Prediction of asymptomatic vertebral fractures by selected clinical risk factors

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SÚHRN

Killinger Z., Čierny D., Jackuliak P., Kužma M., Payer J.: **Predikcia asymptomatických vertebrálnych fraktúr pomocou vybraných klinických rizikových faktorov**

Úvod: Zlomeniny stavcov (VFX) sú asociované so zvýšenou morbiditou a mortalitou a výrazne zhoršujú kvalitu života pacientov s osteoporózou. V klinickej praxi sú vertebrálne fraktúry (dokonca aj stredne ťažkého a ťažkého stupňa) veľmi často nediagnostikované, a preto aj neliečené.

Cieľ štúdie: Stanoviť prevalenciu vertebrálnych fraktúr s využitím bočného zobrazovacieho skenu chrbtice pri meraní kostnej denzity (DXA) u dvoch rôznych rizikových skupín pacientov. 1. skupinu tvoria pacienti odoslaní na meranie kostnej denzity (BMD) na základe štandardných kritérií Medzinárodnej spoločnosti pre klinickú denzitometriu (ISCD) a druhú skupinu pacienti selektovaní na základe vybraných jednoduchých klinických rizikových faktorov. Sekundárnym cieľom bolo posúdenie korelácií medzi vybranými rizikovými faktormi a vertebrálnymi fraktúrami.

Pacienti a metódy: Anyalyzovali sme 277 postmenopauzálnych žien odoslaných na meranie kostnej denzity, ktoré boli rozdelené do dvoch rizikových skupín. Skupina 1 (n = 147, priemerný vek 75,3 roka) pozostáva z pacientiek spĺňajúcich kritériá ISCD pre meranie BMD. Skupina 2 (n = 130, priemerný vek 77,6 roka) pozostáva z pacientiek vybraných na základe prítomnosti ďalšieho aspoň jedného rizikového faktora z nasledujúcich: strata výšky viacej ako 3 cm, vzdialenosť tyla od steny viac ako 0 cm, vzdialenosť medzi posledným rebom a lopatou panvovej kosti menej ako 2 prsty, hmotnosťou menej ako 51 kg, alebo počet zubov pod 20. Hodnotenie zlomenín stavcov bolo založené na zhodnotení bočného zobrazovacieho skenu pri DXA, pričom na klasifikáciu závažnosti fraktúr bolo použité semi-kvantitatívne hodnotenie podľa Genanta.

Výsledky: Zistili sme v skupine pacientov vybraných na základe klinických rizikových faktorov významne vyšší počet zlomenín stavcov (67 %) v porovnaní s neselektovanou skupinou, kde bolo detegovaných „iba" 32 % zlomenín stavcov. Rozdiel vo výskyte viacpočetných a závažných zlomenín stavcov medzi oboma skupinami bol ešte vyšší (56 % vs. 6 % a 16 % vs. 6 % v uvedenom poradí). Okrem toho 20 % pacientov s diagnostikovanou fraktúrou malo kostnú denzitu v pásme osteopénie.

Záver: Použitie týchto jednoduchých klinických rizikových faktorov, ako aj použitie DXA metódy pre detekciu zlomenín stavcov sú schopné v klinickej praxi zvýšiť podiel pacientov s diagnostikovanou asymptomatickou VFX. Bez tohto merania by mnohí z týchto pacientov zostali bez liečby, pretože nespĺňajú kritériá pre začatie antiporotickej liečby (na základe nameranej BMD, alebo na základe anamnézy prekonanej osteoporotickej zlomeniny po neadekvátnej traume). Detekcia zlomenín stavcov (aj asymptomatických) s následným zahájením antiporotickej liečby môže výrazne znížiť riziko následných zlomenín v tejto veľmi vysoko rizikovej skupine.

Kľúčové slová: zlomeniny stavcov, osteoporóza, bočný denzitometrický sken, meranie kostnej denzity

SUMMARY

Killinger Z., Čierny D., Jackuliak P., Kužma M., Payer J.: **Prediction of asymptomatic vertebral fractures by selected clinical risk factors**

Introduction: In clinical practice vertebral fractures (VFx) are associated with increased morbidity and mortality and significantly impaired quality of life in patients suffering from osteoporosis. In clinical practice VFx (even moderate and severe) are very often undiagnosed and untreated.

The aim of the study: To asses the prevalence of vertebral fractures using lateral spine imaging by dual-energy x-ray absorptiometry (DXA) in two different risk groups (1) patients referred for bone mineral density (BMD) testing according to International Society for Clinical Densitometry (ISCD) recommendations, (2) patients selected according to additional simple clinical risk factors. The second end-point was to assess a correlation between selected risk factors and vertebral fractures.

Patients and methods: 277 postmenopausal women sent for BMD testing, were divided in two risk groups. Group 1 (n = 147, mean age 75.3 years) consist of patients referred for BMD testing according to ISCD criteria. Group 2 (n = 130,

mean age 77.6 years) consist of patients selected by additional clinical risk factors as loss of height more than 3 cm, thoracic kyphosis and occiput to wall distance more than 0 cm, "Rib – pelvis" distance below 2 fingers, weight below 51 kg and number of teeth below 20. Vertebral fracture detection in both groups was based on lateral spine imaging by dual-energy x-ray absorptiometry (DXA). Semi-quantitative method according to Genant was used for fracture severity classification.

Results: We found in patients selected according to simple clinical tests a significantly higher number of vertebral fractures (67 %) in comparison to non-selected patients group, where "only" 32 % of vertebral fractures were detected. The difference in multiple and severe fractures occurrence between both groups was even higher (56 % vs 6 % and 16 % vs 6 % respectively). In addition, 20 % of the patients diagnosed as fractured had a BMD in osteopenic range.

Conclusion: The use of these simple tests as well as the use of non invasive DXA method for vertebral fracture recognition is able to improve the proportion of patients identified as having asymptomatic VFx in clinical practice. Without this measurement these patients will remain untreated, because many of them do not meet the criteria for treatment initiation (osteoporosis based on BMD or prior history of low trauma osteoporotic fracture). Recognition of vertebral fractures (even asymptomatic) followed by antiporotic treatment can significantly decrease the risk of subsequent fractures in this very high risk group.

Keywords: vertebral fractures, osteoporosis, lateral densitometric scan, BMD testing

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Introduction

A significant increase in the age-adjusted incidence of osteoporotic fractures has been reported from many countries and osteoporosis will become an increasing public health problem in the future due to the world's aging population. Osteoporosis is a disease that may cause no symptoms until a fracture occurs. Vertebral fractures (VFx) are the most common type of fragility fracture with their prevalence increasing with age. At 80 years of age, the prevalence of vertebral fractures is about 25 % [1].

Fractures of the spine are associated with reduced pulmonary function, chronic back pain, loss of height, kyphosis, loss of self-esteem, abdominal discomfort, disability, loss of independence and contribute to the increased morbidity and mortality of patients suffering from osteoporosis [2]. Patients with prior vertebral fractures, including not clinically recognized, are associated with 4 to 5 fold increased risk of future spinal fractures. 20 % of patients will develop a new vertebral fracture within one year independent of their bone mineral density (BMD). Many patients with VFx do not meet the criteria for osteoporosis according to BMD measurement [3]. It means, that treatment decision based on BMD alone, overlooks many individuals who are at high risk of sustaining VFx and who might therefore benefit from therapeutic intervention. Vertebral fractures are a much more important factor in determining therapeutic interventions than low bone mineral density (BMD) [4].

Recognition of asymptomatic vertebral fractures may change our clinical management. The International Osteoporosis Foundation recommends that patients with a prior low trauma VFx should receive drug therapy regardless of BMD results [5]. From a clinical point of view it is important to detect vertebral fractures in asymptomatic patients and to start the treatment in an effort to avoid the next fracture.

In clinical practice, X-raying of the spine is an infrequent examination also in patients who complain of back pain (due to many reasons such as radiation, cost, availability, etc). In patients who do not complain of back pain, the likelihood of performing a spinal x-ray is even lower. Another well known problem is, that vertebral deformities are often not recognized. This is especially true for mild and moderate vertebral deformities which commonly escape the attention of radiologists. In many cases it is common in practice that VFx that are visible on X-rays are not reported by radiologists [6]. Under-diagnosis of VFx the rate of false-negative results on spinal X-rays worldwide has been 30–45 % [7].

In the last few years, lateral spine imaging with VFx assessment (VFA) by dual-energy x-ray absorptiometry (DXA) has been used. VFA is a relatively new technology than can reliably and accurately diagnose VFx with greater patient convenience, minimal radiation exposure, and lower cost than the standard spinal radiography. An important advantage of VFA is that it can be done with the same densitometer, in same sit-

ting [8]. The clinical utility of VFA has led many clinicians to recommend its use as a complement to BMD testing to identify the patients most likely to benefit from pharmacological therapy especially those with osteopenia, who might otherwise be untreated.

For identification of patients with vertebral fractures it is of the essence to know risk factors that provide an accurate basis for referral for further investigation such as VFA or simple X-ray. Several simple clinical factors such as decreased height of patient, decreased lower chest margin to upper pelvis border distance and decreased occiput to wall distance, presence of thoracic kyphosis, low number of teeth or low weight may increase the proportion of patients diagnosed as having a vertebral fracture when referred to VFA testing [9].

Unfortunately, the correlation between these risk factors and vertebral fractures in different ethnic groups has not been conclusively proven [10].

Aim of the study

1. To assess the prevalence of asymptomatic vertebral fractures using lateral spine imaging by DXA in patients referred for BMD testing.
2. To compare the prevalence of vertebral fractures between a group of patients referred for BMD testing according to standard ISCD (International Society for Clinical Densitometry) recommendations and the group of patients selected by additional simple clinical risk factors.
3. To assess the correlation between selected risk factors and vertebral fractures.

Patients and methods

Prior to data collection, the study protocol had been approved by the Comenius University and University Hospital research boards. The regional medical ethics committee also approved the study. All subjects prior to study inclusion signed informed consent.

We included a total of 277 postmenopausal women with low bone mineral density defined according to WHO criteria as osteopenia (T-score from –1 to –2.5SD) or osteoporosis (T-score below –2.5 SD) referred to BMD testing by their GP (*Table 1*). *Group I* consisted of 147 women, which fulfilled the criteria for BMD testing according to International Society for Clinical Densitometry (ISCD) without any other risk factors. The ISCD indications for BMD testing are in *Table 2*. *Group II* consisted of 130 patients selected according to additional clinical risk factors (at least one) listed in *Table 3*.

Wall-occiput distance was defined as inability to touch occiput to the wall when standing with back and heels to the wall. *Low rib-pelvis distance* was defined as less than 2 finger breadths between the inferior margin of the ribs and the superior surface of the pelvis in the midaxillary line.

Evaluation of VFx was performed on densitometer (Hologic, Discovery) using a special software – instant vertebral assessment (IVA) (*Fig. 1*). The vertebral fractures and their severity were classified using semiquantitative method according to the Genant s classification. This method classifies VFs as :

- Grade 1 or mild (20–25 % loss of vertebral height).
- Grade 2 or moderate (25–40 % loss of vertebral height).
- Grade 3 or severe (greater than 40 % loss of vertebral height).

Examiners in our study did not know whether the patient belongs to the group I or II.

Statistical significance of correlations among selected risk factors was based on Pearson s correlations and Kruskall-Wallis test.

Table 1
Characteristic of patients

	Group I	Group II
Number of patients	147	130
Age range	52–84 years	59–89 years
Mean age	75.3 ± 8,6 years	77.6 ± 7,9 years
Years after menopause	25.8 ± 2,1 years	28.3 ± 1,4 year

Table 2
ISCD recommendations for BMD testing

Women aged 65 and older	
Postmenopausal women	- Low body weight
younger than age 65	- Prior fracture
if they have	- High risk medication use
a risk factor as:	- Disease or condition associated with bone loss

Table 3
Additional selected risk factors in group II and numbers of patients with risk factors

Risk factor	Number of patients
Weight below 51 kg	32 pts
Loss of high more than 3 cm	82 pts
Thoracic kyphosis	56 pts
Number of teeth below 20	94 pts
"Rib – pelvis" distance below 2 fingers	37 pts
Occiput to wall distance more than 0 cm	59 pts

Figure 1
Vertebral fractures visualized by DXA scan

Results

From total number of 277 patients 147 patients belonged to group I (mean age 75,3 years) and 130 to group II (mean age 77,6 years) (see *Table 1*). Number and severity of the vertebral fractures in each group are listed in *Table 4*. In the group I, 47 (32 %) patients were identified to have vertebral fracture, from whom 3 (6 %) had a multiple fracture, mostly grade 1. In the group II a greater number (87; 67 %) of fractures were identified. 44 (56,6 %) patients had multiple fractures, mostly grade 1 or 2. Correlations between selected risk factors, BMD and fractures are in *Table 5*. A significant correlations were found in grade 2 fractures between BMI, weight and kyphosis. DXA was positively associated with rib-pelvis distance, kyphosis wall-occiput distance and BMI.

Discussion

Our study identified in the group 1 (selected according to the standard ISCD recommendations for BMD testing) 32 % patients (with no prior history of VFx) with vertebral fractures. The prevalence of fractures was significantly higher than expected VFx prevalence in the general population of the same mean age [11,12]. It means that use of ISCD recommendations in clinical practice is capable of selecting more patients with VFx compared to non-selected population. In the group of patients selected according to the above mentioned additional clinical risk factors, published by Green et al. [13] we even found two times higher VFx prevalence (67 %). 47 % fractures in this group were classified as moderate or severe compared to only 16 % in the group without these additional risk factors. The most important finding in our study was the difference in multiple vertebral fractures. We found multiple fractures in 56 % of pts in the risk group vs 6 % in the standard group. Multiple fractures, especially moderate or severe, are the most significant with regard to morbidity, mortality and decreased quality of life. In addition, 20 % of the patients diagnosed as fractured had a BMD results in osteopenic range. Without knowledge of VFx occurrence, these osteopenic women might not have been considered for antiporotic therapy. Netelenbos found the same proportion of vertebral fractures (21 %) in osteopenic patients with clinical risk factor using spinal radiographs for fracture detection [14]. Based on high proportion of patients diagnosed as having VFx and differences between both groups in fracture prevalence, the described simple clinical test proved to be sufficiently sensitive detection criterion.

In recent years, there have been a clear tendency to move the treatment decision from BMD based interventional threshold to threshold based on individual risk of fracture. Fracture Risk Assessment Tool (FRAX) was introduced as a clinical tool to evaluate

an individual's 10 year probability in sustaining a femoral neck or other major osteoporotic fractures and is based on clinical risk factors [4]. The presence of a fragility fracture is considered as one of the most important risk factors in FRAX tool and can significantly increase estimated fracture risk. National Osteoporosis Foundation (NOF) in US recommends antiporotic treatment if the fracture risk exceeds 3 % for femoral neck fractures and 20 % for other major osteoporotic fractures. In most countries by FRAX recommended interventional threshold is not accepted. Chen et al. used spinal fracture status, along with age and BMD and predicted future fracture risk with greater simplicity and higher prognostic accuracy compared to using risk factor criteria such as those used in the FRAX tool [15]. Our results show the statistically significant correlation between grade II fractures and BMI, weight and kyphosis and grade III fractures and kyphosis. We found significant correlations between BMD and both "*occiput-wall distance*" and presence of the kyphosis. Correlations among other selected clinical parameters and fractures did not reach statistical significance.

The limitation of our study was the relatively small sample of patients, which may have contributed to only a borderline significance of correlations between the other clinical risk factors mentioned and spinal fractures. Another limitation of the study was relatively poor quality of DXA scans in the upper part of thoracic spine. On the other hand, vertebral fractures mostly occur in the region of thoracic – lumbar junction.

Table 4
Numbers and severity of the vertebral fractures in both groups

	Group I	Group II
Number of patients	147	130
Patients with fracture	47 (32 %)	87 (67 %)
Patients with multiple fracture	3 (6 %)	44 (56.6 %)
Number of fractured vertebrae	50	172
Mild fracture (grade 1)	42 (84 %)	93 (54 %)
Moderate fracture (grade 2)	5 (10 %)	51 (30 %)
Severe fracture (grade 3)	3 (6%)	28 (16%)
Number of patients with		
1 fracture	44	43
2 fractures	3	24
3 fractures	0	7
4 fractures	0	6
5 fractures	0	6
6 fractures	0	1

Table 5
Correlations between fractures, risk factors and BMD

	Level of significance	Coefficient of correlation
Correlation with fracture		
Grade 2 fractures/BMI	$p < 0{,}0198$	–0.521
Grade 2 fractures/weigh	$p < 0{,}0458$	–0.458
Grade 2 fractures/kyphosis	$p < 0{,}0429$	0.494
Grade 3 fractures/kyphosis	$p < 0{,}0389$	0.574
Correlation with densiometry		
DXA femur/rib-pelvis distance	$p < 0{,}0143$	0.369
DXA spine/rib-pelvis distance	$p < 0{,}0334$	0.327
DXA femur/kyphosis	$p < 0{,}0056$	0.397
DXA femur/wall-occiput distance	$p < 0{,}0005$	0.472
DXA femur/BMI	$p < 0{,}0002$	0.403

Conclusions

Vertebral fractures are the most common type of osteoporotic fracture and in daily practice, high proportion of patients with VFx are not recognised and therefore not treated appropriately [16].

Vertebral fracture assessment using lateral DXA scan is new quick and non-invasive method that allows health practitioners to identify VFx in high risk individuals during routine BMD testing. The use of selected simple clinical criteria can significantly improve the proportion of patients diagnosed as having the vertebral fracture. The test is simple, takes no more than 5 minutes and can be done in outpatient clinic without any specific equipment.

Early detection of vertebral fractures may alter fracture risk stratification, and help identify patients likely to benefit from pharmacological therapy who otherwise might not be treated.

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