Combined Vertebral Fracture Assessment and Bone Mineral Density Measurement: A Patient-friendly New Tool with an Important Impact on the Canadian Risk Fracture Classification

Pieter L. Jager, MD, PhD^{a,*}, Riemer H. J. A. Slart, MD, PhD^b, Colin L. Webber, PhD^a, Jonathan D. Adachi, MD^c, Alexandra L. Papaioannou, MD^d, and Karen Y. Gulenchyn, MD^a

^aDepartment of Nuclear Medicine, Hamilton Health Sciences, McMaster University, Hamilton, Ontario, Canada ^bDepartment of Nuclear Medicine, University Medical Center, Groningen, The Netherlands ^cDepartment of Rheumatology, St Joseph's Healthcare, Hamilton, Ontario, Canada ^dDepartment of Internal Medicine, Hamilton Health Sciences, McMaster University, Hamilton, Ontario, Canada

Abstract

Purpose—Vertebral fractures often go unnoticed, while they constitute a significant risk factor for new fractures, independent of the bone density. Vertebral Fracture Assessment (VFA) is a new feature on DXA bone densitometry equipment. Our purpose was to determine the added value of VFA and its impact on the Canadian fracture risk classification using data from a Dutch academic cohort.

Methods—All 958 consecutive patients (64% female, mean age 53 [20–94], mean weight 75 kg [32–150]) who underwent BMD measurement at the University Medical Center Groningen, The Netherlands also underwent VFA in the same session.

Results—The prevalence of vertebral fractures was 26%. In 68% of these patients this fracture was unknown. The severity was “mild” (20%–25% height loss) in 43%, “moderate” (25%–35%) in 44% and “severe” (>35% height loss) in 13%. Even after excluding mild fractures, the prevalence of vertebral fractures was 17%. In the 28% with normal BMD the vertebral fracture prevalence was still 18%, in the 43% with osteopenia 23%, and in the 29% with osteoporosis 36%. The Canadian risk classification was “low fracture risk” in 68%, “moderate” in 19%, and “high” in 13%. Adding VFA altered the classification in 20% of the patients, to become 54%, 27%, and 19%, respectively.

Conclusions—VFA added to BMD is a patient friendly diagnostic tool with a high diagnostic yield, as it detected unknown vertebral fractures and altered diagnostic classification in approximately 1 out of every 5 patients. These results suggest that BMD plus VFA may become the new standard in osteoporosis testing.

*Address for correspondence: Pieter L. Jager, MD, PhD, Department of Nuclear Medicine, MUMC P1.14, Hamilton Health Sciences, McMaster University, Hamilton, Ontario L7R 3J6, Canada. jager@hhsc.ca (P. L. Jager).

Osteoporosis is a systemic disease of the skeleton, characterized by low bone mass and deterioration of bone microstructure. Osteoporosis can be “primary” or “secondary.” Primary osteoporosis is caused by genetic factors, aging, and/or lifestyle factors, and is especially present in postmenopausal women. Secondary osteoporosis is a result of a wide variety of medical disorders, such as hyperthyroidism, hyperparathyroidism, malabsorption, or use of medication, such as corticosteroids.

By definition, osteoporosis is associated with an increased risk of fracture. Osteoporosis Canada estimates that approximately 2 million Canadians suffer from osteoporosis, including 1 in 4 women over 50 years old, and 1 in 8 men over 50 years of age. The cost of treating osteoporosis, the associated fractures, and the resulting requirements for hospital care, long-term care, and chronic care are estimated to be \$1.3 billion [1]. Osteoporosis significantly lowers quality of life. Based on extrapolation from Dutch data, an estimated 100 000 quality-adjusted life-years are lost each year as a result of osteoporosis and fractures in the population over 50 years old [2]. In 1993, approximately 25 000 hip fractures were diagnosed in Canada, 70% of which were considered osteoporosis related. Such fractures result in death in up to 20% of cases and disability in 50% of those who survive [2].

The main aim of diagnosing and treating osteoporosis is prevention of osteoporotic fractures. Low bone mineral density (BMD) is one of the most predictive factors for osteoporotic fracture [3,4]. The presence of a vertebral fracture is also a strong predictor of new fractures, and this risk is independent of BMD [3–8]. Therefore, even with only modestly decreased or even normal BMD vertebral fractures can be present. When both these risk factors, low BMD, and prevalent vertebral fracture, are present, risks for a new fracture may be increased by a factor of 25 [9].

Clearly, the vertebral fracture status of a patient is an important and independent predictive factor for new future fractures. Therefore, it is useful to obtain a lateral radiographic image of the spine in all patients with suspected osteoporosis. However, in daily practice, this is usually not done, presumably because of lack of awareness, costs, radiation exposure, and additional clinic visits for patients.

New developments in BMD measurement equipment, however, now include the possibility to measure both BMD and vertebral fracture status in a single short session. After dual energy x-ray absorptiometry (DXA) BMD measurement, an additional single (usually) monoenergetic radiographic image can be acquired by using the DXA machine. This radiographic image visualizes the lateral spine from approximately T4 through L4 and takes only a few seconds. Radiation exposure is negligible, because it is over a factor of 100 lower than conventional radiographs [10,11]. The radiation dose of BMD and vertebral fracture assessment (VFA), together is reported to be approximately 3 microSv, which is near the same dose as 2 days of background radiation [11].

The image quality is lower than in conventional radiographs but improves with every new version of the DXA equipment. After image acquisition, a software application is able to analyse the shape of the vertebral bodies for wedge, biconcave, or other fractures. This

image procedure has been called “vertebral morphometry,” “instant vertebral assessment,” “spine assessment,” but the term “vertebral fracture assessment” is now preferred. Combined BMD measurement with VFA, therefore, allows documenting the 2 main risk factors in osteoporosis in a single session in a very patient-friendly way.

At the University Medical Center of Groningen, The Netherlands, a VFA-capable DXA machine has been operational since mid 2005. For the evaluation of the added value of the VFA feature, a prospective study was carried out in which each patient referred for BMD measurement underwent VFA, combined with a short questionnaire for patients and their referring physicians. The results of the first 958 patients were recently reported (in the Dutch language) [12]. The current article places these data in a Canadian perspective, and we calculate the impact VFA would have on the Canadian risk classification, in which absolute risk assessment has been identified as one of the main conclusions of a BMD article [13].

Patients and Methods

Patients

The study population consisted of all patients 18 years or older who were referred for BMD measurement to the Department of Nuclear Medicine of the University Medical Center Groningen, in the north east of The Netherlands. These patients came from many different departments and outpatient clinics, including internal medicine, endocrinology, immunology, rheumatology, and gynecology, and also included patients referred by a recently started “osteoporosis and fracture clinic,” where every patient over 50 years old and with a low-energetic fracture is assessed for osteoporosis. More than 99% of the population was of the white race.

The study was approved by the institutional ethics review board and was considered to be evaluation of modern patient care, therefore, patients did not need to consent to the procedure itself but were only asked whether their data might be used for the evaluation. All patients gave this permission. A brief questionnaire was obtained to record information on demographics, some risk factors, and data on the disease or condition that led to the referral for BMD measurement. Both DXA and VFA were acquired by using a Hologic Discovery A densitometer (Hologic Inc., Bedford, MA).

BMD Measurement

BMD was measured by using standard methods over the lumbar spine, the proximal femur, and the distal radius, and results were expressed as T-scores. The reference standard of a T-score is the peak bone density, as reached in men or women between 20–30 years of age. The T-score is then defined as the number of standard deviations from this value. According to the commonly used World Health Organization definition, “osteoporosis” is defined as a T-score lower than -2.5 ; “osteopenia” as a T-score between -2.5 and -1.0 ; and when the T-score is greater than -1.0 , the BMD is “normal.”

VFA

Immediately after BMD measurements, VFA was performed. While the patient remained in a supine position, the scanning arm (similar to a C-arm) of the machine revolved around the patient to acquire the lateral radiographic image of the spine. In older machines, the patients had to be scanned after they rotated to the lateral position. The maximum range of vertebral visualization is from the level of T4 through L4. Three experienced technologists analysed all images under the supervision of nuclear medicine specialists and radiologists. These technologists had all been trained both for nuclear medicine and radiology procedures, and had more than 5 years of work experience and followed specific courses on vertebral fracture recognition. Image quality was qualitatively scored by the technologist who also did the processing and was scored as “poor,” “moderate,” or “good,” based on how well vertebral outlines could be seen and with how much confidence markers could be placed. In agreement with the instructions of the manufacturer, dedicated software was used to place markers on cranial and caudal aspects of vertebral bodies, anterior, posterior, and in the middle. The original Genant classification and International Society of Clinical Densitometry (ISCD) recommendations suggest performing a visual analysis and to only do the morphometry measurement in those vertebrae that seem abnormal. However, we thought that would again induce significant subjectivity and decided to refrain from visual assessment only and analyse all vertebral bodies in each patient by using the software. In a large proportion (estimated 80%) of vertebrae, manual correction of software-based marker placement was necessary. Most corrections were applied to T4–T11. After correct marker placement was verified, software calculated the degree and shape of vertebral-shape anomalies by using the Genant classification. In this classification, a relative height reduction between 20%–25% was designated a “mild” fracture, 25%–40% was a “moderate” fracture, and >40% was a “severe” fracture [14–16].

Results

Patients

This article focuses on the first 958 patients who underwent VFA. Most patients were referred because of suspected secondary osteoporosis. Only 10% of these patients were known to have a vertebral fracture. Two-thirds of the group came for a first BMD measurement; in the remaining patients, this was a follow-up test. More patient data are presented in Table 1.

VFA Methodology

In 937 of the patients (98%), VFA was considered technically adequate. The quality of the VFA image was subjectively considered “good” in 739 (77%), “moderate” in 172 (20%), and “poor” in 34 (3%) of the patients. In 21 of the patients (2%) in whom VFA was technically inadequate, the cause was severe scoliosis, deformities, or extreme adiposity, and these patients were excluded from this analysis.

As stated above, we had chosen to perform the quantitative analysis on all individual vertebra in all patients. By clicking on this vertebra, the software automatically places 6 marker points on the anterior, mid, posterior, upper, and lower limits. From these marker

points, heights and height differences are measured, which determine the percentage height loss and the type of fracture. Although the software is nearly always correct in the lower levels of the spine, manual corrections were considered necessary between T4–T11 in approximately 80% of the patients.

Reproducibility was measured in the first 100 patients, and the overall agreement rate for the presence of vertebral fractures was 97% among the technologists, on a per patient basis. Differences were resolved by consensus. All findings were always checked by the physicians.

VFA Results

In 667 (71%) patients VFA visualized vertebrae from L4 through L4, which is the maximum number of vertebrae that can be imaged with VFA. The lowest visualized vertebra was L4 in 913 (95%). The highest visualized vertebra was T4 in 667 (71%) and T5 in 135 (14%) (Figure 1).

VFA demonstrated a vertebral fracture in 244 of the patients (26%). An example is presented in Figure 2. These 244 patients all together had 436 vertebral fractures, which is a mean of 1.8 fractures per patient with a fracture. In 164 patients (67%), these fractures were not demonstrated earlier and were unknown. Most fractures were present in T11, T12, and L1 with numbers of 76 (17%), 67 (15%), and 65 (15%), respectively. In 189 (43%), the severity of the fracture was mild, in 191 (44%) was moderate, and in 56 (13%) was severe. If mild fractures would have been omitted, then the frequency of vertebral fractures was 157 (17%) in our cohort. The fracture was wedge shaped in 76% ($n = 332$), biconcave in 22% ($n = 95$), and “crush” in 2% ($n = 9$).

The prevalence of vertebral fractures was 37% in the subgroup of patients referred for primary osteoporosis assessment vs 22% in those studied for secondary osteoporosis ($P < .001$). The higher prevalence in primary osteoporosis was consistent in all 3 classes of BMD.

BMD and VFA

A relationship was found between the BMD and the prevalence of vertebral fractures (Figure 3). In the entire cohort, 28% of the patients had a normal BMD. In this subgroup, a vertebral fracture was still found by using VFA in 18%, which was unknown in 80%. Osteopenia was found in 43% of the cohort, and, in 23% of that subgroup, a vertebral fracture was detected, which was unknown in 73%. Osteoporosis was diagnosed in 29% of the cohort. In 36% of these patients, a vertebral fracture was found, which was unknown in 56%.

In patients with “osteoporosis” by BMD criteria, the severity of the fractures was mild, moderate, and severe in 19%, 50%, and 31%, respectively. These figures were 46%, 42%, 12% in those with “osteopenia” and 49%, 43%, and 9% in “normal” BMD, which indicated that the severity of fractures increases with lower BMD.

Converting Data to Canadian Risk Categories

Based on age, BMD T-score, and sex, the patients in this cohort would have been classified with having “low,” “moderate,” and “high” fracture risk in 650 (68%), 184 (19%), and 124

(13%), respectively, without taking the vertebral fracture status into account [13]. After performing VFA, 133 of the patients with a low risk (26%) were found to have 1 or more vertebral fractures, which moves them to the moderate risk class. Similarly, 59 of 184 moderate risk patients were diagnosed with a vertebral fracture (32%), which converts them to high risk. There were 52 patients with a vertebral fracture of 124 who already had high risk. Therefore, in total, 192 patients (20% of the whole cohort) were moved up 1 risk class, roughly two-thirds from low to moderate and one-third from moderate to high risk. The addition of VFA data changed the distribution over the low, moderate, and high risk categories from 68%, 19%, and 13% based on BMD alone to 54%, 27%, and 19%, respectively. In future revisions of this classification, the presence of a vertebral fracture has been suggested to upgrade the classification to high risk in all patients, independent of baseline classification (Dr Papaioannou, personal communication). This would imply 54% low, 13% moderate, and 33% high risk, which would more than double the number of patients classified as being at high fracture risk.

If mild fractures were omitted, then upstaging from low to moderate would occur in 75 patients with low risk and in 38 patients from moderate to high risk. Overall, upstaging, therefore, would occur in 113 patients or 12% of the entire cohort.

Discussion

The aim of this study was to determine the value of VFA added to BMD measurement and its impact on fracture risk classification in consecutive patients scheduled for BMD assessment in an academic center. This is a specific population, and the results do not apply to the population in general. The results show that addition of VFA enabled the detection of one or more vertebral fractures in 26% of this population, and, in approximately two-thirds of these patients, the fracture was unknown. VFA, therefore, detected in 1 of each 5 patients an unknown vertebral fracture (this is the diagnostic equivalent to a number-needed-to-treat of 5). Even when mild fractures would have been omitted, the method still detected vertebral fractures in 17% of this population or approximately 1 in 6 patients (number-needed-to-treat of 6).

To determine the cost-effectiveness of this new diagnostic technique, several factors need to be considered. The high diagnostic yield is associated with a low burden for patients, because VFA only takes a few additional minutes and has a negligible radiation dose, which is in the order of 1% of radiographs. Costs are in the order of several tens of dollars. The detection of a vertebral fracture presumably leads to medical treatment in many patients who would otherwise not have been treated, because it increased the risk class in 20%. It was demonstrated in many studies that treatment reduces future fracture risks and that this might lead to decreased hospitalizations [17–19]. Indeed, there is 1 report that suggests cost-effective application of VFA in post-menopausal women with osteopenia [20]. Therefore, although it is not formally proven, it would seem reasonable that the balance between costs and advantages is favorable. The addition of VFA to BMD, therefore, appears to give a valuable and presumably cost-effective contribution to the diagnosis of osteoporosis.

Several comparisons between the yield of radiographs and VFA are available. The resolution of radiographs is better than that of VFA. However, radiographs also have difficulty visualizing the upper thoracic levels. In addition, the quality of radiographs varies considerably, and overprojection of skeletal and lung structures decreases readability. Because the x-ray beam is divergent, standard radiographs also contain variable degrees of magnification and distortion for different vertebrae, whereas VFA images all vertebrae in an orthogonal direction without parallax artifact. It may also be difficult to determine from a standard lateral radiograph of the thoracic spine which vertebral vertebra is affected, which is easier in VFA, which shows all levels in a single image from L4 up to T4.

In many articles, comparisons between radiographs and VFA used a less optimal method of VFA, in which the patient is scanned in the lateral position that may cause sagging of the lumbar spine. In the current study, the patient could remain in a supine position, with a straight spine, which improves accuracy. Multiple studies have now demonstrated good agreement between both methods, with very good sensitivities and specificities when using radiographs as a gold standard, especially for the moderate and severe fractures [21–28]. In a side study, we also confirmed excellent agreement between VFA and radiographs, both with visual and semiquantitative analysis, in a 250-patient subgroup of the current cohort [29]. The slightly decreased reliability for assessment of mild fractures of the upper-thoracic levels does not seem to preclude the added value of VFA, because vertebral fractures are considerably less common in that range, which was also evident in our study, and, even when all mild fractures were disregarded, a vertebral fracture was still found in 17%, which is 1 of 6 patients.

These results seem to confirm again that the vertebral fractures status is independent of bone density and that the bone microarchitecture is an important parameter, because, even in patients with normal bone density, a vertebral fracture was found in 18%. This percentage rose to 23% in patients with osteopenia and to 36% in patients with osteoporosis. Our findings and interpretations are also in agreement with the conclusions of the comprehensive review on VFA by Lewiecki and Laster [28]. In addition, the 26% overall fracture rate is within the same order of magnitude as reported in studies from Europe and slightly lower than data from Minnesota, but these were population-based studies, with likely lower fracture rates as in our university hospital population. [30]. This study was performed in an “academic” Dutch population, where many patients used corticosteroids for a large spectrum of medical indications. Ethnicity would be different in similar Canadian populations, which may influence the numbers. Most patients were assessed because of suspected secondary osteoporosis. It would be reasonable to assume that the prevalence of vertebral fractures will be lower in a more general population with a larger fraction of primary osteoporosis. However, we found it quite remarkable that, even in this population referred from a large university medical center, where patients and their conditions are often extensively documented, the prevalence of unknown vertebral fractures was that high.

In conclusion, VFA combined with BMD assessment is a simple, patient-friendly procedure that provides important additional information in a large proportion of our academic patients at minimal costs. The method alters the risk classification in 1 of each 5 patients. We,

therefore, suggest that this method should become the standard diagnostic tool in every new patient who is referred for BMD assessment.

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Figure 1.

Frequency distribution of the upper and lower vertebrae that can be imaged by using vertebral fracture assessment.

Figure 2.

Example of a vertebral fracture assessment study. Left panel: spine image with markers placed on vertebral edges. Upper right panel shows Genant classification. Lower right panel shows a table with measurements and percentage deformity for each vertebra. In this patient, 3 moderate vertebral fractures were detected: wedge shaped in T11 and L1 and biconcave in T12.

Figure 3.
Prevalence of vertebral fractures in relation to bone density.

Table 1**Patient data**

Sex, no. (%)	
Men	349 (36)
Women	609 (64)
Postmenopausal women, no. (%)	
<40 y ^a	81 (8)
>40 y	228 (24)
Mean age, y	53.4 (range, 20–94)
Mean weight, kg	75 (range, 32–150)
Referred from (most frequent), no. (%)	
Orthopaedics or traumatology	326 (34)
Endocrinology	135 (14)
System diseases	112 (12)
General internal medicine	97 (10)
Other	288 (30)
Indication, no. (%)	
Primary osteoporosis	237 (29)
Secondary osteoporosis	685 (71)
Steroid use, no. (%)	
None	669 (70)
<7.5 mg/d	61 (6)
>7.5 mg/d	228 (24)
Therapeutic	244 (25)
Substitution	45 (5)
Known no. (%) with vertebral fracture	93 (10)

^aPartly as a result of endocrine diseases or after ovariectomy.