

Associations between Metabolic Syndrome and Bone Mineral Density and Trabecular Bone Score in Postmenopausal Women with Non-Vertebral Fractures

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Abstract—Medical, social, and economic relevance of osteoporosis is caused by reducing quality of life, increasing disability and mortality of the patients as a result of fractures due to the low-energy trauma. This study is aimed to examine the associations of metabolic syndrome components, bone mineral density (BMD) and trabecular bone score (TBS) in menopausal women with non-vertebral fractures. 1161 menopausal women aged 50-79 year-old were examined and divided into three groups: A included 419 women with increased body weight (BMI - 25.0-29.9 kg/m²), B – 442 females with obesity (BMI >29.9 kg/m²) and C – 300 women with metabolic syndrome (diagnosis according to IDF criteria, 2005). BMD of lumbar spine (L1-L4), femoral neck, total body and forearm was investigated with usage of dual-energy X-ray absorptiometry. The bone quality indexes were measured according to Med-Imaps installation. All analyses were performed using Statistical Package 6.0. BMD of lumbar spine (L1-L4), femoral neck, total body, and ultradistal radius was significant higher in women with obesity and metabolic syndrome compared to the pre-obese ones ($p < 0.001$). TBS was significantly higher in women with increased body weight compared to obese and metabolic syndrome patients. Analysis showed significant positive correlation between waist circumference, triglycerides level and BMD of lumbar spine and femur. Significant negative association between serum HDL level and BMD of investigated sites was established. The TBS (L1-L4) indexes positively correlated with HDL (high-density lipoprotein) level. Despite the fact that BMD indexes were better in women with metabolic syndrome, the frequency of non-vertebral fractures was significantly higher in this group of patients.

Keywords—Bone mineral density, trabecular bone score, metabolic syndrome, fracture.

I. INTRODUCTION

OSTEOPOROSIS and metabolic syndrome are important public health problems, due to the decreasing of quality and reducing life expectancy of patients as a result of low-trauma fractures in a case of osteoporosis and the possibility of cardiovascular, endocrine and other complications in a case of metabolic syndrome development [1], [5]. The frequency of

both diseases increases with age of patient and duration of menopausal period as a result of slowdown in metabolism and estrogen deficiency development [8], [11].

Traditionally, osteoporosis is diagnosed according to the history of low-energy fractures or the results of BMD (T-score), which are determined by using X-ray densitometry [10]; however, BMD provides only 70-75% of bone strength [13]. Other factors that affect it include state of cortical bone macro-geometry and trabecular bone micro-architecture, presence damages and cracks in it, which can be calculated by index TBS, patented by MED-I maps (m. Bordeaux, France) in 2006 [3]. In our opinion, evaluation of TBS is important to perform this work.

Scientists paid much attention to the study of the relationships between metabolic syndrome and osteoporosis. Abdominal obesity, high glucose (as a result of insulin deficiency or insulin resistance), high triglycerides and low high density lipoproteins which are the main components of metabolic syndrome have significant impact on bone tissue and fractures development but published research results are contradictory [4], [7], [12], [14], [16]. The discrepancy of opinions prompted this investigation.

The aim of our study was to evaluate the relationships between metabolic syndrome components and BMD, TBS in postmenopausal women with low-trauma non-vertebral fractures.

II. MATERIALS AND METHODS

The study involved 1161 postmenopausal women aged 50-79 years (mean age – 63.977±7.961 years; mean body mass index (BMI) – 31.587±4.739 kg/m²; mean waist circumference – 92.524±11.466 cm; mean duration of menopause period – 13.858±8.014). Patients were divided into three groups: A – 419 women with increase body weight (pre-obese) defined on the basis of WHO criteria, [15] BMI 25.0–29.9 kg/m² (mean age – 63.983±8.283 years; mean BMI – 27.547±1.906 kg/m²; mean waist circumference – 79.995±4.511 cm; mean duration of menopause period – 13.809±8.004), B – 442 women with obesity – BMI ≥ 30.0 kg/m² (mean age – 63.884±7.619 years; mean BMI – 34.418±3.864 kg/m²; mean waist circumference – 100.464±6.726 cm; mean duration of menopause period – 13.627±7.847), C – 300 females with metabolic syndrome (diagnosed according to the

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International Diabetic Federation criteria of 2005) [6] (mean age – 64.163±8.017; mean BMI – 33.058±4.812 kg/m²; mean waist circumference – 98.323±8.244 cm; mean duration of menopause period – 14.267±8.280). Additionally, groups were divided according to the presence of low-trauma non-vertebral fractures (202 female had them in history (NVF) and 959 women were without fractures (WF) in the past).

DXA method (Prodigy, GE Medical systems, Lunar, Madison, WI, USA, 2005) was used to investigate BMD of lumbar spine (L1-L4), femoral neck, total body and forearm.

TBS (L1-L4) was estimated by installation of TBS iNsight® software (Med-Imaps, Pessac, France) program on DXA machine.

The Statistical Package 6.0 ©StatSoft, Inc. was used for analyses. Continuous variables were reported as mean ± SD. Pearson correlations examined the relationship between continuous variables, significance set at p<0.05.

III. RESULTS

We found that women with increased body weight have a significantly lower BMD of lumbar spine (A – 0.986±0.178 g/cm², B – 1.109±0.181 g/cm²; C – 1.120±0.199 g/cm²; F=63.814; p<0.001); femoral neck (A – 0.809±0.126 g/cm², B – 0.872±0.134 g/cm²; C – 0.880±0.149 g/cm²; F=32.097; p<0.001), total body (A – 0.876±0.139 g/cm², B – 0.968±0.146 g/cm²; C – 0.978±0.160 g/cm²; F=57.366; p<0.001) and ultradistal forearm (A – 0.378±0.076 g/cm², B – 0.436±0.080 g/cm²; C – 0.435±0.088 g/cm²; F=67.582; p<0.001) compared to women with obesity and metabolic syndrome. The bone tissue quality (TBS L1-L4) was significantly higher in women with increased weight in comparison with metabolic syndrome female (A – 1.188±0.151, B – 1.169±0.163; C – 1.157±0.173 g/cm²; F=3.479; p<0.05).

BMD of lumbar spine (L1-L4) was significantly higher in patients of groups B and C without fractures (Table I). BMD of femoral neck was significantly lower in female with obesity and non-vertebral fractures (Table II). BMD of total body and ultradistal radius significantly better in all groups of women without fractures compared to patients with non-vertebral fractures (Tables III and IV). TBS (L1-L4) was significantly higher in patients without fractures in the groups of women with increased body weight and obesity (p<0.05) (Table V).

The analysis of the metabolic syndrome laboratory components (serum triglycerides and HDL indexes) was carried out. We established significantly higher triglycerides level (A – 1.049±0.381 g/cm², B – 1.030±0.322 g/cm²; C – 1.605±0.703 g/cm²; F=162.669; p<0.001) and significantly lower HDL level (A – 1.531±0.372 g/cm², B – 1.509±0.314 g/cm²; C – 1.170±0.256 g/cm²; F=126.832; p<0.001) in patients with metabolic syndrome. There was no difference of triglycerides level in female with non-vertebral fractures and without them in all investigated groups (Table VI). The level of HDL was significantly lower in patients with non-vertebral fractures and metabolic syndrome (Table VII).

TABLE I
BMD OF LUMBAR SPINE (L1-L4) IN GROUPS OF WOMEN

Groups of patients	Subgroups of patients	BMD lumbar spine (L1-L4), g/cm ²	P
A	without fractures (n=358)	0.992±0.180	>0.05
	with non-vertebral fractures (n=61)	0.955±0.164	
B	without fractures (n=365)	1.119±0.183	<0.001
	with non-vertebral fractures (n=77)	1.059±0.163	
C	without fractures (n=236)	1.139±0.199	<0.001
	with non-vertebral fractures (n=64)	1.052±0.860	

TABLE II
BMD OF FEMORAL NECK IN GROUPS OF WOMEN

Groups of patients	Subgroups of patients	BMD femoral neck, g/cm ²	P
A	without fractures (n=358)	0.814±0.130	>0.05
	with non-vertebral fractures (n=61)	0.780±0.101	
B	without fractures (n=365)	0.879±0.135	<0.001
	with non-vertebral fractures (n=77)	0.834 ±0.119	
C	without fractures (n=236)	0.888±0.153	>0.05
	with non-vertebral fractures (n=64)	0.852±0.133	

TABLE III
BMD OF TOTAL BODY IN GROUPS OF WOMEN

Groups of patients	Subgroups of patients	BMD total body, g/cm ²	P
A	without fractures (n=358)	0.884±0.140	<0.001
	with non-vertebral fractures (n=61)	0.832±0.119	
B	without fractures (n=365)	0.977±0.148	<0.001
	with non-vertebral fractures (n=77)	0.928±0.129	
C	without fractures (n=236)	0.991±0.163	<0.001
	with non-vertebral fractures (n=64)	0.931±0.140	

TABLE IV
BMD OF ULTRADISTAL RADIUS IN GROUPS OF WOMEN

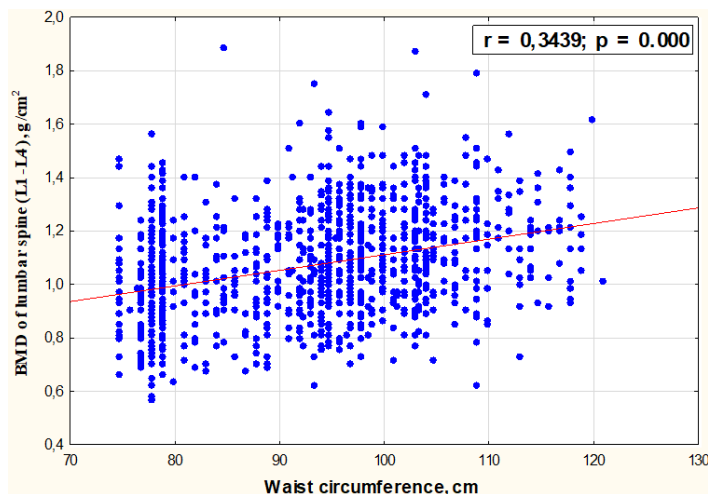
Groups of patients	Subgroups of patients	BMD ultradistal radius, g/cm ²	P
A	without fractures (n=358)	0.382±0.077	<0.05
	with non-vertebral fractures (n=61)	0.354±0.071	
B	without fractures (n=365)	0.442±0.079	<0.001
	with non-vertebral fractures (n=77)	0.410±0.083	
C	without fractures (n=26)	0.442±0.088	<0.001
	with non-vertebral fractures (n=64)	0.407±0.842	

TABLE V
TBS (L1-L4) IN GROUPS OF WOMEN

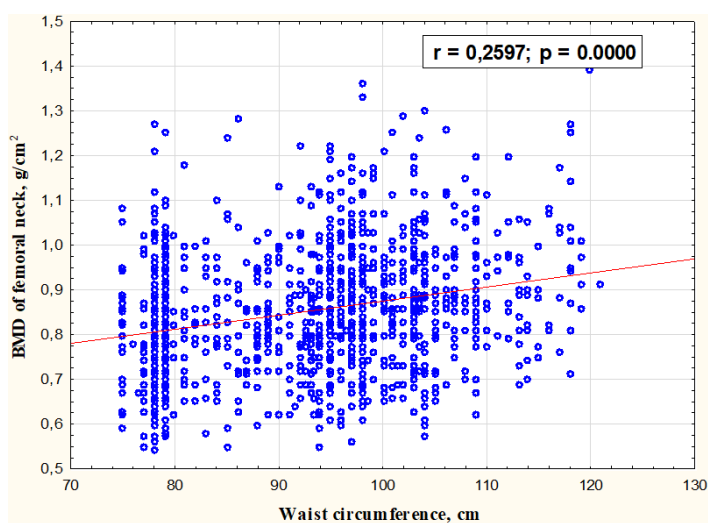
Groups of patients	Subgroups of patients	TBS (L1-L4)	P
A	without fractures (n=358)	1.194±0.151	<0.05
	with non-vertebral fractures (n=61)	1.152±0.439	
B	without fractures (n=365)	1.179±0.150	<0.001
	with non-vertebral fractures (n=77)	1.119±0.171	
C	without fractures (n=236)	1.156±0.177	>0.05
	with metabolic syndrome (n=73)	1.158±0.156	

TABLE VI
TRIGLYCERIDES LEVEL IN GROUPS OF WOMEN

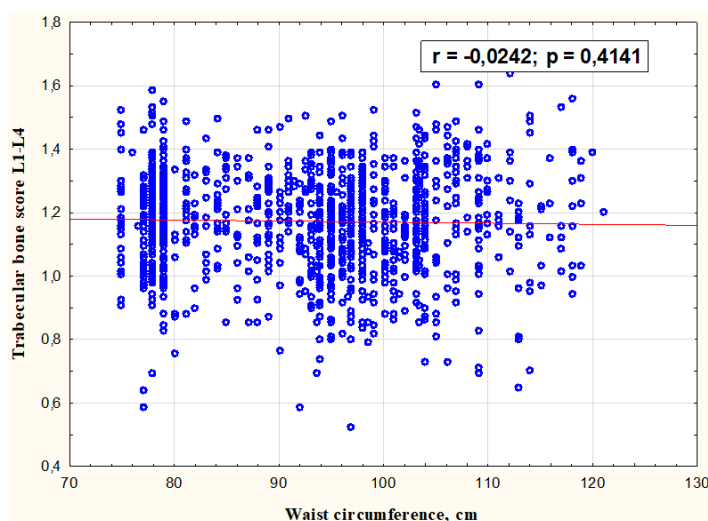
Groups of patients	Subgroups of patients	triglycerides level, mmol/l	P
A	without fractures (n=358)	1.057±0.393	>0.05
	with non-vertebral fractures (n=61)	0.996±0.288	
B	without fractures (n=365)	1.035±0.332	>0.05
	with non-vertebral fractures (n=77)	1.006±0.273	
C	without fractures (n=236)	1.643±0.708	>0.05
	with non-vertebral fractures (n=64)	1.465±0.668	



(a)



(b)



(c)

Fig. 1 Correlation between waist circumference and BMD of (A) lumbar spine (L1-L4), (B) femoral neck, (C) TBS

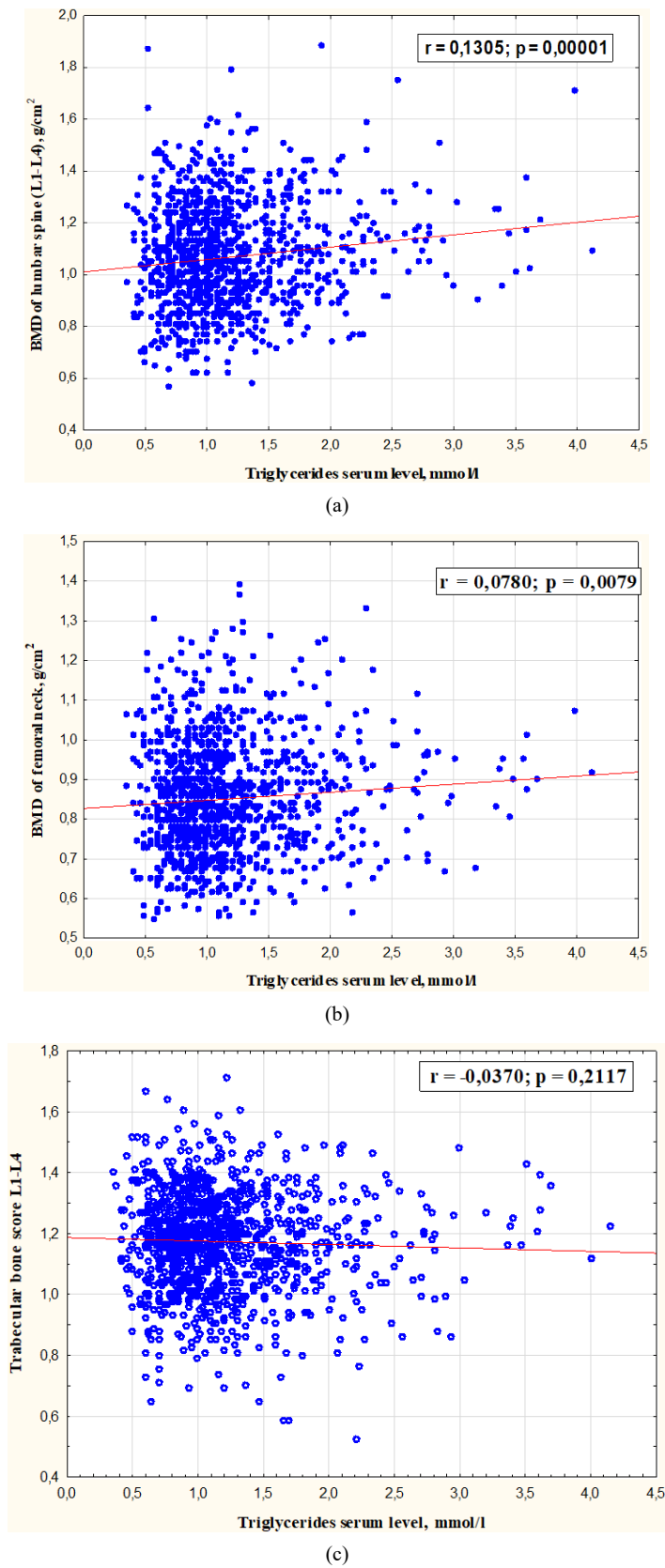
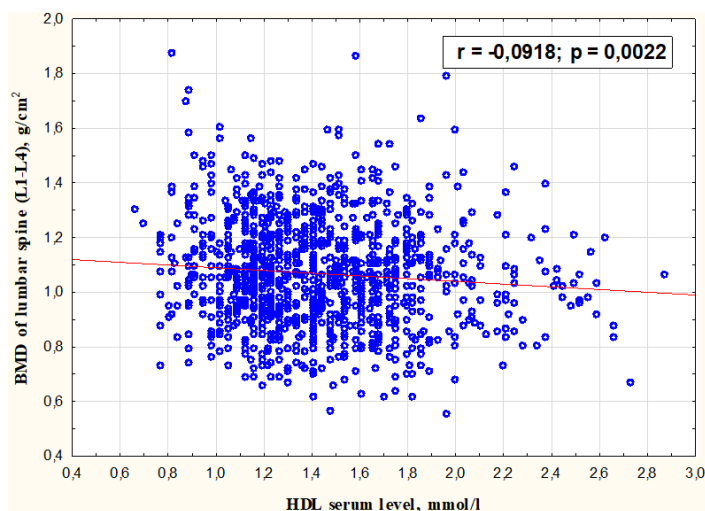
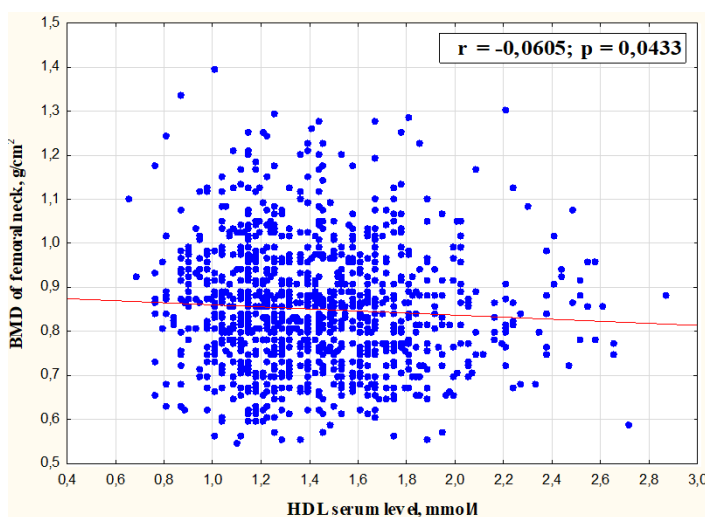


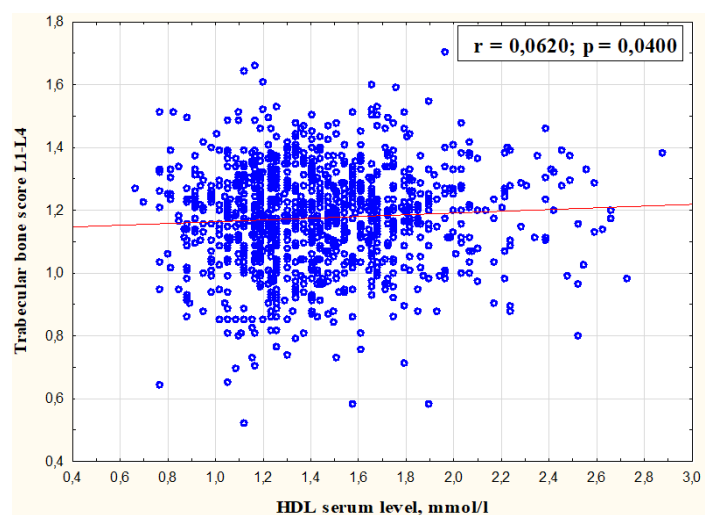
Fig. 2 Correlation between triglycerides serum level and BMD of (A) lumbar spine (L1-L4), (B) femoral neck, (C) TBS



(a)



(b)



(c)

Fig. 3 Correlation between HDL serum level and BMD of (A) lumbar spine (L1-L4), (B) femoral neck, (C) TBS

TABLE VII
HDL LEVEL IN GROUPS OF WOMEN

Groups of patients	Subgroups of patients	HDL level, mmol/l	P
A	without fractures (n=358)	1.523±0.037	>0.05
	with non-vertebral fractures (n=61)	1.579±0.327	
B	without fractures (n=365)	1.501±0.319	>0.05
	with non-vertebral fractures (n=77)	1.546±0.272	
C	without fractures (n=236)	1.148±0.229	<0.001
	with non-vertebral fractures (n=64)	1.252±0.325	

In analysis of metabolic syndrome components, the waist circumference component was positively associated with BMD of lumbar spine and femur (Fig. 1). The study reveals significant positive correlation between serum triglycerides level and both investigated BMD sites (Fig. 2). A number of investigators have suggested relationship in accordance with our own findings [2]. It was found a significant positive correlation between HDL serum level and TBS and inversely association with BMD of lumbar spine and femur (Fig. 3).

We calculated the percentage of non-vertebral fractures in anamnesis (Fig. 4).

Low-trauma non-vertebral fractures occurred in 14.6% female with increased body weight, 17.4% of women with obesity and 21.3% of patients with metabolic syndrome.

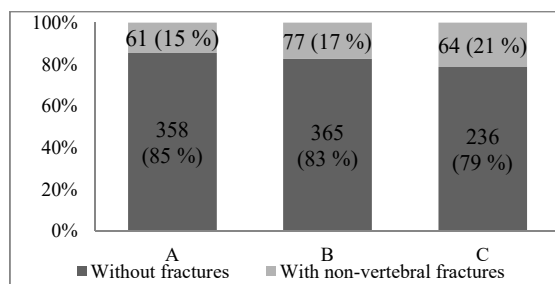


Fig. 4 Frequency of low-trauma vertebral fractures in women with increase body weight (A), obesity (B) and with metabolic syndrome (C)

Significant differences were not found in the frequency of non-vertebral fractures in the groups of women with obesity and increased body weight or metabolic syndrome ($X^2=1.312$, $p>0.05$ and $X^2=1.780$, $p>0.05$, respectively), but it was significant in the groups of pre-obese female and patients with metabolic syndrome ($X^2=5.590$, $p<0.05$). The similar results were found by other investigators [9].

IV. CONCLUSION

Menopausal women with obesity and metabolic syndrome have a significantly higher BMD at all measured sites compared to females with pre-obesity. TBS is significantly lower in women with non-vertebral fractures and increased body weight or obesity. A significant positive correlation is established between waist circumference, triglycerides level and BMD of lumbar spine and femoral neck. Correlation between HDL level and BMD at all levels is significant and negative. At the same time, it is positively associated with

TBS indexes. There is no significant difference in frequency of low-trauma non-vertebral fractures in the groups of pre-obese and obese women. At the same time, the incidence of osteoporotic non-vertebral fractures is significantly higher in female with metabolic syndrome in compared to other patients. Metabolic syndrome may not protect from any type of fractures, but future investigations are necessary.

REFERENCES

- [1] Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR. 'Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women', *JAMA*, 301:513–521, 2009; doi: 10.1001/jama.2009.50.
- [2] Dennison E.M., Syddall H.E., Aihie Sayer A., Martin H.J., Cooper C. Lipid profile, obesity and bone mineral density: the Hertfordshire Cohort Study. *QJM: An International Journal of Medicine*, Volume 100, Issue 5, 1 May 2007, Pages 297–303, <https://doi.org/10.1093/qjmed/hcm023>. (Accessed on 09/01/2018, open access).
- [3] Didier Hans, Andrew L Goertzen, Marc-Antoine Krieg, William D Leslie. "Bone Microarchitecture Assessed by TBS Predicts Osteoporotic Fractures Independent of Bone Density: The Manitoba Study", *Journal of Bone and Mineral Research*, Vol. 26, No. 11, November 2011, pp 2762–2769/ DOI: 10.1002/jbmr.499.
- [4] Gonelli S., Caffarelli C., Nuti R. "Obesity and fracture risk" *Clin. Cases Miner. Bone Metab.*, Jan; 11 (1): 9-14, 2014.
- [5] Huang CY, Liao LC, Tong KM, Lai HL, Chen WK, Chen CI, Lu CY, Chen FJ. Mediating effects on health-related quality of life in adults with osteoporosis: a structural equation modeling. *Osteoporos. Int.* 2015; 26(3):875–883. doi: 10.1007/s00198-014-2963-3.mc.
- [6] International Diabetes Federation. Worldwide definition of the metabolic syndrome. Available at: http://www.idf.org/web-data/docs/IDF_Metasyndrome_definition.pdf. Accessed, August 24, 2005.
- [7] Kan Sun; Jianmin Liu; Nan Lu; Hanxiao Sun; Guang Ning "Association between metabolic syndrome and bone fractures: a meta-analysis of observational studies," *BMC Endocr Disord.*; 14(13), 2014, Published online 2014 Feb 9. doi 10.1186/1472-6823-14-13.
- [8] Maghraoui A1, Rezqi A, Mrad S, Sadni S, Ghazlani I, Mounach A. "Osteoporosis, vertebral fractures and metabolic syndrome in postmenopausal women" *BMC Endocr Disord.*, Dec 10;14:93, 2014; doi: 10.1186/1472-6823-14-93.
- [9] Von Muhlen D, Safii S, Jassal SK, Svartberg J, Barrett-Connor E. Associations between the metabolic syndrome and bone health in older men and women: The Rancho Bernardo Study. *Osteoporos Int.* 2007; 18:1337–1344. doi: 10.1007/s00198-007-0385-1.
- [10] Official Positions of the International Society for Clinical Densitometry, Copyright ISCD, October 2007, Supersedes all prior "Official Positions" publications.
- [11] Poiana C, Carsote M, Radoi V, Mihai A, Capatina C. "Prevalent osteoporotic fractures in 622 obese and non-obese menopausal women", *J Med Life*, Oct-Dec; 8(4): 462–466, 2015.
- [12] Sun K, Liu J, Lu N, Sun H, Ning G. Association between metabolic syndrome and bone fractures: a meta-analysis of observational studies. *BMC Endocr Disord.* 2014 Feb 9;14:13. doi: 10.1186/1472-6823-14-13.
- [13] Susan M. Ott. "Bone strength: more just density", *Kidney International*, 89; p.16-19, 2016.
- [14] Taulant Muka, Katerina Trajanoska, Jessica C. Kieffe-de Jong, Ling Oei, et al. The Association between Metabolic Syndrome, Bone Mineral Density, Hip Bone Geometry and Fracture Risk: The Rotterdam Study. Published: June 12, 2015, <https://doi.org/10.1371/journal.pone.0129116>. (Accessed on 09/01/2018, open access).
- [15] World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation on obesity. World Health Organization: Geneva, 2000, p.9.
- [16] Yang L, Lv X, Wei D, Yue F, Guo J, Zhang T. "Metabolic syndrome and the risk of bone fractures: A Meta-analysis of prospective cohort studies", *Bone*, Mar; 84:52-6, 2016; doi: 10.1016/j.bone.2015.12.008. Epub 2015 Dec 18.