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Review

Radiographic methods for evaluating osteoporotic vertebral fractures

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Abstract

Reproducible methods for the radiological assessment of osteoporotic vertebral fractures, defined based on accurate criteria, are needed in everyday practice and in therapeutic trials and epidemiological studies.
Objectives: To describe and to evaluate methods for osteoporotic vertebral fracture assessment based on standard radiographs or dual-energy X-ray absorptiometry (DXA) and to determine the role for each method in clinical practice, therapeutic trials, and epidemiological studies.
Methods: A review written by a rheumatologist based on his clinical experience and on a literature review was submitted to four experts. Studies in English or French published between 1975 and February 2008 were retrieved from Medline using the keywords vertebral fracture, osteoporosis, vertebral deformity, and vertebral fracture assessment.
Results: One hundred forty-nine articles were selected and read in their full-text version. There was no consensus regarding the definition of osteoporotic vertebral fractures. The following methods were evaluated: visual assessment, Genant's semi-quantitative assessment, Jiang's algorithm-based qualitative method, morphometric radiography, and DXA of the spine. In everyday practice, Genant's semi-quantitative assessment on standard radiographs may provide useful information on the severity and prognosis of osteoporosis. DXA done for bone mineral density measurement may detect vertebral fractures in asymptomatic patients. Assessment of standard radiographs remains the reference standard for diagnosing vertebral fractures in patients with suggestive symptoms (e.g., pain in the thoracic or lumbar spine, height loss, or thoracic kyphosis). For therapeutic trials and epidemiological studies, Genant's semi-quantitative assessment used by a trained and experienced observer is the preferred method, based on its good reproducibility and ability to differentiate fractures from other deformities. However, thousands of radiographs may be needed, making routine interpretation by an expert impractical. A visual semi-quantitative method may be used to separate normal radiographs from radiographs showing possible or obvious fractures, which can then be read by an expert. Alternatively, radiomorphometric indices can be determined on digitized radiographs in combination with a semi-quantitative assessment, with discordant cases being reviewed by an expert. We do not recommend Jiang's method at present, as it is still undergoing validation.

Keywords: Vertebral fracture; Osteoporosis; Vertebral fracture assessment

1. Introduction

The radiographic assessment of osteoporotic vertebral fractures is important for several reasons. In everyday clinical practice, it ensures the diagnosis of osteoporosis with vertebral fractures. Osteoporotic vertebral fractures are both underestimated [1,2] and common, with at least one such fracture being present in 22.8% (95% confidence interval [95% CI], 19.8–25.8%) of ambulatory women older than 75 years in France [3]. A diagnosis of vertebral fracture carries prognostic information, independently from the results of dual-energy X-ray absorptiometry (DXA) measurements [4]. Thus, patients with at least one vertebral fracture have a 4- to 5-fold increase in the risk of further vertebral fractures [5–8] and a 3-fold increase in the risk of hip fracture [6,7]. In women

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with osteoporotic vertebral fractures, poor quality of life [9,10] and increased mortality [11,12] have been reported. Availability of a reliable method for diagnosing vertebral fractures is crucial in epidemiological studies and trials of osteoporosis treatments. However, there is no consensus regarding criteria for the radiographic diagnosis of vertebral fractures. Compared to peripheral fractures, vertebral fractures have a number of features that complicate the diagnosis [13] (Table 1). Thus, there is often no initiating trauma, and the symptoms may be minimal or absent. Back pain and height loss are nonspecific symptoms that have many causes in older individuals. Vertebral fractures vary in severity. The fracture may escape detection on standard radiographs, being seen only by magnetic resonance imaging (MRI) [14]. Mobility at the fracture site is noted in 35% of cases [15]. Worsening of pre-existing vertebral fractures is common. Osteoporotic vertebral fractures may be difficult to differentiate from deformities (e.g., variants of normal, Scheuermann's disease, or degenerative disease), artifacts produced by an oblique X-ray beam, or fractures caused by tumors. Furthermore, the radiographic diagnosis may be difficult between recent and long-standing fractures or between osteoporotic and trauma-related fractures.

The objective of this study was to describe and to evaluate the various available methods for vertebral fracture assessment based on standard radiographs or DXA. We also define the role for each method in everyday practice, therapeutic trials, and epidemiological studies.

2. Methods

A literature review written by a rheumatologist (FG) based on his clinical experience and on a Medline search (FG, EF) was submitted to four physicians: two experts in osteoporotic vertebral fracture assessment (JF, SK) and two rheumatology professors specialized in osteoporosis (PF, CR). Medline was searched for articles in English or French published between 1975 and February 2008. The following key indexing terms were used: vertebral fracture, osteoporosis, vertebral deformity, and vertebral fracture assessment. Articles that evaluated techniques other than standard radiography and DXA were excluded. There was no financial support or influence from industrials.

Table 1
Comparison of the features of vertebral and peripheral fractures, from Kleerekoper et al. [13].

	Vertebral Fractures	Peripheral Fractures
Absence of pain	Possible	Rare
Severity	Variable	All or nothing
Absence of radiological changes	Possible	Rare
Restoration of normal anatomy	Impossible	In most cases
New fracture at same site	Common	Rare
Trauma	None or minimal	Often high impact
Long-term persistence of fracture site mobility	Possible	Rare

3. Results

The Medline search retrieved 149 relevant articles, which were read in their entirety. The methods used were visual assessment of standard radiographs, Genant's semi-quantitative assessment, Jiang's qualitative method, morphometric radiography, and DXA measurements. Because no reference standard was available, we assessed reproducibility, performance compared to consensus reading by experts, and predictive value of detected fractures for subsequent fractures.

3.1. Subjective visual assessment

Visual assessment of radiographs is the most widely used method in everyday practice. The results are highly dependent on the experience of the observer. Visual assessment is simple and is mandatory for ruling out vertebral deformities due to other conditions. However, reproducibility is low. Intra-observer agreement is 87% ($\kappa = 0.62$) and interobserver agreement 75% ($\kappa = 0.47$) [16]. (The κ score takes into account the proportion of agreement ascribable to chance alone and can range from 0 (no agreement) to 1 (complete agreement); values greater than 0.8 are considered satisfactory and values lower than 0.6 poor). Therefore, visual assessment is not suitable for therapeutic trials or epidemiological studies.

3.2. Genant's semi-quantitative assessment

Genant et al. [17] developed an evaluation method based on vertebral shape (wedge, concave, or crush) and on decreases in anterior, posterior, and/or middle vertebral height (grade 0, no reduction; grade 1, minimal fracture, 20%–25% height decrease; grade 2, moderate fracture, 25%–40% height decrease; and grade 3, severe fracture, greater than 40% height decrease) (Fig. 1). The spinal deformity index computed as the sum of the grades from T4 to L4 reflects the number and the severity of the vertebral fractures.

Using an illustrated atlas [17] and adding a quantitative criterion to the visual assessment improves the reproducibility of the diagnosis of prevalent and incident vertebral fractures (Tables 2 and 3, respectively) [17–19]. However, the results

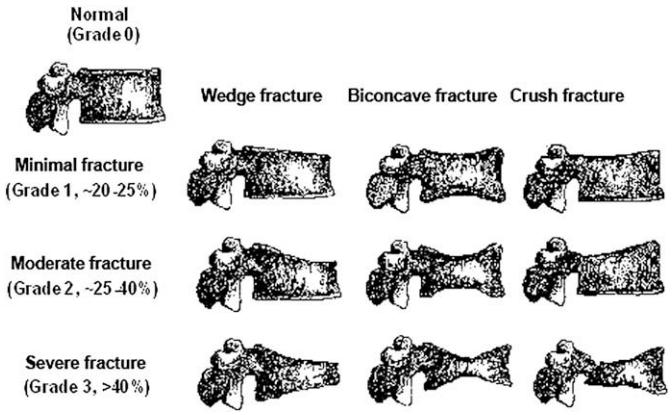

Fig. 1. Genant's semi-quantitative classification [17], with permission.

Table 2
Reproducibility of Genant's semi-quantitative assessment for diagnosing prevalent vertebral fractures.

Authors	Concordance (%)	κ	95% Confidence interval
Genant et al [17]			
Intraobserver			
Inexperienced observer	93	0.73	0.66–0.80
Experienced observer	97	0.89	0.84–0.94
Interobserver	94	0.74	0.67–0.81
Wu et al [18]			
Interobserver	94.2	0.80	
	94.3	0.80	
	94.4	0.81	
One observer	95.5	0.84	
versus consensus reading	96.2	0.87	
by four radiologists	96.3	0.87	
Grados et al [19]			
Intraobserver	96.4	0.91	0.87–0.95
One observer versus consensus reading by three experts	98	0.95	0.92–0.97

are dependent on training and experience. Intraobserver agreement is 97% ($\kappa = 0.89$) for experienced observers and 93% ($\kappa = 0.73$) for inexperienced observers [17]. Thus, although Genant's method is simple and accessible to all physicians, it has a learning curve. In the hands of trained and experienced observers, Genant's method is effective in ruling out vertebral deformities due to other causes. The number and severity of vertebral fractures is associated with the outcome independently from DXA measurements [4]. Thus, each 1-point increase in the baseline spinal deformity index is associated with a 5% increase in the 3-year vertebral fracture risk [20]. Women with grade 1 vertebral fractures have a relative risk of further vertebral fractures within 4 years of 1.8 (95% CI, 1.3–2.4; $P < 0.001$), compared to 2.7 (2.3–3.3, $P < 0.001$) in women with at least one grade 2 vertebral fracture [21]. Patients with grade 3 vertebral fractures at baseline have a significantly higher 3-year risk of peripheral fractures than patients with no vertebral fractures or only grade 1 vertebral fractures at baseline ($P < 0.05$), even after adjustment for bone mineral density values [22]. Bone microarchitecture alterations are more severe in patients who have grade 3 vertebral fractures. [23]. Thus, Genant's method is a useful diagnostic and prognostic tool, both for everyday practice and for therapeutic trials and epidemiological studies.

Table 3
Reproducibility of Genant's semi-quantitative assessment for diagnosing incident vertebral fractures.

Authors	Concordance (%)	κ	95% Confidence interval
Genant et al [17]			
Intraobserver			
Inexperienced observer	98	0.76	0.63–0.90
Experienced observer	99	0.93	0.86–1.00
Interobserver	99	0.80	0.68–0.92
Wu et al [18]			
One observer	99.6	0.86	0.79–0.93
versus consensus reading	99.7	0.87	0.80–0.94
by four radiologists	99.7	0.96	0.90–0.99

3.3. Jiang's algorithm-based qualitative method

Based on the appearance of the central endplate, each vertebra is categorized as osteoporotic fracture (endplate collapse), nonfracture deformity (≥15% height loss without endplate collapse), or normal [24]. As with Genant's method, three severity grades exist, but there is no lower limit for defining grade 1 fractures (grade 1 ≤ 25%, grade 2 > 25%, and grade 3 > 40%). Interobserver reproducibility is good ($\kappa = 0.74$) [25,26]. Intraobserver reproducibility has not been evaluated. In both women [27] and men [25], osteoporotic fractures diagnosed using Jiang's method were associated with low BMD values, whereas nonfracture deformities were not. Prospective studies are under way in women [27] and men [25] to assess the hypothesis that nonfracture deformities are not associated with an increased fracture risk. Until the results are available, we do not recommend the use of Jiang's method.

3.4. Morphometric radiography

Digitized radiographs are used to measure the anterior height (AH), posterior height (PH), and middle height (MH) of each vertebral body (Fig. 2). Vertebral height ratios are computed to define vertebral shape: AH/PH reflects wedging, MH/PH reflects concavity, and PH/PH' of the supra- and infrajacent vertebras reflects posterior compression. The reproducibility of vertebral height measurement is good in healthy individuals, with coefficients of variation (CV) of less than 2% [28]. In patients with osteoporotic vertebral fractures, however, reproducibility is lower (interobserver CV, 3.6% for AH, 5% for MH, and 3.8% for PH), with the greatest variation occurring when the same observer assesses MH on serial radiographs (intraobserver CV, 6.3%) [19]. A prevalent vertebral fracture is defined as a decrease in at least one of the three heights that is greater than 15% [29] or 3 SDs from

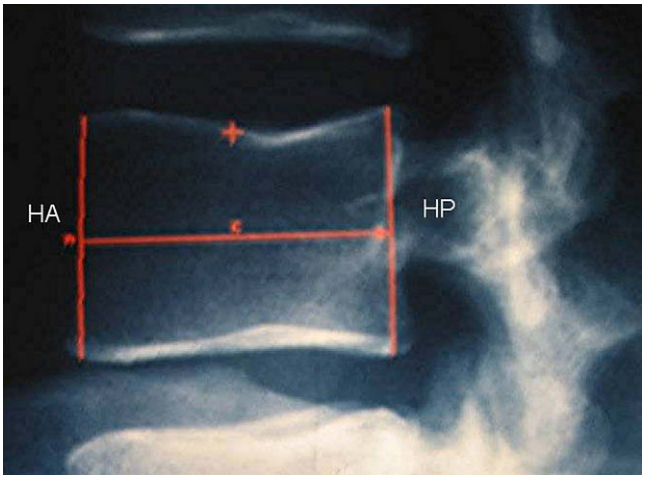

Fig. 2. Radiographic morphometry measurement of anterior height (AH) and posterior height (PH).

the mean in a reference population [30]. Although complex algorithms have been developed [31,32], they do not improve concordance with consensus evaluation by three experts using Genant's method [19]. When selecting the reference population, the ethnicity [33] and the age and sex distributions of the study population should be taken into account [34]. Presence of at least one prevalent vertebral fracture, defined as an at least 3 SDs difference in at least one of the three vertebral height ratios [30], is associated with an increased risk of subsequent vertebral and femoral fracture [6]. An incident vertebral fracture is defined as a change over time in at least one of the three vertebral heights by at least 15%–20% or 3–4 mm. Positioning of the points used for vertebral height measurement is partly subjective, most notably for MH, where the edges of the vertebra may be difficult to detect when obliquity of the X-ray beam creates a double contour simulating a concave fracture (particularly at the periphery of the radiograph). Scoliosis, even when moderate, precludes morphometric radiography. Despite efforts to standardize the method for obtaining radiographs, it is often difficult to obtain good-quality radiographs without variations in X-ray obliquity and vertebral positioning in older patients with osteoporosis. Therefore, fairly large deviations must be used for diagnosing fractures, and consequently a number of small uniconcave fractures are missed. Simplifying the shape of the vertebra into three heights causes loss of information that is visible to the naked eye, such as lack of parallelism of the endplates. Morphometric radiography fails to distinguish between deformities due to osteoporotic fractures and deformities due to other causes. In the European Study of Vertebral Osteoporosis, among women with prevalent vertebral deformities by quantitative morphometry of digitized radiographs, 31%–68% – depending on the criterion used (Eastell et al [30] 3 or 4 SDs, McCloskey et al [32]) – were classified as having non-fracture deformities based on a combined qualitative and quantitative assessment. [35]. Therefore, morphometric radiography must be combined with a visual evaluation.

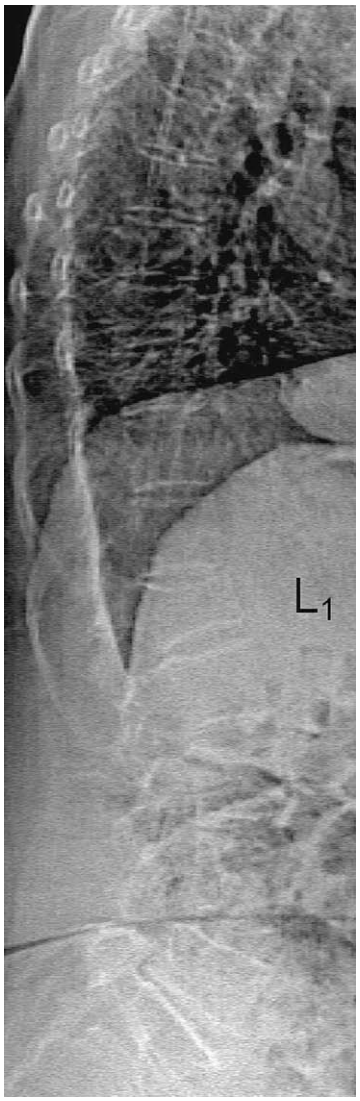

Fig. 3. Grade 2 wedge fracture of L1 on a dual-energy X-ray absorptiometry scan.

3.5. Dual-energy X-ray absorptiometry assessment

Vertebral morphometry can be assessed on lateral views of new generation dual-energy X-ray absorptiometry (DXA) scans, either by using a rotating arm (Hologic QDR 4500 A, QDR Delphi) or by placing the patient on the side (Hologic Discovery (Fig. 3), Lunar Prodigy). "Vertebral fracture assessment" (VFA) is now the preferred term for designating this technique, having replaced previously used terms such as instant vertebral assessment (IVA), lateral vertebral assessment (LVA), dual-energy vertebral assessment (DVA), and morphometric X-ray absorptiometry (MXA) [36]. The X-ray beam is parallel to the endplates, instead of being fan-shaped as during standard radiography, which eliminates problems related to image amplification and geometric distortion. In a single session, a single machine supplies the two pieces of information that are crucial to the diagnosis and prognosis of osteoporosis, namely, BMD values and prevalent vertebral fractures. Image acquisition requires only a few minutes [36]. Radiation exposure is only 3 micro-Sieverts (μSv), compared to 600 μSv for a lateral radiograph of the thoracic and lumbar spine [36]. In the US, Medicare covers VFA in many regions, with a cost reimbursement of $40, which is only half the cost of thoracolumbar spine radiographs [37]. Image resolution is less good than with standard radiography [38]. Correct positioning of the patient in lateral decubitus is crucial to obtain optimal image quality with the Hologic Discovery and Lunar Prodigy machines. In clinical practice, Genant's semi-quantitative assessment can be used to evaluate the images [36]. Quantitative morphometric assessment should not be used alone, as numerous sources of error exist (e.g., problems with positioning the measurement points on the vertebras, anatomic variants, and deformities related to degenerative disease) [36]. When VFA detects a vertebral fracture, standard radiographs should be obtained to confirm the presence of the abnormality and to determine whether it is a fracture or a deformity. VFA showed good agreement with quantitative morphometry of digitized radiographs (94.8%, $\kappa = 0.70$, 95%

Table 4
Indications for vertebral fracture assessment according to a panel of experts convened by the International Society for Clinical Densitometry [51].

1 Postmenopausal women with osteopenia by densitometry and any of the following criteria:
- Age ≥ 70 years
- Historical height loss greater than 4 cm since young adulthood
- Documented height loss greater than 2 cm
- History suggestive of vertebral fracture not documented by prior investigations
- At least two of the following:
  - Age between 60 and 69 years
  - Self-reported prior non-vertebral fracture
  - Historical height loss of 2–4 cm since young adulthood
  - Chronic disease associated with an increased risk of vertebral fractures (e.g., chronic obstructive lung disease, rheumatoid arthritis, or Crohn's disease)

  Level of proof: fairly good. Grade B recommendation

2 Men with osteopenia by densitometry and any of the following criteria:
- Age ≥ 80 years
- Historical height loss greater than 6 cm since young adulthood
- Documented height loss greater than 3 cm
- History suggestive of vertebral fracture not documented by prior investigations
- At least two of the following:
  - Age between 70 and 79 ans.
  - Self-reported prior non-vertebral fracture.
  - Historical height loss of 3–6 cm since young adulthood
  - Androgen antagonist therapy or orchidectomy
  - Chronic disease associated with an increased risk of vertebral fractures (e.g., chronic obstructive lung disease, rheumatoid arthritis, or Crohn's disease)

  Level of proof: fairly good. Grade C recommendation (expert opinion).

3 Women and men taking glucocorticoids (≥5 mg prednisone-equivalent per day for at least 3 months)
Level of proof: fairly good. Grade B recommendation

4 Postmenopausal women and men with osteoporosis by densitometry in whom discovery of one or more vertebral fractures would affect treatment decisions
Level of proof: good. Grade C recommendation.

CI = 0.65–0.76 [39], $\kappa = 0.67$ [40]), consensus qualitative radiograph assessment by two experts ($\kappa = 0.71$, 95% CI = 0.66–0.75) [41], and Jiang's qualitative assessment ($\kappa = 0.62$ and 0.81 in low-risk and high-risk populations, respectively) [26]. A lower level of agreement was found between VFA and Genant's semi-quantitative assessment (95%, $\kappa = 0.545$) [42]. VFA has a high negative predictive value (>80% between T7 and L4 [43], 95.5% [44]): thus, a negative result makes presence of a fracture highly unlikely. Image quality may be poor, most notably at the upper thoracic spine [43]. The κ-value for agreement between VFA and morphometric radiography was 0.32 from T4 to T7 and 0.71 from T8 to L4 [40]. VFA has only 50% sensitivity for detecting grade 1 vertebral fractures [26,42,45]. Poor image quality precluding assessment occurred for a far larger number of vertebras by VFA (11% [45] or 13% [38] among women undergoing routine BMD measurement, 14% in the general population, and 15% in osteoporotic patients) than by morphometric radiography (<1% and 1%, respectively) [41]. Lower levels of interobserver agreement were found with VFA than with Genant's semi-quantitative assessment of standard radiographs ($\kappa = 0.56$, 95% CI = 0.541–0.580; and $\kappa = 0.599$, 95% CI = 0.580–0.618, respectively [45]; $\kappa = 0.69$ and $\kappa = 0.86$, respectively [44]). VFA cannot be performed in patients with scoliosis or severe multilevel degenerative disk disease. Thus, although VFA holds promise, technological improvements are needed. VFA might help to detect vertebral fractures, which escape clinical detection in about two-thirds of cases [46]. Furthermore, VFA may prove a useful complement to BMD measurement, which is not sufficient to identify women at high risk for vertebral fractures, as about half the vertebral fractures occur in women with BMD values in the osteopenic range [47,48]. In clinical practice today, VFA performed during routine densitometry may detect previously unrecognized vertebral fractures in asymptomatic women (and men [49]) with no known fractures and with T-score values < -1 [50]. VFA may also show a second vertebral fracture in an osteoporotic woman with a single known vertebral fracture on old radiographs. In these situations, detection of a new vertebral fracture confirmed by standard radiographs influences the treatment strategy. A panel of experts recently discussed the indications for VFA [51] (Table 4). However, plain radiography remains the reference standard in patients with a clinical suspicion of vertebral fracture (thoracic or lumbar spinal pain in a postmenopausal woman or in a patient with risk factors for osteoporosis, thoracic kyphosis, greater than 6 cm height loss compared to the tallest recalled height, [52], or height loss ≥ 2 cm from one visit to the next [53]). Given the performance characteristics of currently available

Table 5
Methods used to identify incident osteoporotic vertebral fractures in the main therapeutic trials.

Name of the study	Medication	Criteria used to diagnose incident vertebral fractures
FIT [54]	Alendronate	Morphometric radiography (at least 20% and 4 mm decrease in at least one vertebral height versus baseline) confirmed by SQA
VERT [55]	Risedronate	Morphometric radiography (at least 15% decrease in at least one vertebral height versus baseline) confirmed by SQA
BONE [56]	Ibandronate	Morphometric radiography (at least 20% and 4 mm decrease in at least one vertebral height versus baseline) confirmed by qualitative assessment
MORE [57]	Raloxifene	Combined morphometric radiography (at least 20% and 4 mm decrease in at least one vertebral height versus baseline) and SQA
SOTI [58]	Strontium ranelate	Morphometric radiography (at least 15% or 3 mm decrease in at least one vertebral height versus baseline) confirmed by SQA
NEER [59]	Teriparatide	SQA
HORIZON [60]	Zoledronate	Morphometric radiography (at least 20% and 4 mm decrease in at least one vertebral height versus baseline) confirmed by SQA

SQA: Genant's semi-quantitative assessment.

Table 6
Main features of five methods for evaluating osteoporotic vertebral fractures.

	Advantages	Disadvantages	Reproducibility	Use		
				Routine	Epidemiology	Therapeutic trials
Subjective visual assessment	Simple	Subjective	Poor	Yes	No	No
Genant's semi-quantitative assessment	Simple Proven to predict subsequent fractures Differential diagnosis	Training and experience needed	Very good	Yes	Yes	Yes
Jiang's qualitative assessment	Simple Differential diagnosis	Validation ongoing Not proved to predict subsequent fractures	Good	Yes	No	No
Morphometric radiography	Objective vertebral height measurement Proven to predict subsequent fractures	Tedious No differential diagnosis	Good	No	Yes If concomitant qualitative assessment	Yes
Dual-energy X-ray absorptiometry	Simultaneous BMD measurement Lower radiation exposure, lower cost	No differential diagnosis Thoracic vertebras poorly visualized	Fair	Yes	No	No

machines, we do not recommend VFA for therapeutic trials or epidemiological studies.

Table 5 shows the methods used to diagnose incident vertebral fractures in the main therapeutic trials published to date [54–60]. Table 6 summarizes the main characteristics of available methods for evaluating osteoporotic vertebral fractures.

Overall, our review suggests that the preferred method may be Genant's semi-quantitative assessment by a trained and experienced observer. When the number of radiographs needed for a study is too large to allow routine interpretation by an expert, visual semi-quantitative assessment can be used to separate normal vertebras from doubtful or fractured vertebras, which can then be examined by an expert [61]. Alternatively, examination by an expert can be reserved for vertebras with a discrepancy between the results of quantitative morphometry and semi-quantitative assessment. VFA by DXA can detect vertebral fractures in asymptomatic patients undergoing routine BMD measurements. At present, we do not recommend Jiang's method, which is still being evaluated.

4. Conflict of interest

None of the authors has any conflicts of interest to declare.

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