Annals of Agricultural and Environmental Medicine 2021, Vol 28, No 4, 654–658
www.aaem.pl

ORIGINAL ARTICLE

Characteristics of osteoporotic vertebral fractures in association with symptomatic status in postmenopausal women – a retrospective study of a single centre in Poland

Piotr Sawicki[1,A-F], Marek Tałałaj[2,A-B], Katarzyna Życińska[1,3,E-F], Wojciech S. Zgliczyński[4,E-F], Agata Bogołowska-Stieblich[2,A-B], Jan Krakowiak[5,E-F], Waldemar Wierzba[6,C-F]

[1] *Department of Rheumatology, Systemic Connective Tissue Diseases and Rare Diseases, Central Clinical Hospital MSWiA, Warsaw, Poland*
[2] *Department of Geriatrics, Internal Medicine and Metabolic Bone Diseases, Centre of Postgraduate Medical Education, Warsaw, Poland*
[3] *Department of Family Medicine, Medical University, Warsaw, Poland*
[4] *School of Public Health, Centre of Postgraduate Medical Education, Warsaw, Poland*
[5] *Department of Social Medicine, Medical University, Łódź, Poland*
[6] *University of Humanities and Economics, Łódź, Poland*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article

Sawicki P, Tałałaj M, Życińska K, Zgliczyński WS, Bogołowska-Stieblich A, Krakowiak J, Wierzba W. Characteristics of osteoporotic vertebral fractures in association with symptomatic status in postmenopausal women – a retrospective study of a single centre in Poland. Ann Agric Environ Med. 2021; 28(4): 654–658. doi: 10.26444/aaem/133230

Abstract

Introduction and objective. Vertebral compression fractures (VCFs), which are a complication of osteoporosis, often cause diagnostic and therapeutic difficulties. The aim of this study was to find association between the characteristics of VCFs and the symptomatic status of patients.

Materials and method. The study involved a total of 437 women with diagnosed postmenopausal osteoporosis (193 with at least one compression fracture and 244 without VCFs). To identify VCFs, all patients underwent morphometry using dual-energy X-ray absorptiometry. Based on the history of VCFs, subjects were divided into two groups: with symptomatic (n=59) and asymptomatic (n=134) VCFs.

Results. Each patient had, on average, 2.03 ± 1.50 VCFs. Patients with VCFs were older [p<0.001] and shorter [p<0.001] than those without VCFs. VCFs located in the thoracic spine and the lumbar spine occurred with similar frequency (p=0.112). Multiple fractures in both spine segments (50.13%) were more frequent than fractures limited to only one section of the spine, either thoracic (22.76%) or lumbar (27.11%). The decreasing number of subjects was exponentially associated with the increasing number of VCFs (p<0.001). Symptomatic patients compared to asymptomatic patients had a higher serum concentration of 25-hydroxyvitamin D, and lower serum activity of alkaline phosphatase (p<0.01; p<0.005, respectively). In the lumbar spin, the risk of symptomatic VCFs was more than twofold higher compared to asymptomatic VCFs (p <0.001, OR=2.57, 95% CI: 1.57–4.19). Symptomatic status depended on the number of lumbar VCFs (p<0.001, OR=2.47, 95% CI: 1.68–3.63), as well as higher T-score L1-L4 (p=0.009, OR=1.43, 95% CI: 1.09–1.88).

Conclusions. Patients' symptomatic status depends on the location and number of VCFs, as well as T-score L1-L4.

Key words

osteoporosis, spinal fractures, densitometry

INTRODUCTION

Osteoporosis is a chronic metabolic bone disease, characterized by progressive bone loss and greater susceptibility to fracture [1, 2]. One of the main types of osteoporotic fractures are vertebral compression fractures (VCFs) that occur in the thoracic and lumbar spine [3]. According to the Genant classification, VCFs can be divided into mild – 1st degree, when vertebral body compression is 20–24%, moderate – 2nd degree, when compression is 25–39% and severe – 3rd degree, when compression reaches at least 40% [4]. Regardless of the severity, VCFs can be classified as wedge, biconcave or crush fractures [5]. The most common method used to diagnose VCFs is the X-ray examination [6]. An alternative method, having high sensitivity and specificity, is morphometric assessment of the thoracic and lumbar spine using the dual-energy X-ray absorptiometry [7]. Most of the fractures are spontaneous, unrelated to trauma [8], and nearly 70% of patients experiencing this type of fracture, report weak or non-specific pain or do not feel any pain. The occurrence of one vertebral fracture significantly increases the risk of subsequent fractures [9].

Address for correspondence: Waldemar Wierzba, University of Humanities and Economics, Łódź, Poland
E-mail: wwierzba@post.pl

Received: 04.01.2021; accepted: 11.02.2021; *first published: 23.02.2021*

OBJECTIVES

The aim of this study was to find an association between the characteristics of osteoporotic vertebral fractures and the symptomatic status of patients. Finding this type of relationship could improve the diagnosis of VCFs and accelerate the start of osteoporosis treatment.

MATERIALS AND METHOD

A total of 437 postmenopausal women were recruited for the study (193 with at least one vertebral fracture and 244 without diagnosed vertebral fractures). Patients were hospitalized in the bone metabolic department or remained under the care of an osteoporotic clinic. Study inclusion criterion was diagnosed postmenopausal osteoporosis [10]. All patients with: 1) the presence of severe scoliosis or overlapping of calcifications or structures of the mediastinum and abdominal cavity (which preclude identification of the borders of many vertebral bodies), 2) suspected or diagnosed secondary osteoporosis, including post-steroid, and 3) high-energy, non-osteoporotic vertebral fractures, were excluded from the study.

Patients' height and weight were measured in a standing position, without shoes. Height was measured using a stadiometer with 1 mm accuracy and weight measured by means of a calibrated digital electronic weighing scale with an accuracy of ±100 grams. VCFs were identified by performing morphometry, using dual-energy X-ray absorptiometry of Horizon W bone densitometer (Hologic, Inc., Bedford, MA, USA). Osteoporosis was diagnosed using bone mineral density (BMD) measurements in lumbar spine and hip [11]. To ensure repeatability of measurements, all tests were performed by the same qualified person, using the same densitometer. The device was calibrated once a day with the spine phantom. Vertebrae from Th6 – L4 were assessed. Pathological lateral curvatures of the spine and the overlapping of mediastinal structures (calcification and fibrosis in the bronchial tree) and abdominal organs (gas-filled intestinal loops) on the vertebral bodies, can limit visualization of the vertebral borders [12]; therefore, if there were doubts about the presence of a vertebral fracture or the degree of fracture, equivocal images were not analyzed. Measurements of the anterior, middle and posterior heights of the vertebral bodies were performed to determine the type and degree of VCFs.

All subjects were asked about their symptoms' related history of VCFs. If the subject did not report a vertebral fracture, or if the fracture was diagnosed accidentally, it was classified as asymptomatic. The number of asymptomatic patients was 134 (69.43%) and the number of symptomatic patients was 59 (30.57%). Patients were grouped according to the number of fractures, as well as according to their symptomatic status. VCFs were classified according to their location (thoracic vs. lumbar vs. both), type (wedge vs. biconcave vs. crush) and severity (mild vs. moderate vs. severe). Serum concentration of calcium, 25-hydroxyvitamin D, phosphate and serum activity of alkaline phosphatase were measured in all patients.

Statistical analysis. Statistical analysis was performed using Statistica TIBCO Software Inc. (data analysis software system – version 13.3, 3307 Hillview Avenue Palo Alto, CA, USA). Continuous data are presented as mean ± SD and categorical data were evaluated in terms of percentage, with the evaluation of significance using a structure indicators test. For continuous data, depending on the distribution of variable, parametric (t-Student test) or non-parametric (Kolmogorow-Smirnov test) comparison was performed. To determine the type of distribution of a variable, which assigns the number of vertebral fractures to the number of subjects, the Chi-square test was used. For the differentiation of symptomatic and asymptomatic vertebral fractures univariate and multivariate logistic regression analysis was performed.

RESULTS

The mean age of the study group was 71.54 ± 9.90 years (range 48–92 years), the mean body weight was 64.1 kg ± 11.51 (range 35.0–106.7) and the mean BMI was 26.1 kg/m^2 ± 4.55 (range 14.95–44.43). Patients with VCFs vs. patients without VCFs were older – 73.93 ± 9.96 years vs. 69.63 ± 10.15 years [p<0.001] and had shorter height – 1.56 ± 0.06 m vs. 1.58 ± 0.07 m [p<0.001]. The total number of examined thoracic and lumbar vertebrae was 2,766 and 1747, respectively. Th6 vertebra was visible in 57.7% of subjects, Th7 in 85.7%, Th8 in 94.7%, Th9 in 97.7%, Th10 in 98.4%, Th11 in 99.3%, Th12 in 99.5%, L1 in 99.8% and vertebrae from L2 to L4 were visible in all subjects. The total number of diagnosed VCFs in thoracic and lumbar spine was 191 and 200, respectively. At least one vertebral fracture was found in 193 patients (44.16%). The total number of fractures in one patient was 2.03 ± 1.50 (max. 8), wherein in the thoracic spine was found 1.04 ± 1.13 (max. 6) fractures and in the lumbar spine 1.06 ± 1.01 (max. 4) fracture were found. There was no difference between the frequency of VCFs in the thoracic and lumbar spine (6.91% and 11.45%, respectively, p=0.112). 47.67% patients with VCFs suffered only one fracture, 74.09% no more than two fractures and 3.62% had more than five fractures. Among patients with VCFs, there was no difference between thoracic and lumbar spine in percentage of subjects with at least one fracture (63.73% and 66.32%, respectively, p=0.33), no more than two fractures (53.37% and 54.93%, respectively; p=0.82), and more than two fractures (10.36% and 11.39%, respectively; p=0.46). Most fractures were found on the border of the thoracic and lumbar spine [13]. L1, Th12 and L2 fractures were the most frequent (Fig. 1). Multiple fractures in both the thoracic and lumbar spine (50.13% of all fractures) were more frequent, compared to fractures limited only to one segment of the spine, either thoracic (22.76%) or lumbar (27.11%) (Fig. 2).

Biconcave fractures (70.08%) were more frequent than wedge (23.27%) and crush fractures (6.65%). In correlation with the severity of the fracture, without division into segments, moderate fractures (48.85% of total fractures) were more frequent than mild (35.04%) and severe fractures (16.11%). There was no difference in the frequency of mild (p=0.474), moderate (p=0.463), severe (p=0.450), wedge (p=0.229), biconcave (p=0.227) and crush (p=0.370) fractures between the thoracic and lumbar spine.

Asymptomatic fractures and symptomatic fractures accounted for 59.80% and 40.20% of total VCFs, respectively. There was no association of symptoms with the presence

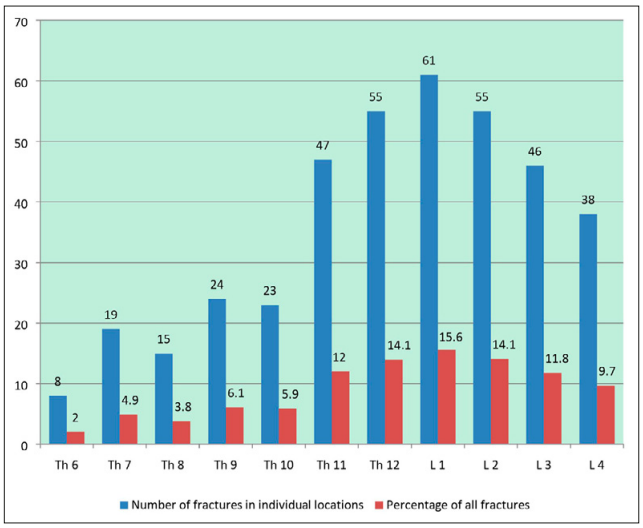

Figure 1. Distribution of compression fractures in vertebral bodies

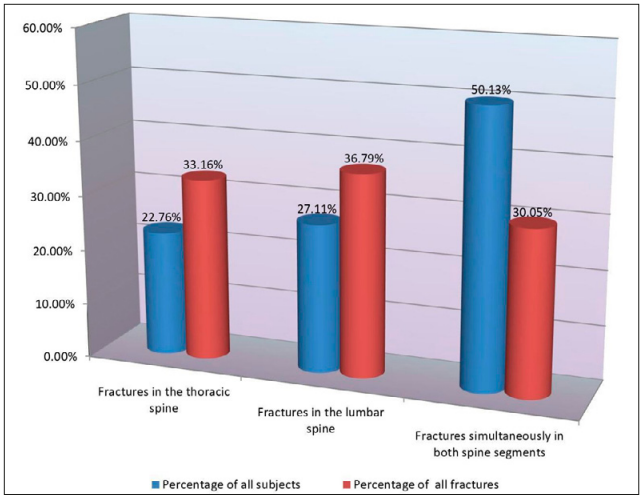

Figure 2. Distribution of compression fractures in spine segments

of VCFs in individual locations for any of the vertebrae from Th6 – L4, but for the entire lumbar spine the risk of symptomatic fractures increased by more than twofold than asymptomatic fractures (p<0.001, OR=2.57, 95% CI: 1.57–4.19). There was no differences in the frequency of mild (p=0.118), moderate (p=0.374), severe (p=0.390), wedge (p=0.337), biconcave (p=0.336) and crush (p=0.482) fractures between symptomatic and asymptomatic patients. The presence of fracture symptoms depended on the number of lumbar VCFs (p<0.001, OR=2.47, 95% CI: 1.68–3.63), but not for VCFs in the thoracic spine. Patients with symptomatic fractures were characterized by higher T-score L1-L4 (p=0.009, OR=1.43, 95% CI: 1.09–1.88).

Using multivariate logistic regression analysis, a statistically significant model was created (p<0.01) which confirmed that the presence of fracture symptoms depends on the location of VCFs in the lumbar spine (OR=1.84, 95% CI: 1.36–2.93), the number of lumbar VCFs (OR=1.58, 95% CI: 1.23–2.38), and the T-score L1-L4 (OR=1.32, 95% CI: 1.03–1.64)

Among symptomatic patients, a higher serum concentration of 25- hydroxyvitamin D (48.64 ng/ml ± 14.24) and lower serum activity of alkaline phosphatase (65.16 U/l ± 20.48) was found, compared to asymptomatic patients (39.08 ng/ml ± 16.34 and 79.37 U/l ± 24.24, respectively) (p<0.01; p<0.005, respectively). There was no difference between symptomatic and asymptomatic patients in the serum concentration of calcium and phosphate.

The decreasing number of subjects was exponentially associated with the increasing number of VCFs (p<0.001) (Fig. 3).

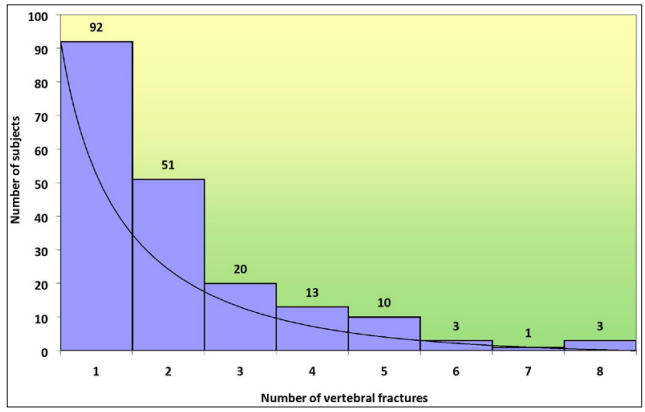

Figure 3. Exponentially decreasing number of subjects associated with the increasing number of vertebral fractures

DISCUSSION

The study demonstrated a significant association between symptomatic status, location and number of lumbar VCFs. A slightly higher percentage of patients with present VCFs in the study group compared to the values reported in the literature [14, 15], can be explained by the specific characteristics of the study group. Patients often had severe, clinically apparent osteoporosis and numerous fractures. Densitometric morphometry, used for the diagnosis of fractures, is also more sensitive for mild fractures than conventional X-ray examination [16].

The study showed that the location of fractures can have important clinical implications. Due to similar occurrence of VCFs in the thoracic and lumbar spine, it is important to consider diagnostic imaging of both spine segments when a compression fracture is suspected. This is the advantage of densitometric morphometry in the preliminary diagnosis of VCFs [17], because this method allows the examination of both spine segments [18] simultaneously, with routine BMD assessment. Furthermore, compared to classic X-ray examination, densitometric morphometry is associated with significantly less exposure to ionizing radiation [17].

The exponentially decreasing number of patients with an increasing number of fractures can be associated with the use of anti-osteoporotic therapies and reduction of the risk of fractures [19–21]. This hypothesis can confirm a higher serum concentration of 25-hydroxyvitamin D and lower serum activity of alkaline phosphatase, demonstrated by the authors in symptomatic patients [22, 23]. Furthermore, worse mental status and physical quality of life among patients with osteoporosis [24] and previous VCFs [25] could lead to reduced physical activity, limiting the risk of falls and further fractures. Changes in the biomechanics of the spine, observed among patients with previous VCFs, could be significant determinants of the subsequent VCFs [26]. Further investigations are required to look for other

factors that reduce the incidence of multiple fractures and are responsible for such a strictly mathematical relationship.

Because of the more frequent coexistence of VCFs simultaneously in the thoracic and lumbar spine, it can be concluded that the appearance of a first vertebral fracture increases the risk of a subsequent fracture [27, 28], and simultaneously, as described above, there are factors that significantly reduce the risk of multiple fractures. The study showed that symptomatic fractures are more common in the lumbar spine and that the presence of symptoms is associated with the number of VCFs in the lumbar spine [29]. Such relationships have not been demonstrated for the thoracic spine. Patients with a higher value of the T-score in the lumbar spine significantly more often experienced symptomatic VCFs. Despite the well-documented association between low BMD and an increased risk of VCFs [30–33], the occurrence of symptoms in the current study probably depended on concentrating the same mass of vertebral bone tissue in a smaller volume due to a fracture, resulting in an increase of mineral density and the T-score. This hypothesis requires further investigation.

Study limitations. Not all patients answered the question about previous VCFs; therefore, the total number of fractures classified as symptomatic or asymptomatic was lower than the total number of diagnosed fractures (301 vs. 391, respectively). Another limitation was that densitometric morphometry used to diagnose VCFs. Although the compatibility of this method with conventional radiography can reach high agreement [34], the 'gold' standard in the diagnostics of VCFs remains the X-ray examination.

CONCLUSIONS

The study shows a strictly mathematical, exponential relationship regarding the number of patients assigned to the number of VCFs. In the lumbar spine, the risk of symptomatic fractures was more than twofold higher compared to asymptomatic fractures. Patients' symptomatic status also depended on the number of fractures in the lumbar spine and T-score L1-L4. Symptomatic patients had higher serum concentration of 25-hydroxyvitamin D and lower serum activity of alkaline phosphatase, compared to asymptomatic patients. The obtained results may be helpful in the diagnosis of VCFs.

Ethical aspects. Research protocols were approved by the Ethics Committee of the Centre for Postgraduate Medical Education in Warsaw (No. 64/PB/2018). The study complied with the 1964 Declaration of Helsinki with its later amendments. All participants received detailed instructions regarding the protocols and written consent was obtained from all patients.

Declaration of competing interest

The authors declare no conflict of interests.

Financial disclosure

Publication of this study was financed from the authors' own funds.

REFERENCES

1. Lorentzon M, Branco J, Brandi ML, et al. Algorithm for the Use of Biochemical Markers of Bone Turnover in the Diagnosis, Assessment and Follow-Up of Treatment for Osteoporosis. Adv Ther. 2019; 36(10): 2811–2824. https://doi.org/10.1007/s12325-019-01063-9
2. Janiszewska M, Kulik T, Dziedzic M, et al. Knowledge of osteoporosis prophylaxis and health behaviours of the population of chosen countries of the world. Ann Agric Environ Med. 2014; 21(2): 364–368. https://doi.org/10.5604/1232-1966.1108606
3. Schousboe J, Vo T, Taylor B. Prediction of Incident Major Osteoporotic and Hip Fractures by Trabecular Bone Score (TBS) and Prevalent Radiographic Vertebral Fracture in Older Men. J Bone Miner Res. 2016; 31(3): 690–697. https://doi.org:10.1002/jbmr.2713
4. Rud B, Vestergaard A, Hyldstrup L. Accuracy of densitometric vertebral fracture assessment when performed by DXA technicians--a cross-sectional, multiobserver study. Osteoporos Int. 2016; 27(4): 1451–1458. https://doi.org/10.1007/s00198-015-3395-4
5. Karlsson M, Kherad M, Hasserius R, et al. Characteristics of Prevalent Vertebral Fractures Predict New Fractures in Elderly Men. J Bone Joint Surg Am. 2016; 98(5): 379–385. https://doi.org/10.2106/JBJS.15.00328
6. McCarthy J, Davis A. Diagnosis and Management of Vertebral Compression Fractures. Am Fam Physician. 2016; 94(1): 44–50.
7. Zeytinoglu M, Jain R, Vokes T. Vertebral fracture assessment: Enhancing the diagnosis, prevention, and treatment of osteoporosis. Bone. 2017; 104: 54–65. https://doi.org/10.1016/j.bone.2017.03.004
8. Cicala D, Briganti F, Casale L, et al. Atraumatic vertebral compression fractures: differential diagnosis between benign osteoporotic and malignant fractures by MRI. Musculoskelet Surg. 2013; 97 Suppl 2: S169–179. https://doi.org/10.1007/s12306-013-0277-9
9. Balasubramanian A, Zhang J, Chen L, et al. Risk of subsequent fracture after prior fracture among older women. Osteoporos Int. 2019; 30(1): 79–92. https://doi.org/10.1007/s00198-018-4732-1
10. Wu Q, Xiao X, Xu Y. Evaluating the Performance of the WHO International Reference Standard for Osteoporosis Diagnosis in Postmenopausal Women of Varied Polygenic Score and Race. J Clin Med. 2020; 9(2): 499. https://doi.org/10.3390/jcm9020499
11. Kanis JA, Cooper C, Rizzoli R, et al. Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF). Executive summary of the European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Calcif Tissue Int. 2019; 104(3): 235–238. https://doi.org/10.1007/s00223-018-00512-x
12. Muszkat P, Camargo M, Peters B, et al. Digital vertebral morphometry performed by DXA: a valuable opportunity for identifying fractures during bone mass assessment. Arch Endocrinol Metab. 2015; 59(2): 98–104. https://doi.org/10.1590/2359-3997000000020
13. Wood K, Li W, Lebl D, et al. Management of thoracolumbar spine fractures. Spine J. 2014; 14(1): 145–164. https://doi.org/10.1016/j.spinee.2012.10.041
14. Stanghelle B, Bentzen H, Giangregorio L, et al. Associations between health-related quality of life, physical function and pain in older women with osteoporosis and vertebral fracture. BMC Geriatr. 2019; 19: 298. https://doi.org/10.1186/s12877-019-1268-y
15. Che H, Breuil V, Cortet B, et al. Vertebral fractures cascade: potential causes and risk factors. Osteoporos Int. 2019; 30(3): 555–563. https://doi.org/10.1007/s00198-018-4793-1
16. Van der Velde R, Ozanian T, Dumitrescu B, et al. Performance of statistical models of shape and appearance for semiautomatic segmentations of spinal vertebrae T4-L4 on digitized vertebral fracture assessment images. Spine J. 2015; 15(6): 1248–1254. https://doi.org/10.1016/j.spinee.2015.02.018
17. Oh S, Kim D, Lee Y, et al. Comparison of screening strategies for prevalent vertebral fractures in South Korea: vertebral fracture assessment vs. spine radiograph. BMC Musculoskelet Disord. 2018; 19(1): 46. https://doi.org/10.1186/s12891-018-1958-1
18. Shetty S, John B, Mohan S, et al. Vertebral fracture assessment by dual-energy X-ray absorptiometry along with bone mineral density in the evaluation of postmenopausal osteoporosis. Arch Osteoporos. 2020; 15(1): 25. https://doi.org/10.1007/s11657-020-0688-9
19. Dennison E, Cooper C, Kanis J, et al. Fracture risk following intermission of osteoporosis therapy. Osteoporos Int. 2019; 30(9): 1733–1743. https://doi.org/10.1007/s00198-019-05002-w
20. Cummings S, Ferrari S, Eastell R, et al. Vertebral Fractures After Discontinuation of Denosumab: A Post Hoc Analysis of the Randomized

Placebo-Controlled FREEDOM Trial and Its Extension. J Bone Miner Res. 2018; 33(2): 190–198. https://doi.org/10.1002/jbmr.3337
21. Vandenbroucke A, Luyten F, Flamaing J, et al. Pharmacological treatment of osteoporosis in the oldest old. Clin Interv Aging. 2017; 12: 1065–1077. https://doi.org/10.2147/CIA.S131023
22. Nurmi-Lüthje I, Lüthje P, Kaukonen J, et al. Positive Effects of a Sufficient Pre-fracture Serum Vitamin D Level on the Long-Term Survival of Hip Fracture Patients in Finland: A Minimum 11-Year Follow-Up. Drugs Aging. 2015; 32(6): 477–486. https://doi.org/10.1007/s40266-015-0267-8
23. Bone HG, Wagman RB, Brandi ML, et al. 10 years of denosumab treatment in postmenopausal women with osteoporosis: results from the phase 3 randomised FREEDOM trial and open-label extension. Lancet Diabetes Endocrinol. 2017; 5(7): 513–523. https://doi.org/10.1016/S2213-8587(17)30138-9
24. Janiszewska M, Firlej E, Dziedzic M, et al. Health beliefs and sense of one's own efficacy and prophylaxis of osteoporosis in peri- and postmenopausal women. Ann Agric Environ Med. 2016; 23(1): 167–173. https://doi.org/10.5604/12321966.1196875
25. Al-Sari U, Tobias J, Clark E. Health-related quality of life in older people with osteoporotic vertebral fractures: a systematic review and meta-analysis. Osteoporos Int. 2016; 27(10): 2891–2900. https://doi.org/10.1007/s00198-016-3648-x
26. Aebi M, Maas C, Di Pauli von Treuheim T, et al. Comparative biomechanical study of a new transpedicular vertebral device and vertebroplasty for the treatment or prevention of vertebral compression fractures. Clin Biomech (Bristol, Avon). 2018; 56: 40–45. https://doi.org/10.1016/j.clinbiomech.2018.05.001
27. Kanis JA, Johansson H, Odén A, et al. Characteristics of recurrent fractures. Osteoporos Int. 2018; 29(8): 1747–1757. doi: 10.1007/s00198-018-4502-0
28. Johansson H, Odén A, McCloskey E, et al. Mild morphometric vertebral fractures predict vertebral fractures but not non-vertebral fractures. Osteoporos Int. 2014; 25(1): 235–241. https://doi.org/10.1007/s00198-013-2460-0
29. Ren H, Jiang J, Chen J, et al. Risk factors of new symptomatic vertebral compression fractures in osteoporotic patients undergone percutaneous vertebroplasty. Eur Spine J. 2015; 24(4): 750–758. https://doi.org/10.1007/s00586-015-3786-4
30. Simpson EL, Martyn-St James M, Hamilton J, et al. Clinical effectiveness of denosumab, raloxifene, romosozumab, and teriparatide for the prevention of osteoporotic fragility fractures: A systematic review and network meta-analysis. Bone. 2020; 130: 115081. https:// doi.org/10.1016/j.bone.2019.115081.
31. Iconaru L, Moreau M, Kinnard V, et al. Does the Prediction Accuracy of Osteoporotic Fractures by BMD and Clinical Risk Factors Vary With Fracture Site? JBMR Plus. 2019; 3(12): e10238. https://doi.org/10.1002/jbm4.10238
32. Okubo N, Matsui S, Matsumoto T, et al. Relationship Between Bone Mineral Density and Risk of Vertebral Fractures with Denosumab Treatment in Japanese Postmenopausal Women and Men with Osteoporosis. Calcif Tissue Int. 2020; 107(6): 559–566. https://doi.org/10.1007/s00223-020-00750-y
33. Bouxsein ML, Eastell R, Lui LY, et al. Change in Bone Density and Reduction in Fracture Risk: A Meta-Regression of Published Trials. J Bone Miner Res. 2019; 34(4): 632–642. https://doi.org/10.1002/jbmr.3641
34. Drampalos E, Nikolopoulos K, Baltas C, et al. Vertebral fracture assessment: Current research status and application in patients with kyphoplasty. World J Orthop. 2015 Oct 18; 6(9): 680–687. https://doi.org/10.5312/wjo.v6.i9.680