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A cross-sectional comparison of selected anthropometric, laboratory, and densitometric parameters in postmenopausal osteoporotic women with and without vertebral compression fractures

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Abstract

Introduction: Osteoporosis leads to an increased risk of vertebral compression fractures (VCFs). Most of them are spontaneous, which makes early diagnosis difficult. The aim of the study was to find parameters that distinguish osteoporotic women with and without vertebral compression fractures.

Material and methods: A total of 437 women with postmenopausal osteoporosis were enrolled to the study. Based on the results of densitometric vertebral fracture assessment, patients were divided into 2 groups: with (n = 193) and without (n = 244) VCFs. Then selected anthropometric, laboratory, and densitometric parameters as well as questionnaire data were compared.

Results: The following distinguishing factors were found among patients with VCFs in comparison to patients without such fractures: older age – 73.93 years *vs.* 69.63 years [p(1) < 0.001, p(2) < 0.001], shorter height — 1.56 m *vs.* 1.58 m [p(4) < 0.001], lower value of glomerular filtration rate (GFR) according to Cockcroft-Gault formula — 58.22 mL/min. *vs.* 66.25 mL/min. [p(1) < 0.025, p(2) = 0.002], lower peripheral blood haemoglobin and serum albumin concentration (OR = 1.24, 95% CI: 1.02–1.51, p(5) = 0.03; OR = 2.29, 95% CI: 1.09–4.80, p(5) = 0.03, respectively), and higher 10-year risk of major osteoporotic fracture (FRAX MOF) –12.01% *vs.* 9.69% [p(1) < 0.01, p(2) < 0.001] and hip fracture (FRAX HIP) — 3.85% *vs.* 2.55% [p(1) < 0.01, p(2) < 0.001]. In addition, among patients with VCFs a greater severity of back pain was found in the 11-grade scale of pain intensity — 6.12 *vs.* 4.29 [p(1) < 0.001, p(2) < 0.001, p(3) < 0.001]. The bone mineral content (BMC) and bone mineral density (BMD) of the hip were lower in patients with VCFs — 25.25 *vs.* 26.2 g and 0.72 g/cm^2 *vs.* 0.75 g/cm^2, respectively [p(4) = 0.04 and p(4) < 0.001, respectively].

Conclusions: Patients with VCFs were characterised by greater back pain intensity, higher fracture risk according to the FRAX calculator, and lower values of the following: GFR according to Cockcroft-Gault formula, peripheral blood haemoglobin and serum albumin concentration, and BMD of the hip. Further studies are required to validate the FRAX calculator to assess not only the risk of future fractures but also unrecognised VCFs. **(Endokrynol Pol 2021; 72 (3): 191–197)**

Key words: *osteoporosis; spinal fractures; back pain; cross-sectional studies*

Introduction

Osteoporosis is a chronic metabolic bone disease, leading to fractures, and it is estimated that osteoporosis affects 22 million women and 5.5 million men in the European Union [1]. With an ageing population, not only the medical but also the socioeconomic effect of osteoporosis will increase further, making it a major public health problem. Osteoporotic fractures can be classified as fractures occurring in locations such as the hip, proximal humerus, pelvis, distal radial bone, thoracic, and lumbar spine [2, 3]. To consider a fracture as osteoporotic, it should be associated with low-energy injury [4, 5]. In particular, osteoporotic fractures can occur spontaneously [6], without injury. These types of fractures occur most often in the thoracic and lumbar spine, and due to their inherent nature they cause great diagnostic difficulties [7]. It has been proven that the occurrence of the first vertebral compression fracture significantly increases the risk of subsequent fractures [8–10]; therefore, early diagnosis of vertebral compression fractures (VCFs) is very important [11].

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However, considering the common prevalence of back pain among older people, including those with osteoporosis [12–16], frequently occurring fluctuations in pain intensity [17], as well as the potentially harmful radiation dose of numerous imaging tests, it seems important to look for additional differentiating factors in patients with and without VCFs [18]. The aim of the study was to find parameters that distinguish osteoporotic women with and without VCFs.

Material and methods

Patients

A total of 437 women with diagnosed postmenopausal osteoporosis based on WHO criteria [19], extended to patients with osteopaenia with T-score equal to or less than –1.5 in densitometric measurements of central skeleton bone mineral density (BMD) and a coexisting low-energy fracture in a major location [3], were recruited for the study. All patients were hospitalised in the Department of Geriatrics, Internal Medicine, and Metabolic Bone Diseases, Centre of Postgraduate Medical Education or remained under the care of an osteoporosis clinic. Patients with suspected or diagnosed secondary osteoporosis, including steroid-induced, as well as patients who suffered high-energy, non-osteoporotic vertebral fractures were excluded from the study. In addition, patients were not included in the study in the presence of severe scoliosis or overlapping calcifications or structures of the mediastinum and abdominal cavity, which preclude identification of the borders of vertebral bodies.

Anthropometric, laboratory, and densitometric data

Measurements of bone mineral density in the central skeleton were conducted for each subject. To identify VCFs, patients underwent vertebral fracture assessment of Th6–L4 vertebrae by dual-energy X-ray absorptiometry (DXA) using a Horizon W bone densitometer (Hologic, Inc., Bedford, MA, USA). To ensure repeatability of measurements, all tests were performed by the same qualified person using the same scanning mode. Before the DXA examination, each patient's height was measured in a standing position, without shoes, using a stadiometer with 1 mm accuracy. Weight was measured using a calibrated digital electronic weighing scale with an accuracy of ± 100 grams. Based on the results of vertebral fracture assessment, patients were divided into 2 groups: with VCFs, regardless of the number of fractures (n = 193) and without VCFs (n = 244). In both groups selected anthropometric parameters (age, height, weight), laboratory parameters [peripheral blood haemoglobin, serum calcium, inorganic phosphate, albumin, 25-hydroxyvitamin D, alkaline phosphatase, creatinine with glomerular filtration rate (GFR) calculated according to the Modification of Diet in Renal Disease (MDRD) and Cockcroft-Gault formula and daily urinary calcium excretion], and densitometric parameters were compared. In addition to vertebral fracture assessment and measurements of bone mineral density, densitometric examination of body composition was performed. Also, a questionnaire taking into account the severity of back pain in an 11-point scale of pain assessment, the tendency to stumble and have falls, and the maximum individual height was conducted. Based on the latter parameter, growth loss was calculated and compared. 322 of the 437 subjects answered the questions in the questionnaire, of whom 143 were with and 179 were without VCFs.

Statistical analysis

Statistical analysis was performed using Statistica data analysis software system — version 13.3 (TIBCO Software Inc., 3307 Hillview Avenue, Palo Alto, CA 94304, USA). Continuous data were presented as mean ± SD and categorical data were presented in terms of percentage in Table 1. For the variables without normal distribution or characterised by a heterogeneous variance despite the normality of the distribution, a nonparametric comparison was performed by 3 tests for each variable: the Kolmogorov-Smirnov test (indication p[1]), the Mann-Whitney U test (indication p[2]), and the Wald-Wolfowitz test (indication p[3]). For all examined interval-quotient variables, characterised by normal distribution (which was confirmed by the Shapiro-Wilk test), the homogeneity of variance was verified by the Leven and Brown-Forsythe test. For this type of variable a parametric comparison using the "z" test or Student's t-test was conducted (indication p[4]). The odds ratios (ORs) and 95% confidence intervals (CIs) for selected variables using logistic regression were analysed (indication p[5]). The chi-square test was used to assess the significance of the data in Table 2. The p-value < 0.05 was considered as significant.

Results

Anthropometric parameters

Older age was identified among patients with VCFs (73.93 years ± 9.95) than without VCFs (69.63 years ± 10.15), ($p[1] < 0.001$, $p[2] < 0.001$). The significance of the difference in body weight between the groups was not shown, although its value was higher by an average of about 2 kilograms for the group without VCFs. A shorter stature was observed in patients with a history of vertebral fractures (1.56 m ± 0.06), compared to patients without VCFs (1.58 m ± 0.07), ($p[4] < 0.001$).

Laboratory parameters

Patients with VCFs had a lower GFR, calculated according to the Cockcroft-Gault formula (58.22 mL/min. ± 20.80) than did patients without VCFs (66.25 mL/min. ± 23.04), ($p[1] < 0.025$ and $p[2] = 0.002$, OR = 0.98, 95% CI: 0.97–0.99, $p[5] = 0.002$) (Fig. 1). There was no difference between the groups regarding laboratory parameters such as alkaline phosphatase, phosphate, calcium, creatinine, and 25-hydroxyvitamin D serum concentration. Lower daily urinary calcium excretion was found in patients with VCFs (145.12 mg/24 h ± 84.70) compared to those without VCFs (175.46 ± 84.61), ($p[2] = 0.02$). Peripheral blood haemoglobin (Fig. 2) and serum albumin concentration were lower among patients with VCFs (OR = 1.24, 95% CI: 1.02–1.51, $p[5] = 0.03$; OR = 2.29, 95% CI: 1.09–4.80, $p[5] = 0.03$, respectively).

Densitometric parameters and questionnaire data

A higher 10-year risk of major osteoporotic fracture (FRAX MOF) and hip fracture (FRAX HIP) for patients with VCFs has been demonstrated (Fig. 3) (12.01% ± 4.71; 3.85% ± 2.52, respectively) in comparison to patients without VCFs (9.69% ± 4.75; 2.55% ± 1.85, respectively), ($p[1] < 0.01$ and $p[2] < 0.001$, OR = 1.11, 95% CI: 1.06–1.16, $p[5] < 0.001$; $p[1] < 0.01$ and $p[2] < 0.001$, OR = 1.31, 95% CI: 1.18–1.46, $p[5] < 0.001$, respectively).

Table 1. *Comparison of statistically significant results of densitometric measurements among subjects with (n = 193) and without (n = 244) vertebral compression fractures (VCFs)*

Parameter	Subjects with VCFs	Subjects without VCFs	p value
BMC — hip [g]	25.25 ± 4.70	26.2 ± 4.03	p(4) = 0.04
BMD — hip [g/cm2]	0.72 ± 0.10	0.75 ± 0.09	p(4) < 0.001
T-score — hip	–1.78 ± 0.80	–1.55 ± 0.76	p(4) < 0.001
PR — hip (%)	76.49 ± 9.89	79.78 ± 9.73	p(4) < 0.001
BMD — femoral neck [g/cm2]	0.61 ± 0.08	0.63 ± 0	p(1) < 0.05, p(2) = 0.01
T-score — femoral neck	–2.15 ± 0.74	–1.98 ± 0.73	p(1) < 0.025, p(2) < 0.01
PR — femoral neck (%)	71.76 ± 9.86	74.16 ± 9.41	p(1) < 0.025, p(2) < 0.01
BMD L1 [g/cm2]	0.76 ± 0.13	0.74 ± 0.11	p(1) < 0.05, p(2) < 0.05
BMD L3 [g/cm2]	0.85 ± 0.17	0.83 ± 0.14	p(1) < 0.05
BMD L1–L4 [g/cm2]	0.83 ± 0.14	0.80 ± 0.11	p(1) < 0.05
T-score L1	–1.98 ± 1.19	–2.22 ± 0.96	p(2) < 0.05
T-score L3	–2.14 ± 1.51	–2.33 ± 1.24	p(1) < 0.05
T-score L1–L4	–1.98 ± 1.30	–2.21 ± 1.03	p(1) < 0.05
PR L1 (%)	77.83 ± 13.39	74.96 ± 10.53	p(2) < 0.05
PR L2 (%)	77.51 ± 14.06	76.44 ± 10.88	p(3) < 0.05
PR L3 (%)	78.17 ± 15.35	76.15 ± 12.25	p(1) < 0.05
PR L1–L4 (%)	78.93 ± 13.29	76.70 ± 10.57	p(1) < 0.05
Z-score L1	0.00 ± 1.27	–0.41 ± 1.08	p(1) < 0.01
Z-score L2	0.14 ± 1.44	–0.18 ± 1.19	p(2) < 0.05
Z-score L3	0.19 ± 1.64	–0.24 ± 1.36	p(2) < 0.005
Z-score L4	0.56 ± 1.72	0.16 ± 1.50	p(2) = 0.01
Z-score L1–L4	0.27 ± 1.45	–0.17 ± 1.20	p(1) < 0.01

BMC — bone mineral content; BMD — bone mineral density; PR — percentage of measured bone mineral density in relation to peak BMD

Table 2. *Frequency of stumbles and falls among subjects with (n = 143) and without (n = 179) vertebral compression fractures (VCFs)*

Frequency of stumbles and falls	Subjects with VCFs	Subjects without VCFs
Rarely (less than once a week)	128 (89.51%)	163 (91.05%)
Once a week	4 (2.80%)	2 (1.12%)
Not every day (but more often than once a week)	11 (7.69%)	11 (6.15%)
Every day	0 (0.00%)	3 (1.68%)

A comparison of statistically significant results of densitometric parameters is presented in Table 1. There was no difference between groups in the frequency of stumbles and falls, as shown in Table 2 (p = 0.658). In the DXA total body examination, there were no differences between groups in parameters such as the following: total weight, fat mass, muscle mass, total mass of bone and soft tissues, and percentage fat content in the upper and lower limbs, head, and trunk. The study

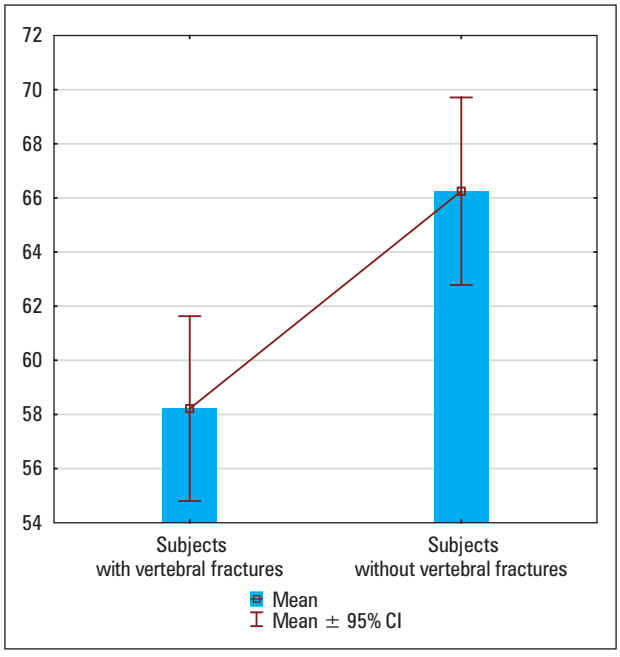

Figure 1. *Glomerular filtration rate according to Cockcroft-Gault formula (mL/min) in subjects with and without vertebral compression fractures (VCFs)*

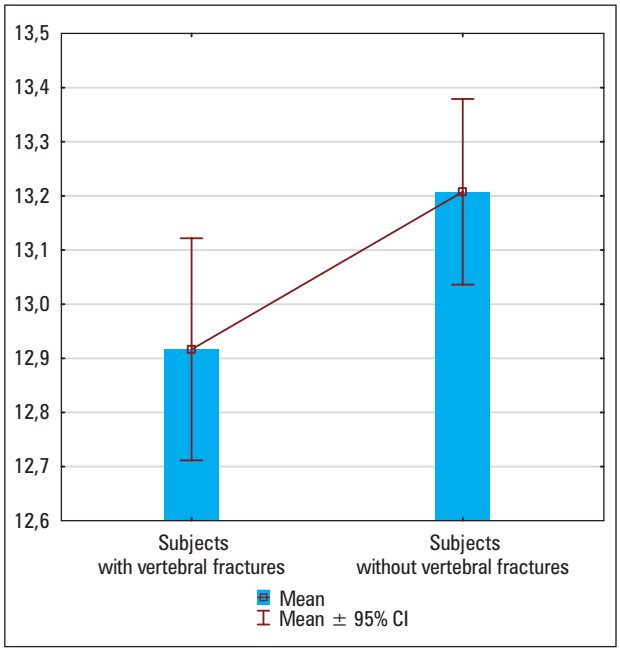

Figure 2. *Peripheral blood haemoglobin concentration [g/dL] among subjects with and without vertebral compression fractures (VCFs)*

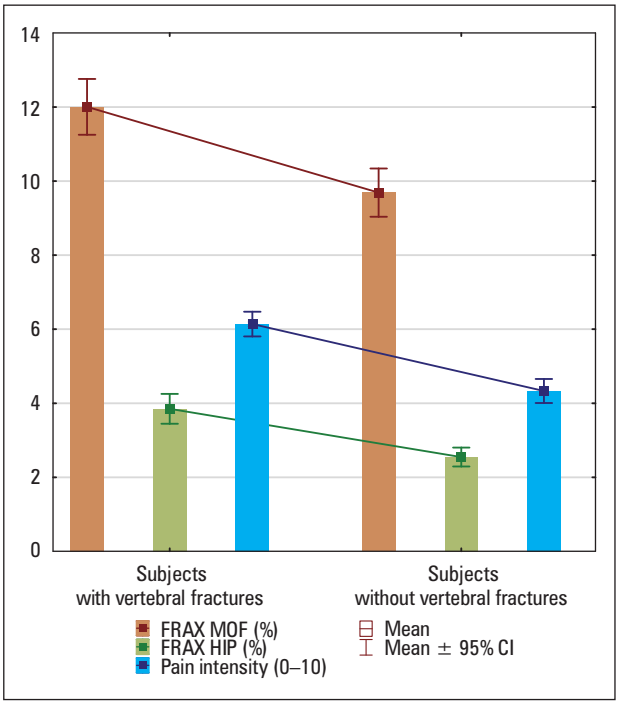

Figure 3. *Pain intensity and 10-year risk of major osteoporotic fracture (FRAX MOF) and hip fracture (FRAX HIP) among subjects with and without vertebral compression fractures (VCFs)*

groups also did not differ in terms of weight, volume, and surface of visceral adipose tissue, percentage of android and gynoid adipose tissue, as well as factors such as the following:

— the ratio of total body fat mass, expressed in kilograms, and the square of height, expressed in metres;
— the ratio of android and gynoid fat mass;
— the ratio of the percentage of body fat within the trunk and lower limbs;
— the ratio of the total soft tissue mass, expressed in kilograms, and the square of height, expressed in metres.

More severe back pain on an 11-point scale of pain intensity was found among patients with VCFs compared to those without (6.12 ± 2.09 and 4.29 ± 2.34, respectively), ($p[1] < 0.001$, $p[2] < 0.001$, $p[3] < 0.001$) (Fig. 3). Groups were not shown to differ in maximum individual height. We observed that patients with VCFs were characterised by greater growth loss – defined as the difference between maximum individual height and actual height (0.0587 m ± 0.039) — than subjects without VCFs (0.0364 m ± 0.026), ($p[1] < 0.001$, $p[2] < 0.001$, $p[3] < 0.001$).

Discussion

Patients with VCFs were over 4 years older than subjects without such fractures. Older age significantly increases the likelihood of VCFs [20, 21], and this is related to the greater advancement of osteoporosis in older patients [22, 23]. Subjects with previous VCFs were significantly shorter than patients without VCFs [24] and were characterised by much greater growth reduction [25]. Nevertheless, there was no significant difference between the groups in terms of maximum individual height; therefore, this parameter is irrelevant in the prediction of the presence of VCFs.

Due to the lack of differences between the groups in terms of total body weight as well as muscle mass, fat mass, and total bone mass, it can be concluded that the greater muscle mass, and thus better overall fitness and coordination, does not fulfil a protective role against VCFs [26]. Body fat content does not affect VCFs in any direction [27]. There is a cause-and-effect relationship: the lack of differentiation of groups in terms of total body weight and muscle mass causes a lack of differentiation in the degree of general fitness and coordination, which entails no significant difference in the frequency of stumbles and falls [26]. Therefore, injuries do not play a significant role in the prevalence of osteoporotic VCFs. In contrast to our results, in several reports the correlation between sarcopaenia [28, 29], visceral and subcutaneous adipose tissue [30], and increased risk of VCFs was confirmed.

A significantly lower value of GFR, calculated according to the Cockcroft-Gault formula, was found among patients with osteoporotic VCFs. The average

difference between the groups was > 8 mL/min. The results obtained by the authors are consistent with previous studies, because the lower GFR calculated according to the Cockcroft-Gault formula, mostly recommended for the elderly, is associated with a higher prevalence of VCFs [31]. Interestingly, no significant difference was observed for isolated creatinine serum concentration or for GFR calculated according to the MDRD formula [32, 33]. Irrespective of the glomerular filtration rate, among patients with type 2 diabetes association was demonstrated between albuminuria and higher frequency of VCFs [34]. The lack of differences in serum calcium and 25-hydroxyvitamin D concentration suggests that supplementation of calcium and vitamin D does not affect the likelihood of VCFs [35, 36]. Despite the significance of calcium and vitamin D supplementation in the course of osteoporosis, early diagnosis and the introduction of anti-resorptive therapy is most important to reduce the risk of VCFs [37]. The lower serum albumin concentration among patients with VCFs can be explained by the older age of these patients [38], but in the cross-sectional study performed by van der Jagt-Willems et al. [39], despite the lack of age difference between geriatric patients with and without VCFs, significantly lower serum albumin concentration among patients with VCFs was demonstrated. Several studies have shown an association between decreased haemoglobin level and an increased risk of non-vertebral fractures in men [40-42] as well as vertebral and non-vertebral fractures in women [42]. In addition, pernicious anaemia is associated with the prevalence of VCFs [43].

Reduced urinary calcium excretion in patients with VCFs can be explained by a higher frequency of anti-resorptive therapy used by these patients [44]. However, due to the small number of patients for whom this test was performed (n = 146) and the significant value obtained for only one statistical test, the result should be confirmed in further investigations.

According to parameters obtained from the densitometric examinations of the central skeleton, the higher bone mineral density of vertebral bodies in patients with VCFs is an obvious consequence of compression and condensing the same mass of bone mineral in a smaller volume [45] and does not contradict the proven relationship between reduced BMD of lumbar spine and increased risk of compression fractures [46]. Simultaneously in subjects with VCFs more advanced osteoporosis was confirmed by lower values of T-score of femoral neck and hip [47, 48].

The finding of a higher 10-year risk of major osteoporotic fracture and hip fracture among patients with VCFs confirms the results of previous studies [49] but can also be considered as a tool to assess the probability of the present undiagnosed VCFs [50]. Due to the greater severity of back pain among patients with VCFs, these fractures should not be considered as asymptomatic or even oligosymptomatic. Because of the spontaneous and non-traumatic nature of this type of fractures, unawareness among patients, and often also among healthcare workers, of the high frequency of spontaneous VCFs in the course of osteoporosis and the common occurrence of back pain in older age, the severity of back pain is often underreported. Even if the severity of pain is reported by the patient, it is often associated with osteoarthritis. At the same time, it should not be assumed that the detected difference in the severity of pain is caused entirely by degenerative changes in patients with or without VCFs.

The main limitation of the study is to include only hospitalised patients or patients remaining under the care of one osteoporosis clinic, so results obtained by authors cannot be extended to the whole population. The size of the study group is relatively small, and further investigations are required to confirm our findings. However, this study is based on one of the first such surveys performed in Poland.

Conclusions

Among patients with diagnosed postmenopausal osteoporosis and the presence of VCFs, in comparison to patients without this type of fractures, the following were demonstrated: a significant loss of growth, lower GFR calculated according to Cockcroft-Gault formula, lower peripheral blood haemoglobin concentration and serum albumin concentration, lower BMD and T-score of femoral neck and hip in DXA examination, an increased 10-year risk of major osteoporotic fracture and hip fracture according to FRAX calculator, and at least moderate severity of back pain. Further studies are required to validate the FRAX calculator to assess not only the risk of future fractures but also unrecognised VCFs.

Conflicts of interest

All authors have no conflicts of interest to declare in relation to this article.

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