



Bone mineral density measurement combined with vertebral fracture assessment increases diagnosis of osteoporosis in postmenopausal women

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Abstract

Objective Osteoporosis is diagnosed based on the results of BMD assessment and/or fragility fractures. Vertebral fracture is the most common fragility fracture. Many vertebral fractures are asymptomatic and are not clinically recognized. Early detection of vertebral fracture may increase diagnosis of osteoporosis. In this study, we performed BMD measurement combined with vertebral fracture assessment (VFA) by DXA for the postmenopausal women receiving the first bone densitometry and studied the impact of VFA on the diagnosis of osteoporosis.

Methods A total of 502 postmenopausal women were enrolled in our study. Patients' age was 66.7 ± 9.5 years. All patients had BMD assessment and VFA by dual-energy X-ray absorptiometry. Genant's semiquantitative assessment was used. The impact of VFA on the diagnosis of osteoporosis was studied. All parameters of groups were compared using the Chi-squared test.

Results There were 257 patients with T-score ≤ -2.5 , 202 patients with a T-score between -1 and -2.5 , and 43 patients with BMD within the normal range. There were 162 patients with 345 fractured vertebrae identified by VFA, among which 84% of patients were previously unknown. Osteoporosis or severe osteoporosis was presented in 51.2% patients diagnosed by BMD alone, in 55.2% patients diagnosed by BMD plus fracture history, and in 62.4% of patients diagnosed by BMD plus fracture history and VFA. Severe osteoporosis significantly increased by 17.2% in patients receiving VFA.

Conclusions VFA combined with BMD can detect previously unknown vertebral fractures and increase clinical diagnosis of osteoporosis. It is plausible to speculate that this method should be considered in postmenopausal women for the first BMD assessment.

Keywords Osteoporosis · Diagnosis · Vertebral fracture assessment · Bone mineral density assessment

Abbreviations

BMD Bone mineral density
DXA Dual-energy X-ray absorptiometry
VFA Vertebral fracture assessment
ISCD International Society for Clinical Densitometry

Introduction

Osteoporosis is a systemic skeletal disease characterized by an increased risk of fractures. Vertebra, hip, proximal humerus, and distal radius are the common sites of fragility fractures.

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Bone mineral density (BMD) measured by dual X-ray absorptiometry (DXA) is regarded as the gold standard for diagnosing osteoporosis. Low BMD is significantly associated with increased fracture risk. Fracture risk increases by 1.5- to 2.6-fold with each standard deviation reduction in BMD of the lumbar spine or femoral neck [1]. Anti-osteoporosis therapies are recommended for patients with BMD T-score ≤ -2.5 by many guidelines such as European guidance for the diagnosis and management of osteoporosis in postmenopausal women and the UK clinical guideline for the prevention and treatment of osteoporosis [2, 3]. However, BMD explains only a part of the fracture risk. Many patients with fragility fractures have baseline BMD above the diagnostic threshold of osteoporosis [4]. Osteoporosis diagnosis is based on BMD measured by DXA and/or fragility fractures diagnosed clinically. Osteoporosis can be diagnosed and anti-osteoporosis therapy is needed for prevention of future fractures if patients have fragility fracture of the hip and spine. Early detection of vertebral fracture may improve the diagnosis and treatment of osteoporosis. Vertebral fracture assessment (VFA) using densitometric lateral spine images has been advocated for clinical use by the International Society for Clinical Densitometry (ISCD) [5]. Vertebral fracture is the most common fragility fracture. However, many vertebral fractures are asymptomatic and not recognized by physicians and surgeons. The radiological under-diagnosis of vertebral fracture is a worldwide problem. The vertebral fracture assessment is not performed in many hospitals. In this study, we performed BMD assessment combined with VFA by DXA for the patients receiving first bone densitometry and studied the impact of VFA on the diagnosis and treatment of osteoporosis.

Materials and methods

Study population

We retrospectively included consecutive postmenopausal women aged 50 years or above who took the first BMD assessment and VFA in the radiology department of the Second Affiliated Hospital of Fujian Medical University between March 2013 and March 2016. The inclusion criteria in our study were postmenopausal women aged ≥ 50 years, first BMD measurement, and no treatment with any anti-osteoporotic therapy. Exclusion criteria were as follows: the patients who used glucocorticoids, had chronic renal dysfunction, rheumatoid arthritis, or hyperparathyroidism, patients with traumatic vertebral fractures or acute severe pain in the thoraco-lumbar spine, pathological fractures caused by metastatic tumors, tuberculosis, and Scheuermann's disease, congenital and degenerative spine deformity, and unclear DXA image of the thoraco-lumbar spine. Approval for this research was given by the

ethics committee of the Second Affiliated Hospital of Fujian Medical University (ERAN No:2017–111) and all methods were performed in accordance with relevant guidelines and regulations. When the participants received BMD measurement, they were informed that their data would be included in a research study and written informed consent was obtained from every patient.

BMD assessment

Bone mineral density of the lumbar spine L₁-L₄ and the proximal femur was measured in the standard position using a Hologic Discovery A densitometer (Hologic, Bedford, MA, USA). BMD of the femoral neck was used for diagnosis and study because vertebral fracture, bone osteophytes, and osteoarthritis of the facet joints in the lumbar spine are common in postmenopausal women, which leads to the falsely elevated BMD at the lumbar spine.

Vertebral fracture assessment

After a lateral spine image was obtained by the same densitometer, VFA was performed and reported from the thoracic spine T₄ through the lumbar spine L₄ respectively by two study radiologists who were certified clinical densitometrists conferred by the ISCD. A consensus was reached between two radiologists for any difference of interpretation at the time of reporting. Genant's semi-quantitative assessment was used in this study. Suspected vertebral fractures were first identified by visual inspection. The software was used for the accurate measurement for vertebral height by study radiologists and the severity of vertebral fracture was classified with Genant's scale [6]. Vertebral fractures identified in this study were defined as Genant grade 2 or higher on densitometric lateral spine images and patients had a history of no trauma or low trauma. More than 40% reduction in the vertebral height was defined as grade 3 (severe) and 25–40% reduction in the vertebral height was defined as grade 2 (moderate). A grade 1 (mild, 20–25%) reduction in the vertebral height was not calculated as a vertebral fracture in this study.

Diagnosis of osteoporosis: osteoporosis based on DXA is defined as a T-score lower than -2.5 , osteopenia as a T-score between -1.0 and -2.5 , and normal as a T-score equal or greater than -1.0 standard deviation in the BMD of the femoral neck. Severe osteoporosis is defined as a T-score of BMD ≤ -2.5 plus a fracture at least. Osteoporosis can be diagnosed in the following fracture types:

1. A low-trauma hip fracture
2. A low-trauma clinical vertebral fracture, proximal humerus fracture, or pelvis fracture with osteopenia

3. A morphometric vertebral fracture on a radiograph if the clinician has a reason to believe that it is likely to have been the result of low bone mass and reduced bone strength
4. A low-trauma distal forearm fracture in a person with osteopenia at the lumbar spine or hip by BMD testing [7, 8]

To understand the impact of VFA information added to the BMD report on the treatment of osteoporosis, we reviewed the patients' medical records to see whether or not the patients have received the bisphosphonate medications.

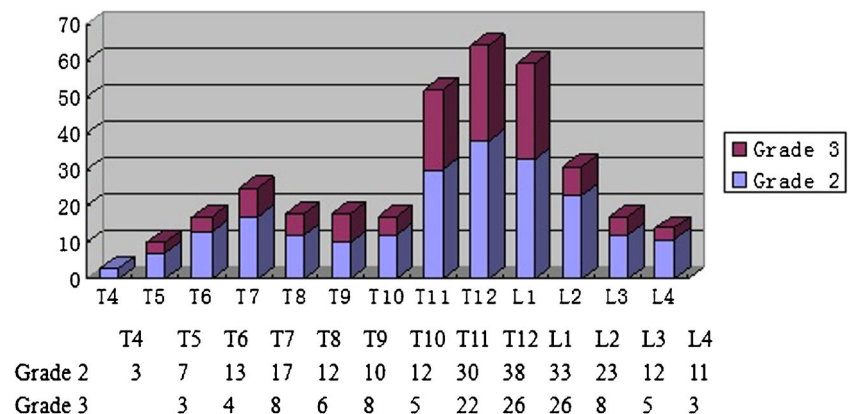
Statistical analysis

All statistical analyses were performed using SPSS statistical software (SPSS, version 25.0; SPSS, Chicago, IL, USA). All parameters of the groups were compared using the Chi-squared test. $p < 0.05$ was considered statistically significant.

Results

A total of 502 patients with no pain or chronic pain in the lumbar spine were enrolled in our study. Patient age ranged between 50 and 91 years, with the average age of 66.7 ± 9.5 years. Postmenopausal duration was between 1 and 54 years, with the average age of 17.6 ± 11.1 years. Body mass index was between 14 and 35 kg/m^2 , with the average of $23.1 \pm 3.7 \text{ kg/m}^2$. Among 71 patients with recognized fragility fractures before BMD assessment, 4 patients had a single level of vertebral fracture, 22 patients had multiple levels of vertebral fractures, and 45 patients had non-vertebral fractures (hip, proximal humerus, distal radius) confirmed by previous medical records and radiographs or MRI.

Fig. 1 Distribution of vertebral fractures between the thoracic spine T₄ and lumbar spine L₄ according to Genant's semi-quantitative scale



BMD assessment

There were 257 patients with a T-score of BMD ≤ -2.5 , 202 patients with a T-score of BMD between -1 and -2.5 , and 43 patients with BMD within the normal range.

Vertebral fracture assessment

There were 162 patients (32.3%) with 345 fractured vertebrae identified by VFA. Among 162 fractured patients identified by VFA, 26 patients had the recognized vertebral fractures before BMD assessment and 136 (84%) were newly identified. There were 84 grade 2 fractured patients with 137 fractured vertebrae and 78 grade 3 fractured patients with 208 fractured vertebrae. Vertebral fractures were the most common in the thoracic-lumbar junction T11-L2 (Fig. 1). Vertebral fractures were found in 43 patients (17.6%) with a BMD T-score > -2.5 , including 6 patients with normal BMD and 37 patients with osteopenia, and in 119 patients (46.3%) with BMD T-score ≤ -2.5 (Table 1). The patients with a BMD T-score ≤ -2.5 had a significantly higher vertebral fracture rate than the patients with a BMD T-score > -2.5 ($p < 0.05$).

Impact of VFA on the diagnosis of osteoporosis and severe osteoporosis

Osteoporosis was diagnosed in 257 patients (51.2%) by BMD alone. Furthermore, osteoporosis or severe osteoporosis was diagnosed in 277 patients (55.2%) by BMD and/or fragility fracture history and in 313 patients (62.4%) by BMD plus fragility fracture history and VFA in this study (Table 2). The diagnosis rate of osteoporosis and severe osteoporosis was increased from 257 patients (51.2%) by BMD alone to 301 patients (60%) by both BMD and VFA. Severe osteoporosis increased from 10.1% in the patients without VFA to 27.3% in the patients with VFA. VFA significantly increased the diagnosis of osteoporosis and severe osteoporosis ($p < 0.05$; Table 1).

Table 1 Comparison of vertebral fractures between patients with a T-score of BMD >−2.5 and patients with a T-score of BMD ≤−2.5

	T-score >−2.5	T-score ≤−2.5	Chi-squared	<i>p</i>
Patients	245	257		
No vertebral fracture, <i>n</i> (%)	202 (82.4)	138 (53.7)	71.077	<0.001
Vertebral fracture, <i>n</i> (%)	43 (17.6)	119 (46.3)		

Impact of VFA on the treatment of osteoporosis

Among 313 patients with osteoporosis or severe osteoporosis, 221 patients received the bisphosphonate medications, including 70 patients receiving alendronate and 151 patients receiving yearly intravenous infusion of zoledronate. Meanwhile, these patients had daily supplementation of calcium and vitamin D. VFA changed the osteoporosis management in 27 patients out of 211 patients receiving bisphosphonate medications, who did not meet the BMD standard of osteoporosis and the indication for bisphosphonate medications by DXA alone (Figs. 2, 3).

Discussion

This study confirmed that VFA combined with BMD assessment dramatically improved the diagnosis of osteoporosis and severe osteoporosis. Vertebral fractures were identified by VFA in 162 (32.3%) patients, including 84% previously undiagnosed vertebral fractures. Low BMD was associated with vertebral fracture. The rate of vertebral fractures significantly increased from 17.6% in the patients with BMD T-score >−2.5 to 46.3% in the patients with BMD T-score ≤−2.5. The diagnosis rate of osteoporosis was 51.2% by BMD alone, and the rate of osteoporosis and severe osteoporosis significantly increased from 55.2% in the patients diagnosed by BMD plus fragility fracture histories to 62.4% in the patients diagnosed by BMD plus fragility fracture history and VFA in this study. VFA increased the diagnosis of severe osteoporosis by 17.2%.

Osteoporosis leads to an increased risk of fragility fractures in the elderly. The lifetime fracture risk is estimated to be between 40 and 44% for women and 13 and 25% for men from age 50 years onward [9, 10]. DXA is good for the

diagnosis of osteoporosis. Although fracture risk is highest in those individuals with a T-score ≤−2.5 in the lumbar spine or in the femoral neck, most fractures occur in osteopenic patients. Vertebral fractures are the most common osteoporotic fractures worldwide. The incidence of new vertebral fracture in women aged 50 years and over was 10.7/1,000 person-years in Europe and the prevalence of vertebral fractures increased from 3% in women below 60 years of age to 20% in women aged over 70 years [11, 12]. Many vertebral fractures are asymptomatic and are not clinically recognized and only one-third of patients with vertebral fractures receive medical care [13]. The presence of vertebral fragility fracture is a marker of reduced bone strength and a predictor of new vertebral and non-vertebral fractures. The number and severity of prevalent vertebral fractures is positively related to the future fracture risk [10, 14]. Radiographs of the spine are important for accurate diagnosis of vertebral fractures, but the radiological under-diagnosis of vertebral fractures is common and the false-negative rates ranged from 27% to 45% [15]. The missed diagnosis of vertebral fracture was as high as 66.8% on chest radiographs [16]. Genant's semiquantitative assessment is recommended for identification of vertebral fractures by the ISCD [7]. Although lateral X-ray images of the thoracolumbar spine is the gold standard for assessment of vertebral fractures, VFA by DXA had a performance comparable with radiographs to identify grades 2 and 3 vertebral fractures [17, 18]. VFA by DXA had very high sensitivity and specificity and excellent agreement with the visual semiquantitative assessment of conventional radiographs [19]. It has the advantage of lower radiation dose and lower cost than lateral radiographs. The entrance dose of radiation to the patient for VFA is about 30–50 μSv and the cost of VFA is about \$25, which is relatively low in China. VFA and BMD assessment can be performed simultaneously, which provides greater

Table 2 Comparison of osteoporosis plus severe osteoporosis among three diagnosis models

	BMD	BMD + fracture history	BMD + fracture history + VFA
Normal, <i>n</i> (%)	43 (8.6)	43 (8.6)	36 (7.2)
Osteopenia, <i>n</i> (%)	202(40.2)	182 (36.3)	153 (30.5)
Osteoporosis + severe osteoporosis, <i>n</i> (%)	257(51.2)	277(55.2)	313 (62.4)*, **

*Comparison with the BMD + fracture history group, *p* < 0.05

**Comparison with the BMD group, *p* < 0.05



Fig. 2 Vertebral fracture assessment (VFA) shows grade 2 vertebral fracture at T12

convenience for radiologists assessing vertebral fractures and diagnosing osteoporosis. An official statement on VFA using DXA spine images was published by the ISCD in 2013 and VFA was suggested to detect vertebral fracture in the screening of people at risk for osteoporosis [7].

The prevalence of vertebral fractures was 32.3% in this study. Our prevalence was higher than the 7.9–22% prevalence reported in other studies of VFA. The reasons for higher fracture prevalence in our study may reflect the older age of our patient cohort, postmenopausal women, and more patients with a BMD T-score ≤ -2.5 . In the study reported by Mrgan et al. [19], male patients were included, 68% patients had a BMD T-score > -2.5 and only 32% had a BMD T-score ≤ -2.5 . In the study reported by Jager et al. [20], the age of study patients was 18 years or older, male patients were included, and only 27% of patients had a BMD T-score ≤ -2.5 . The vertebral fractures were common in the patients with back pain and prevalence was as high as 39% [21]. Low BMD is associated with vertebral fractures. Jager et al. [20] reported that the prevalence of vertebral fracture was 14% in patients with normal BMD, 21% in osteopenia, and 33% in those with osteoporosis. Ehsanbakhsh et al. [21] reported that vertebral fractures were found in 43.6% of patients with osteoporosis, 37.5% of the patients with osteopenia, and 22% of the patients with a normal T-score. The results were similar in this study. Vertebral fractures were identified by VFA in 17.6% of patients with a BMD T-score > -2.5 and 46.3% of patients with a BMD T-score ≤ -2.5 . Recognition of vertebral fracture can increase the diagnosis rate of osteoporosis. Mrgan et al. [19] reported that VFA increased by 9.79% of patients diagnosed with osteoporosis and increased by 14.4% of patients diagnosed with severe osteoporosis referred to DXA. Jager et al. [20] reported that the osteoporosis increased from 27% in the patients depending upon BMD to 40.1% in patients with BMD plus VFA and suggested that combined vertebral fracture assessment and BMD measurement became a new standard in the diagnosis of osteoporosis. In this study, VFA improved the diagnosis of osteoporosis and severe osteoporosis from 51.2% of patients referred to DXA and from 55.2% of patients referred to DXA plus fragility fracture histories to 62.4% and increased severe osteoporosis from 10.2% to 27.3%. VFA combined with BMD assessment significantly improves the diagnosis of osteoporosis and severe osteoporosis. VFA is recommended by the ISCD and is indicated in patients with a T-score < -1.0 , who meet one or more of following conditions: women aged ≥ 70 years or men aged ≥ 80 years, historical height loss > 4 cm, self-reported but undocumented previous vertebral fracture, glucocorticoid therapy equivalent to ≥ 5 mg of prednisone or equivalent per day for ≥ 3 months [7]. We think that the indications recommended by the ISCD are good for confirmation of vertebral fractures; however, they are not best for the evaluation of fracture risk and early diagnosis and treatment of osteoporosis, because

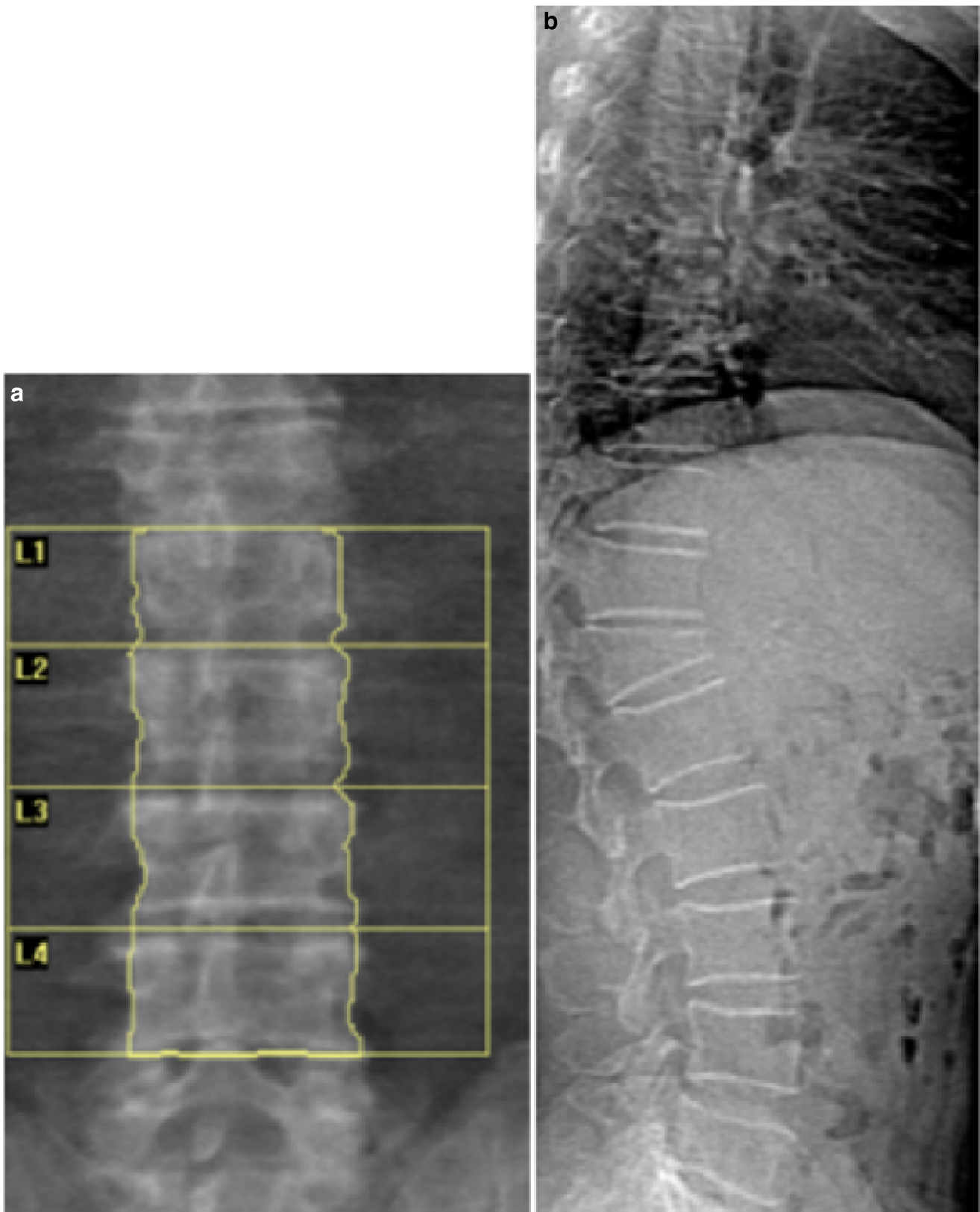


Fig. 3 a DXA image for BMD measurement. b VFA shows grade 3 vertebral fracture at T12

VFA identified that 32.3% patients referred for first BMD assessment had vertebral fractures in this study and a

population-based study in China showed that the prevalence of vertebral fracture was 13.4% in women less than 60 years

of age, 22.6% in women aged between 60 and 69, 31.4% in women aged between 70 and 79, and 58.1% in women aged more than 80 years [22]. The strong impact of VFA on the diagnosis of vertebral fractures and osteoporosis is in accordance with Jager's opinion. Hence, we recommend that VFA should be considered in all postmenopausal women for first BMD assessment. However, this does not imply that spinal radiography should be replaced by VFA, because VFA is inferior to X-ray in visualizing vertebrae properly in the upper spine, and the accuracy of VFA for detecting mild fractures was poor [23, 24].

Anti-osteoporosis therapy is indicated for vertebral fragility fracture. Jager et al. [20] reported that VFA improved physicians' understanding of their patient's osteoporosis status and had an impact on their management. Our study showed the number of patients receiving the bisphosphonate medications after VFA was increased by 12.2%.

There are some limitations to our study. We only included moderate and severe vertebral fractures. Therefore, our prevalence of vertebral fracture may be lower than the real prevalence. Also, we did not compare the diagnostic accuracy of vertebral fracture on VFA and radiographs in our patients. With these limitations in mind, this study identified many vertebral fractures that were previously unknown before VFA and underscores the importance of VFA combined with BMD assessment in the diagnosis of osteoporosis.

In conclusion, VFA combined with BMD assessment can detect previously unknown vertebral fractures and improve the diagnosis rate of osteoporosis and severe osteoporosis. It is recommended that VFA should be considered in all postmenopausal women for the first BMD assessment.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

Ethical approval The participants were informed at the time of BMD measurement that their data would be included in a research study, and provided written consent. Approval for this research was given by the ethics committee of the Second Affiliated Hospital of Fujian Medical University (ERAN No:2017–111).

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