

Vertebral fracture assessment in postmenopausal women with low bone mass: prevalence and risk factors

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Objective The study aimed to use VFA to determine the prevalence of and risk factors associated with unnoticed VFs in postmenopausal women with low bone mass.

Methods A total of 330 consecutive postmenopausal patients with a mean age of 62.7 years (range 43 to 85 years) who had been diagnosed with low bone mass by bone mineral densitometry (BMD) with a T-score between -1.0 and -2.5 and who had undergone VFA study were retrospectively reviewed. No prior vertebral or non-vertebral fragility fractures had been observed in any of the patients. The VFAs were performed in a supine position using Hologic Discovery A. VFA interpretation was done independently by two experienced nuclear medicine physicians using a combination of the Genant visual semi-quantitative method and morphometric measurement. Demographic data from the medical records and questionnaires were reviewed.

Results The prevalence of VFs was 25.8%. Of those, 9.1% had Grade 1 and 16.7% had Grade 2 and/or 3 fractures. VFs were identified in 165 vertebrae of 85 patients who had VFs. Of which 49.7% were wedge and 50.3% were biconcave fractures but without crush fracture. The thoracolumbar junction (T11-L2) was the most common site of VFs. The interobserver agreement between the two nuclear medicine physicians was very good (Cohen's kappa=0.89). Age, years since menopause, and steroid use were identified as independent risk factors.

Conclusion As VFA detected unnoticed VFs in one fourth of postmenopausal women with low bone mass, an additional VFA at the time of BMD study should be considered for this group of patients.

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Keywords: vertebral fracture assessment, low bone mass, postmenopausal women

Introduction

Osteoporosis is a silent disease in which there is no evidence of a problem until a fracture occurs. Osteoporotic fractures can occur anywhere in the skeleton, but the most common sites are the femoral neck, lumbar, and thoracic vertebrae (1).

Almost half of osteoporotic vertebral fractures (VFs) that occur are unnoticed by the individual. VFs occur primarily in women with low bone mass (2), especially postmenopausal women (3,4). Low bone mass, referred to as osteopenia, is defined as a bone mineral density T-score between

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-1.0 and -2.5 (5). Detection of VFs in patients with low bone mass can lead to a change of diagnosis from osteopenia to osteoporosis. In individuals with VF, the likelihood of having additional vertebral or non-vertebral fractures rises 3-fold (6). The incidence of a second VF within one year in untreated subjects has been reported to be 20% (7). Prevalence of VFs is associated with an increased risk of mortality (8) and has a negative effect on quality of life (9). Many pharmacologic therapies can significantly reduce the risk of VF. Therefore, appropriate therapy should be offered as soon as practical when a VF is diagnosed (10). Early detection of asymptomatic fractures can help improve the outcome of treatment and reduce the incidence of future osteoporotic fractures at other sites (11).

The standard method of assessing VFs is a lateral spine radiograph. However, vertebral fracture assessment (VFA) is also a useful technique (12, 13). The advantage of VFA over routine x-rays of the lateral thoracolumbar spine is that it results in much less radiation exposure. In addition, images can be collected at the same time as bone densitometry measurement (14), making the process easier for both the patient and the technician.

Objectives

The objective of the present study was to use VFA to determine the prevalence of and risk factors associated with VFs in postmenopausal women with low bone mass to allow assessment of current recommendations regarding performing VFA in postmenopausal women with low bone mass and to aid patients and physicians in choosing appropriate treatments for osteoporosis.

Methods

Patients

This observational and retrospective study enrolled 330 consecutive postmenopausal patients with a mean age of 62.7 years (range 43 to 85 years) who had been diagnosed with low bone mass based on bone mineral densitometry (BMD) and who had currently undergone a VFA study. The research was conducted at the Division of

Nuclear Medicine, Department of Radiology, Faculty of Medicine, Chiang Mai University between January 2015 and June 2017. All the patients had had amenorrhea for more than one year and had had no identified vertebral or fragility fractures. Demographic data were obtained from medical records and questionnaires. Patient characteristics are summarized in Table 1.

Imaging protocol

VFAs were obtained in the supine position from T4 to L4 using Hologic Discovery A (Hologic Company, Marlborough, Massachusetts, United States). High definition scans were performed with a scan length of 39.9 cm, a scan width of 14.5 cm, line spacing of 0.0241 cm, point resolution of 0.1258 cm with 5.69x0.03 cdl, 140x140 kVp, at an average of 5 mA for 18 seconds at 50 Hz.

Image interpretation

VFAs were classified independently by two experienced radiologists using the Genant visual semi-quantitative approach (15). Three types of VFs were identified: wedge, biconcave, and crush.

Table 1. Patient characteristics

Clinical Characteristics	Mean±SD (range)
Number of Patients	330
Age	62.7±8.8 (43-85)
Age at menopause	48.9±5.0 (25-60)
Years since menopause	13.8±9.3 (0-59)
BMI (kg/m ²)	24.9±3.6 (15.2-35.6)
BMD	
Lumbar spine	0.8513±0.09 (0.705-1.314)
Proximal femur	0.6297±0.06 (0.522-0.833)
T-Score (SD)	
Lumbar spine	-1.3±0.8 (-2.4-+2.7)
Proximal femur	-1.6±0.8 (-2.4-+2.1)
Z-Score (SD)	
Lumbar spine	+0.4±0.8 (-1.6-+3.5)
Proximal femur	+0.0±0.7 (-1.7-+3.1)
Other factors	
Parental hip fracture (%)	43 (13.0)
Steroid use (%)	20 (6.1)
Smoking (%)	10 (3.0)

These fractures are characterized by the prominently decreased height of the anterior part, the biconcave middle part, and the crushed posterior part or the total vertebrae, respectively. Three degrees of severity were confirmed by quantitative morphometric methods (16). Six points were placed on the vertebral body: at the anterior, middle, and posterior points of the upper and the inferior endplates. Reductions in anterior or mid vertebral height in relation to posterior height or reductions in posterior height in relation to posterior height of the adjacent vertebrae were classified as mild (Grade 1; 20 to 25%), moderate (Grade 2; between 25 to 40%), or severe (Grade 3; more than 40%). Unidentifiable vertebrae between T4 to L4 were also recorded. Any non-consensual readings were reviewed, and agreement was reached.

Statistical analysis

IBM Statistical Package for Social Sciences (SPSS) 25.0 software was used for statistical calculations. Demographic and clinical characteristics are shown as mean, standard deviation, and range. The prevalence of VFs, type and degree of VFs, and the number of unidentifiable vertebrae are presented as a percentage. Correlation between VFs and age, years since menopause, body mass index (BMI), BMD, T-score and Z-score of total lumbar spines (L1-L4) and proximal femurs, history of parental hip fractures, smoking, and steroid uses were analyzed using independent sample t-tests with a 95% confidential interval. The interobserver agreement between the two nuclear medicine physicians was calculated using Cohen's kappa statistic.

Ethics approval

The present study was approved by Research Ethics Committee of the Faculty of Medicine, Chiang Mai University (study code: RAD-2560-05203). For this type of study formal consent of the patient is not required. This research did not involve any animal experiments.

Results

Identifiable vertebrae and VFs on VFA

Out of 330 patients, unnoticed VFs were identified in 85 patients (25.8%). Thirty patients (9.1%) had fractures of Grade 1 and 55 patients (16.7%) had Grade 2 and/or 3 (Figure 1). The number (%) of patients with 1, 2, 3, 4, and 5 VFs was 38 (11.5), 23 (7.0), 16 (4.8), 7 (2.1), and 1 (0.3), respectively.

VFs were identified in 165 vertebrae. The number (%) of Grade 1, Grade 2, and Grade 3 VFs was 78 (47.3), 61 (37.0), and 26 (15.8), respectively. There were 82 (49.7%) wedge and 83 (50.3%) biconcave fractures without crush fracture. The most common site of VFs was at L1 level, followed by T12, T11, L2, L3, T10, L4, and T9 where the number (%) of VFs was 48 (29.1), 38 (23.0), 28 (17.0), 26 (15.8), 13 (7.9), 6 (3.6), 4 (2.4), and 2 (1.2), respectively (Figure 2). The agreement between the two nuclear medicine physicians for the presence of VFs from T4-L4 was 0.89.

In 209 patients (63.3%) it was possible to identify all the vertebrae from T4 to L4, while in 268 patients (81.2%) it was possible to identify all T7 to L4 vertebrae. The percentage of identifiable vertebrae was as follows: T4 (67.9), T5 (71.2), T6 (80.6), T7 (83.0), T8 (90.6), T9 (95.8),

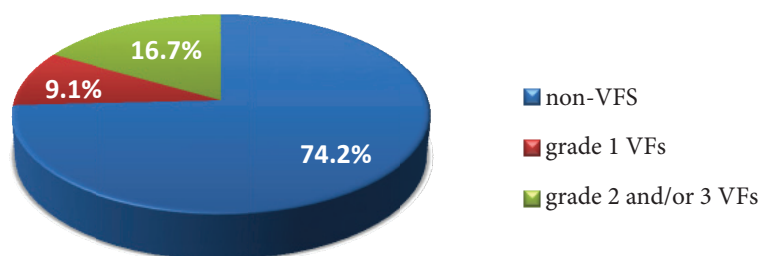


Figure 1. Percentage of patients with non-VFs, Grade 1 VFs, and Grade 2 and/or 3 VFs

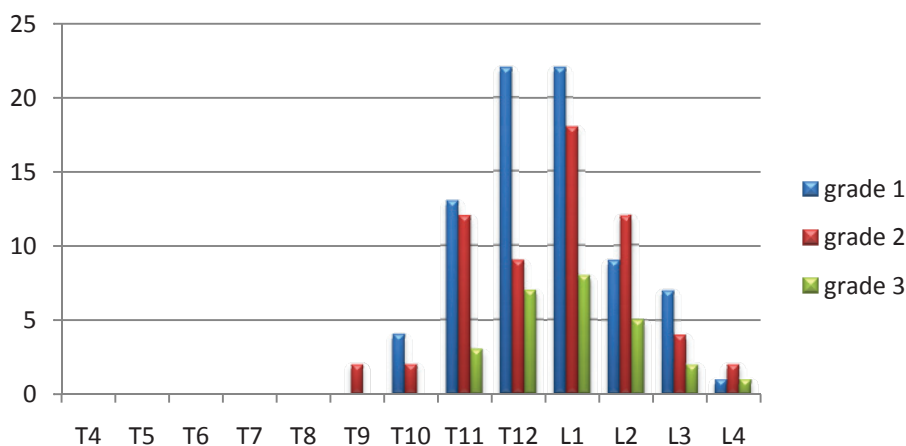


Figure 2. Number of VFs of Grade 1, 2 and 3 from T4 to L4

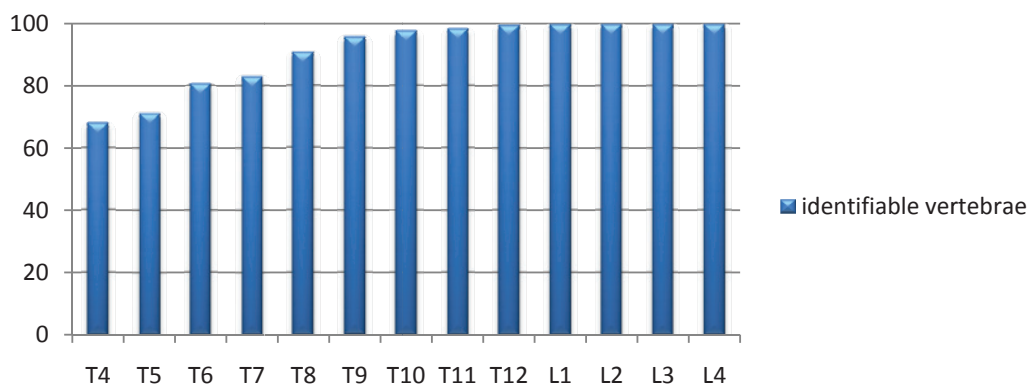


Figure 3. Percentage of identifiable vertebrae from T4 to L4

T10 (97.6), T11 (98.2), T12 (99.4), L1 (99.7), L2 (99.7), L3 (99.7), and L4 (99.7).

Comparison of quantitative variables in the VFs and non-VFs groups are shown in Table 2. Age, years since menopause, history of parental hip fracture, and steroid use were significantly different between patients with VFs and those without VFs.

Discussion

VFAs detected unnoticed VFs in 25.8% of patients (16.7% grade 2 and/or 3 VFs) in postmenopausal women with low bone mass. The prevalence of VFs was consistent with publications which found asymptomatic VFs in approximately one quarter of patients. Muschitz C et al reported 22.6% of VFs in elderly women

with osteopenia (17). Negreiros CC et al found asymptomatic VFs in 24.4% of osteopenia subjects (18). Schousboe JT et al reported VFs in 21.3% of postmenopausal women age over 60 years who had osteopenia according to WHO criteria (19). However, other publications reported a much higher prevalence of VFs. El Maghraoui A et al found a 38.5% prevalence of VFA-detected fractures in postmenopausal Moroccan women with osteopenia (15.7% had grade 2 and/or 3 VFs) (11). This differences among the studies could be related to differences in ethnicity as well as epidemiological heterogeneity in VFs among Asians and Caucasians. VFs are more common among Caucasian women than among people of African-American or Asian ethnicity (20, 21). The prevalence of VFs in the present study was similar to

Table 2. Comparison of clinical characteristics of non-VFs and VFs patients

	Non-vertebral fracture mean±SD (range)	Vertebral fracture mean±SD (range)	p-value
Number (%) of Patients	245 (74.2)	85 (25.8)	
Age	61.4±8.2 (43-81)	66.2±9.6 (48-85)	0.015*
Menopause Age	48.9±4.9 (32-60)	49.0±5.5 (25-59)	0.716
Years Since Menopause	12.5±8.3 (0-37)	17.5±11.1 (0-59)	0.001*
BMI (kg/m ²)	24.74±3.7 (15.2-35.5)	25.4±3.3 (18.7-35.6)	0.227
BMD			
Lumbar spine	0.8541±0.09 (0.730-1.314)	0.8431±0.09 (0.705-1.131)	0.659
Proximal femur	0.6328±0.06 (0.522-0.833)	0.6205±0.05 (0.543-0.817)	0.769
T-Score (SD)			
Lumbar spine	-1.3±0.8 (-2.4-+2.7)	-1.4±0.7 (-2.4-+1.1)	0.466
Proximal femur	-1.6±0.6 (-2.4-+2.1)	-1.7±0.5 (-2.4-+0.1)	0.657
Z-Score (SD)			
Lumbar spine	+0.4±0.8 (-1.6-+3.5)	+0.5±0.8 (-1.2-+2.6)	0.639
Proximal Femur	+0.0±0.7 (-1.7-+2.1)	+0.1±0.7 (-1.6-+3.1)	0.672
Parental Hip Fracture (%)	35 (14.3)	8 (9.4)	0.018*
Steroids Use (%)	12 (4.9)	8 (9.4)	0.003*
Smoking (%)	8 (3.3)	2 (2.4)	0.401

*Statistically significant

that in Caucasian populations and corresponds to the prevalence reported in studies done in Bangkok and Vietnam (22, 23).

The reason for caution in interpretation of VFAs is that there can be differences in interpretation between radiologists in diagnosis of Grade 1 VF. There has been less consistency in diagnosis of Grade 1 VF than with Grade 2 and/or 3 VF reported (24-26). Nevertheless, Grade 1 VFs are not associated with future fractures to the same degree as higher Grade VFs (27). Therefore, in the absence of other risk factors, osteoporosis pharmacotherapy is often postponed (28). In our study, almost 17% of the subjects had Grade 2 and/or 3 VFs.

There are some limitations in using VFAs to evaluate the upper thoracic vertebrae. In our study, only 67.9% of T4, 71.2% of T5, and 80.6% of T6 could be adequately visualized. This rate is similar to previous reports (29, 30). Artifacts from great vessels and mediastinal structures may obscure vertebral structures. Because VFs are most common in the thoracolumbar junction (30), as was the case in this study, and osteoporotic

fractures of the upper thoracic vertebrae without concurrent fractures at the thoracolumbar junction rarely occur, unidentifiable vertebrae at the upper thoracic levels are of much less concern. However, unidentifiable vertebrae between T7-L4 should be followed up with other imaging studies (31).

Our study identified advanced age, years since menopause, and steroid use as the independent risk factors. VFs have been directly correlated with increasing age (32,33). Bone density begins to decrease after age 40 for both men and women, and the process rapidly accelerates in postmenopausal women (34,35), so the longer the time since menopause, the lower the bone density. Glucocorticoid therapy is the most common cause of secondary osteoporosis and osteoporotic-induced fractures (36). Treatment with 10 mg/d of prednisone or equivalent for more than three months leads to a 7-fold increase in hip fractures and a 17-fold increase in VFs (37). Prednisone at doses below 2.5 mg/d has also been documented to increase the relative risk of VF (38). Parental hip fracture could be an incidental independent

risk factor. The non-VF group had a significantly higher frequency of parental hip fracture than the VF group. Some of the risk factors for osteoporotic VFs identified in our study have not been previously reported in the literature (39). Smoking is associated with lower rates of VF. Other factors, including age at menopause, BMD, and BMI, were not significantly different between the groups. The difficulty in identifying risk factors is that osteoporosis is a multifactorial disease which involves both endogenous and environmental factors (40). Additional co-morbid medical conditions of the patients in this study may not have been recognized.

A limitation of the current study is that our sample was not representative of the general population. The subjects were all drawn from an academic hospital setting and all had been referred by physicians for BMD evaluation. The study did, however, reflect the population seen in routine clinical practice.

Conclusion

Among postmenopausal women with low bone mass, treatment decisions based on bone mineral density alone can lead to women not receiving proper treatment. Additional VFA at the time of BMD evaluation should be considered for postmenopausal women with low bone mass.

Conflicts of interest

None

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การตรวจประเมินกระดูกสันหลังหักในหญิงวัยหมดประจำเดือน: ความชุกและปัจจัยเสี่ยง

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ภาควิชารังสีวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

วัตถุประสงค์ การวิจัยนี้มีเป้าหมายเพื่อประเมินความชุกและปัจจัยเสี่ยงของกระดูกสันหลังหักที่ไม่เคยทราบมาก่อนในหญิงวัยหมดประจำเดือนที่มีมวลกระดูกต่ำโดยการตรวจ VFA

วิธีการ หญิงวัยหมดประจำเดือน 330 รายซึ่งมีอายุเฉลี่ย 62.7 ปี, ระหว่าง 43-85 ปี, ที่ได้รับการวินิจฉัยว่ามีมวลกระดูกต่ำจากการตรวจหาความหนาแน่นของมวลกระดูก (BMD) ซึ่งมีค่า T-score ระหว่าง -1.0 และ -2.5 และได้รับการตรวจ VFA ในคราวเดียวกับการตรวจ BMD ถูกทบทวนแบบย้อนหลัง ผู้ป่วยไม่เคยทราบมาก่อนว่ามีการแตกหักของกระดูกสันหลังหรือกระดูกที่ไม่ใช่กระดูกสันหลัง การตรวจ VFA ทำในท่านอนหงายโดยใช้เครื่อง Hologic Discovery A การแปลผลการตรวจ VFA จะทำโดยแพทย์เวชศาสตร์นิวเคลียร์ที่มีประสบการณ์สองคนอย่างเป็นอิสระต่อกัน โดยใช้การประเมินร่วมกันระหว่าง Genant visual semi-quantitative method และ morphometric measurement ข้อมูลประชากรถูกทบทวนจากบันทึกทางการแพทย์และแบบสอบถาม

ผลการศึกษา ความชุกของกระดูกสันหลังหักเท่ากับร้อยละ 25.8, ร้อยละ 9.1 เป็นการหักระดับ 1 และร้อยละ 16.7 เป็นการหักระดับ 2 และ/หรือ 3 กระดูกสันหลังหักถูกตรวจพบ 165 ข้อ ในผู้ป่วยที่พบกระดูกสันหลังหักทั้งหมด 85 ราย ร้อยละ 49.7 เป็นการหักแบบ wedge และร้อยละ 50.3 เป็นการหักแบบ biconcave โดยปราศจากการหักแบบ crush จุดเชื่อมต่อระหว่างกระดูกสันหลังส่วนอกและส่วนเอว (กระดูกสันหลังส่วนอกข้อที่ 11 ถึงกระดูกสันหลังส่วนเอวข้อที่ 2) เป็นจุดที่มีกระดูกสันหลังหักมากที่สุด ความสอดคล้องระหว่างผู้ประเมินดีมาก (ค่าสัมประสิทธิ์แคปปาของโคเฮนเท่ากับ 0.89) อายุ จำนวนปีที่หมดประจำเดือน และการใช้สเตียรอยด์เป็นปัจจัยเสี่ยงอิสระ

สรุป VFA ตรวจพบกระดูกสันหลังหักที่ไม่เคยทราบมาก่อนถึงหนึ่งในสี่ของหญิงวัยหมดประจำเดือนที่มีมวลกระดูกต่ำ การตรวจ VFA เพิ่มเติมขณะที่ตรวจ BMD ควรถูกพิจารณาในผู้ป่วยกลุ่มนี้ **เชียงใหม่เวชสาร 2562; 58(1):23-30.**

คำสำคัญ: การตรวจประเมินกระดูกสันหลังหัก มวลกระดูกต่ำ หญิงวัยหมดประจำเดือน