.38±0.69 Kg/m^2). 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

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

✉ Address for correspondence: Oksana D. LIAKHOVYCH
Department of Internal Medicine, Clinical Pharmacology and Occupational Diseases, Higher State Educational Establishment of Ukraine „Bukovinian State Medical University", Chernivtsi, Ukraine
Email: ksiusuk@gmail.com; Phone +380506222407

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 BMD.

Keywords: non-alcoholic steatohepatitis, osteoporosis, 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

de l'os fémoral proximal a été évaluée sur un densitomètre à rayons X à double énergie utilisant l'appareil STRATOS DMS-APELEM (France) sous un cabinet de densitométrie basé au centre médico-suédo-ukrainien «Angelholm», Chernivtsi. Le diagnostic de l'ostéoporose et de la DMO basse a été réalisé selon les critères des Positions officielles ISCD, 2007 (révisé en 2015). L'analyse statistique a été réalisée à l'aide de SPSS Statistics 20 Multilingual.

Résultats. L'ostéoporose et une faible DMO étaient significativement plus élevées chez les patients atteints d'arthrose par rapport à ceux du groupe arthrose, stéatose hépatique non alcoolique et obésité.

Conclusions. Chez les patients présentant une arthrose isolée, une diminution significative de la densité minérale osseuse, en particulier dans la région intertrochantérienne du fémur, un risque plus élevé de fracture ostéoporotique sans DMO et de fracture du fémur sans DMO sont significativement plus fréquents par rapport aux patients présentant une atteinte concomitante (stéatose hépatique non-alcoolique et obésité).

Mots-clés: stéatose hépatique non-alcoolique, ostéoporose, densité minérale du tissu osseux, obésité.

Introduction

Osteoarthritis (OA) and osteoporosis (OP) are common diseases of the musculoskeletal system, affecting millions of people with significant comorbidity[1]. These are ones of the most common causes of disability in the elderly, especially in postmenopausal women[2].

In a recent review of male osteoporosis, Willson et al[3] argued that osteoporosis is a common pathology of the musculoskeletal system, which occurs as a result of micro-architectural deterioration of bone tissue and low bone mineral density, under conditions of an imbalance between the formation of bone tissue and its resorption[3]. Therefore, in this situation, the significance of resorption may increase the risk of bone fragility[4].

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 disease. NAFLD is more common in diabetes mellitus. Currently, an association between NAFLD and hormonal anomalies of the thyroid gland and chronic kidney disease has been established[5-8].

The liver is the source of many proteins and is the regulator of several metabolic pathways, including 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 anomalies is not unexpected, especially due to the significant 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 activates, then obesity may have a protective effect on bone tissue[9]. Some authors also pointed to the positive effects of obesity on the bone mineral density (BMD)[10]. Other authors[11-13] argue that increased body weight does not always have a protective effect on the development 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, values 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/cm^2, 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)[14]. 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 22.88±0.39 Kg/m^2); group 2 (n = 30) – patients with OA with NASH and obesity (mean BMI 34.38±0.69 Kg/m^2); 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 N^o 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 cytolytic 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 N^o 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 N^o 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 N^o 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/cm^2), 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 Position[14]. 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

Table 1. Mineral density of bone tissue and evaluation of T-score in patients with osteoarthritis depending on the comorbid states.

	Practically healthy persons (n=30)	OA with normal body weight (n = 30) 1 group	NASH + OB+ OA (n = 30) 2 group
BMD, g/cm^2 neck of the femur	1.030±0.020	0.977±0.056	1.013±0.037
BMD, g/cm^2 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/cm^2 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±0.014*/**

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.

the requirements regulated by the 6th chapter of the manual CH GPC (1996) and created on the basis of its national guide "Guidelines for Clinical Research. Medicines. Approved Clinical Practice ", approved by the Order of the MOH of Ukraine No. 373 dated July 22, 2005. In drawing up the protocol, they adhered to the basic principles of the Helsinki Declaration on Biomedical Research (1974), adapted to the 41st International Assembly in Hong Kong (September 1989), as well as "Ethical Principles for Medical Research Involving Human Subjects", adopted by the 52nd Assembly of the World Medical Association (2000).The Committee on Biomedical Ethics of the HSEI of Ukraine „Bukovinian State Medical University" has not revealed any violations of moral and legal standards during the scientific research.

The statistical processing of the research outcomes was carried out with the help of the standard applications Microsoft Excellence 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/m^2. 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/m^2. 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).

In particular, the mineral density of bone tissue at the level of a trochanter minor was significantly lower in patients in group 1 by 15%, compared with the PHP group. Considering the BMD at the level of the intertrochanteric region, it was found that the data of the 1 groups were lower than the PHP group by 24%, and 2 groups by 14% with a reliable difference between the groups. Analyzing the BMD of the entire hip, it was also found to have a significant

Table 2. Assessment of the risk of fractures in patients with OA, NASH and OB (M ± m)

	OA with normal body weight (n = 30) 1 group	NASH + OB+ OA (n = 30) 2 group
Osteoporosis fracture without considering BMD%	8.76±0.35	6.90±0.46*
Osteoporosis fracture considering BMD%	7.00±0.87	6.27±0.82
Hip fracture without considering BMD%	2.17±0.22	1.04±0.17*
Hip fracture considering BMD%	1.08±0.34	0.80±0.47

*Notes: * – 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. Though low BMD was found to be a major determinant of fragility and fractures, some other factors contribute:

1. Individuals with OA tend to suffer from greater bone loss over time.
2. Bone structure and quality of the osseous tissue in the affected joints of patients with OA.
3. Higher occurrence of falling down among OA patients associated with possible postural instability, quadriceps weakness, ache in joints and stiffness (Nguyen et al showed in their works that postural instability, quadriceps weakness, and history of fall or prior fracture were significant predictors of osteoporotic fractures independent of baseline BMD)[16].

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.

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.

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"

„No funding for this study"

References

1. Palazzo C, Ravaud J-F, Papelard A, Ravaud P, Poiraudeau S. The burden of musculoskeletal conditions. *PloS One.* 2014;9(3):e90633.
2. Terracciano C, Celi M, Lecce D, et al. Differential features of muscle fiber atrophy in osteoporosis and osteoarthritis. *Osteoporos Int.* 2013;24(3):1095-100.
3. Willson T, Nelson SD, Newbold J, Nelson RE, La Fleur J. The clinical epidemiology of male osteoporosis: a review of the recent literature. *Clin Epidemiol.* 2015;7:65-76.
4. Pérez-Castrillón JL, Pinacho F, De Luis D, Lopez-Menendez M, Dueñas Laita A. Odanacatib, a new drug for the

treatment of osteoporosis: review of the results in postmenopausal women. *J Osteoporos.* 2010;2010:401581.
5. Eshraghian A, Jahromi HA. Non-alcoholic fatty liver disease and thyroid dysfunction: a systematic review. *World J Gastroenterol.* 2014;20(25):8102-9.
6. Francque SM, van der Graaff D, Kwanten WJ. Non-alcoholic fatty liver disease and cardiovascular risk: Pathophysiological mechanisms and implications. *J Hepatol.* 2016;65(2):425-43.
7. Portillo-Sanchez P, Bril F, Maximos M, et al. High prevalence of non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus and normal plasma aminotransferase levels. *J Clin Endocrinol Metab.* 2015;100(6):2231-8.
8. Musso G, Gambino R, Tabibian JH, et al. Association of non-alcoholic fatty liver disease with chronic kidney disease: a systematic review and meta-analysis. *PLoS Med.* 2014;11(7):e1001680.
9. Freitas PMSS, Garcia Rosa ML, Gomes AM, et al. Central and peripheral fat body mass have a protective effect on osteopenia or osteoporosis in adults and elderly?*Osteoporos Int.* 2016;27(4):1659–63.
10. Fatima SS, Farooq S, Tauni MA, Irfan O, Alam F. Effect of raised body fat on vitamin D, leptin and bone mass. *J Pak Med Assoc.* 2015;65(12):1315–9.
11. Maghraoui AEl, Sadni S, Maataoui AEl, et al. Influence of obesity on vertebral fracture prevalence and vitamin D status in postmenopausal women. *Nutr Metab* (Lond). 2015;12:44.
12. Maïmoun L, Mura T, Leprieur E, Avignon A, Mariano-Goulart D, Sultan A. Impact of obesity on bone mass throughout adult life: Influence of gender and severity of obesity. *Bone.* 2016;90:23-30.
13. Poiana C, Carsote M, Radoi V, Mihai A, Capatina C. Prevalent osteoporotic fractures in 622 obese and non-obese menopausal women. *J Med Life.* 2015;8(4):462–6.
14. The International Society for Clinical Densitometry (ISCD). Official Positions of the International Society for Clinical Densitometry. West Hartford, USA: ISCD; 2007 (cited 2019 Apr 30). Available from: https://www.iscd.org/wp-content/themes/iscd/pdfs/official-positions/ISCD2007OfficialPositions-Adult.pdf
15. Radchenko VO, Kosterin SB, Dedukh NV, Pobel EA. Kostnaya densitometriya v klinicheskoy praktike (Bone densitometry in clinical practice). *Orthopaedics, Traumatology and Prosthetics.* 2015;2:100-7. (in Russian)
16. Nguyen ND, Eisman JA, Center JR, Nguyen TV. Risk factors for fracture in nonosteoporotic men and women. *Osteoporos Int.* 2006;92:955-62.