Identification of Vertebral Fractures

Mohamed Jarraya, Daichi Hayashi, James F. Griffith, Ali Guermazi, and Harry K. Genant

Contents

Abstract

Osteoporosis is characterized by reduced bone mass and microarchitectural deterioration of bone, leading to an increase in bone fragility and susceptibility to low-traumatic or atraumatic fractures, most commonly vertebral fractures. Osteoporotic vertebral fractures have a significant impact on morbidity, mortality, and healthcare costs. Vertebral fracture is an independent and significant predictor of increased risk for further fractures. The occurrence of vertebral fracture is often clinically asymptomatic, and many of these fractures, therefore, remain undiagnosed. Several techniques are available for their reliable identification on radiographs. The two most widely used methods are the semiquantitative (SQ) assessment, which is based on visual evaluation, and the quantitative approach, which is based on morphometric criteria. Genant's SQ approach is an accurate and reproducible method, tested and applied in many clinical studies. The newest generation of fan-beam dual energy *X*-ray absorptiometry (DXA) systems delivering lateral spine images of higher resolution offer a practical alternative to radiographs for vertebral fracture analysis. The advantages of DXA over radiography are its minimal radiation exposure and the practicalities of a one-step image acquisition allowing concurrent evaluation of vertebral fracture and bone mineral density, which are important criteria when assessing the risk of osteoporotic fracture. Standard computed tomography (CT) is not primarily used to detect vertebral fracture, though it often leads to the fortuitous detection of asymptomatic fracture. Magnetic resonance imaging (MRI) is an increasingly used modality for assessing the age and other important aspects of vertebral fracture.

M. Jarraya (✉) · D. Hayashi · J. F. Griffith · A. Guermazi · H. K. Genant
Department of Radiology, 820, Harrison Avenue, FGH building, 3rd floor, Boston, MA 02118, USA
e-mail: mjarraya@bu.edu

G. Guglielmi (ed.), *Osteoporosis and Bone Densitometry Measurements*, Medical Radiology. Diagnostic Imaging,
DOI: 10.1007/174_2012_701, © Springer-Verlag Berlin Heidelberg 2013

1 Significance of Vertebral Fracture

Osteoporosis is a progressive systemic skeletal disease characterized by a loss of bone quantity (low bone mass) and quality (microarchitectural deterioration), leading to increased bone fragility and susceptibility to low-energy traumatic or atraumatic fracture (Guermazi et al. 2002; Siris et al. 2012). Although osteoporotic vertebral fracture is often asymptomatic, it is a serious and irreversible outcome of osteoporosis (Cooper et al. 1992; Lindsay et al. 2001) associated with increased mortality (Ettinger et al. 1992) and morbidity (Ensrud et al. 2000). The decreased physical function and social isolation resulting from osteoporotic vertebral fractures has a significant impact on the patient's overall quality of life and self-esteem (Gold 2001). The economic toll is also considerable. With more than 432,000 hospital admissions, almost 2.5 million medical office visits, and about 180,000 nursing home admissions annually in the US, the cost to the healthcare system associated with osteoporosis-related fractures has been estimated at $17 billion for 2005 (Services. UDoHaH. Bone Health and Osteoporosis: A Report of the Surgeon General. In: Department of Health and Human Services OotSG, ed. Rockville, MD: US 2004). According to the United States Surgeon General, fractures and their associated costs could double or triple by the year 2040 (Services. UDoHaH 2004).

Vertebral fractures are the first osteoporotic fractures to occur and also the most common. The reported prevalence of vertebral fracture varies considerably according to the imaging criteria used to diagnose the fractures and the general health of the populations being studied. Thankfully, more stringent criteria on the reporting of vertebral fractures as well as greater recognition of their importance, are allowing a more reliable assessment of fracture rates in different populations. Fracture incidence increases with advancing age and is greater in women than men. Using comparable diagnostic criteria, vertebral fracture rates are rather similar worldwide (Table 1). Early and accurate recognition of vertebral fracture is essential to comprehensive clinical evaluation, determination of population prevalence, and fracture risk as well as evaluation of treatment efficacy. Although vertebral fractures are strongly linked to osteoporosis (DXA *T*-score at or below −2.5), almost half of them occur in patients with osteopenia (*T*-score at or below −1.0) or normal BMD (*T*-score above −1.0) (Siris et al. 2001; Sanders et al. 2006). Subjects with low-energy vertebral fracture indisputably have reduced bone strength, and are therefore osteoporotic irrespective of BMD measurement. For this reason, the National Osteoporosis Foundation has recommended that patients aged over 50 years with atraumatic new vertebral fractures receive appropriate bone protective/bone enhancing therapy, irrespective of DXA *T*-score (Foundation 2010).

It has been shown that the relative risk of new vertebral fracture increases with the number of baseline vertebral fractures (Black et al. 1999; Siris et al. 2007). Therefore, determining vertebral fracture status in addition to BMD, provides practical information when predicting fracture risk in post menopausal women (Siris et al. 2007). Over an 8-year period, subjects with pre-existing vertebral fractures had a 5-fold increased risk of further vertebral fractures and a 3-fold increased risk of proximal femoral fracture compared to those without a pre-existing vertebral fracture (Black et al. 1999). Incident vertebral fractures also increase risk of future vertebral fractures especially in the year following the fracture; 20 % of women with incidental vertebral fracture experience another fracture within a year (Lindsay et al. 2001). This demonstrates the need for identification and intervention of at-risk patients, especially as early treatment with appropriate anti-fracture medication significantly reduces the occurrence of new vertebral and nonvertebral fractures (Ensrud and Schousboe 2011).

Despite the importance of early vertebral fracture, under diagnosis is an appreciable problem worldwide. There are many reasons. First, vertebral fractures are often asymptomatic with only one-third of retrospectively diagnosed vertebral fractures relating to a clinically symptomatic period (Cooper et al. 1992). Second, the typical clinical symptoms of back pain and restricted movement are usually attributed to spondylosis rather than vertebral fracture so that most patients with vertebral fracture do not seek medical attention. Third, about one-third to one-half of vertebral fractures are under diagnosed in radiology reports (Delmas et al. 2005). Many vertebral fractures are clinically asymptomatic, and radiologists and clinicians who review imaging studies should look specifically for vertebral fractures (Lenchik et al. 2004; Adams et al. 2010). If a vertebral fracture is present, then it is imperative that it is reported clearly as a "vertebral fracture" and not with ambiguous descriptions such as "vertebral collapse", "compressed vertebral body", "loss of vertebral height", "wedging of vertebral body", "wedge deformity", "biconcavity" or "codfish deformity". The location and severity of any vertebral fracture should also be clearly stated.

2 Pathophysiology of Vertebral Fracture

Unlike the diaphyses of long bones, the vertebral body mainly relies on trabecular bone for its strength rather than cortical bone. However, trabecular bone surface area and thinness makes it particularly responsive to change in its microenvironment and, therefore, vertebral bodies are one of

Table 1 Comparison of age-specific vertebral fracture prevalence of women worldwide using comparable assessment methods

Age (years)	Chinese [a, f (%)]	Japanese [b, g (%)]	Latin American [c, g (%)]	European [d, g (%)]	American (white) [e, g (%)]
50 ~ 59		2.7	6.9	6.3	
60 ~ 69	10.8	13.8	10.2	11.7	14.5
70 ~ 79	17.4	17.5	18	20.9	22
80+	29.5		27.8		33.9

LAVOS Latin american vertebral osteoporosis study, EVOS European vertebral osteoporosis study

[a] Ms. OS (Hong Kong) study (Kwok et al. 2012)

[b] The japanese population-based osteoporosis study (Kadowaki et al. 2010)

[c] The latin american vertebral osteoporosis study (Clark et al. 2009)

[d] The European vertebral osteoporosis study (Johnell et al. 1997)

[e] The study of osteoporotic fractures (Clark et al. 2009; Black et al. 1999) (quoted from Table 5 in (Clark et al. 2009))

[f] Genant's SQ system

[g] Quantitative methods of McCloskey–Kanis criteria or McCloskey–Kanis criteria with mean—3SD criteria (population-based reference)

the first bones to be affected in osteoporosis (Griffith et al. in press). The vertebral body is particularly prone to early osteoporotic fracture. The weakest parts of the vertebral body are the central and antero-superior components of the end-plates where lower BMD is not compensated by higher trabecular strength (Banse et al. 2002). Other features such as microarchitecture, collagen composition, microdamage, mineralization, and osteocyte function may also play a role, although their relative contributions to vertebral strength remain ill-defined (Christiansen and Bouxsein 2010). Beside BMD, vertebral strength largely depends on vertebral size. An increase in vertebral body cross-sectional area will increase vertebral body strength (Griffith et al. in press). With age, vertebrae undergo periosteal apposition with resultant outward cortical displacement as a response to diminishing BMD. This enlarges the cross-sectional surface of the vertebral body and increases its resistance to compressive forces. These changes in vertebral body cross-sectional area can help somewhat to offset other changes occurring with age which have a cumulative deleterious effect, such as increased endocortical resorption, increased cortical porosity, and especially, decreased trabecular vertebral BMD (Riggs 2004). A greater lifelong decrease in trabecular and cortical vertebral bone mass coupled with a smaller bone size in women at the end of puberty compared to men helps to explain why osteoporotic fractures are more common in elderly women than in elderly men (Riggs 2004).

Changes in trabecular bone with age have been studied including assessment of the number and thickness of both vertical and horizontal trabeculae. While both horizontal and vertical trabeculae are removed with age, corresponding to a decrease in trabeculae number, only horizontal trabeculae display significant loss of thickness (Thomsen et al. 2002). The horizontal trabeculae are thought to be lost largely because of strain-adaptive resorption, while vertical trabeculae loss is due to perforation from microdamage resorption followed by rapid strain-adaptive resorption of the remaining unloaded trabeculae (Mc Donnell et al. 2009). The predominant loss of horizontal trabeculae and the preservation of the longitudinal trabeculae can result in the radiographic appearance of longitudinal striation (Fig. 1).

A vertebral fracture occurs when the force sustained by the vertebra exceeds its strength. Unlike long bones where fractures occur as a definite event, vertebral fractures often progress incrementally and this incremental nature is reflected in the overlapping of the various stages of fracture healing seen on histology (Diamond et al. 2007). Depending on the sustained force and inherent vertebral body strength, fracture severity can vary from a minor peripheral fracture to an almost complete vertebral body fracture. Most vertebral fractures occur in the mid-thoracic (T6-T8) and thoracolumbar (T11-L2) regions (Genant et al. 1996). Compressive loading is accentuated in the mid-thoracic spine during flexion when increased kyphosis is present, and also in the thoracolumbar region which is the transition zone between the relatively fixed thoracic, and the more mobile lumbar segments. Osteoporotic vertebral fractures are rare above the T4 level (Genant and Jergas 2003). Loading on the spine is determined by gravitational forces and muscle contracture which, in turn, are influenced by body weight, height, muscle action, coordination, and strength as well as spinal curvature and intervertebral disk characteristics (Christiansen and Bouxsein 2010). Fracture of a single vertebral body, particularly of the anterior wedge type, shifts compressive forces toward the anterior aspects of the vertebral bodies, potentially leading to a vertebral fracture "cascade", characterized by fractures in adjacent vertebrae occurring in rapid succession (Christiansen and Bouxsein 2010).

3 Clinical Diagnosis of Vertebral Fracture

Vertebral fractures are difficult to identify clinically. Recent large cohort studies of postmenopausal women with low BMD have shown that only about one-fourth of incident

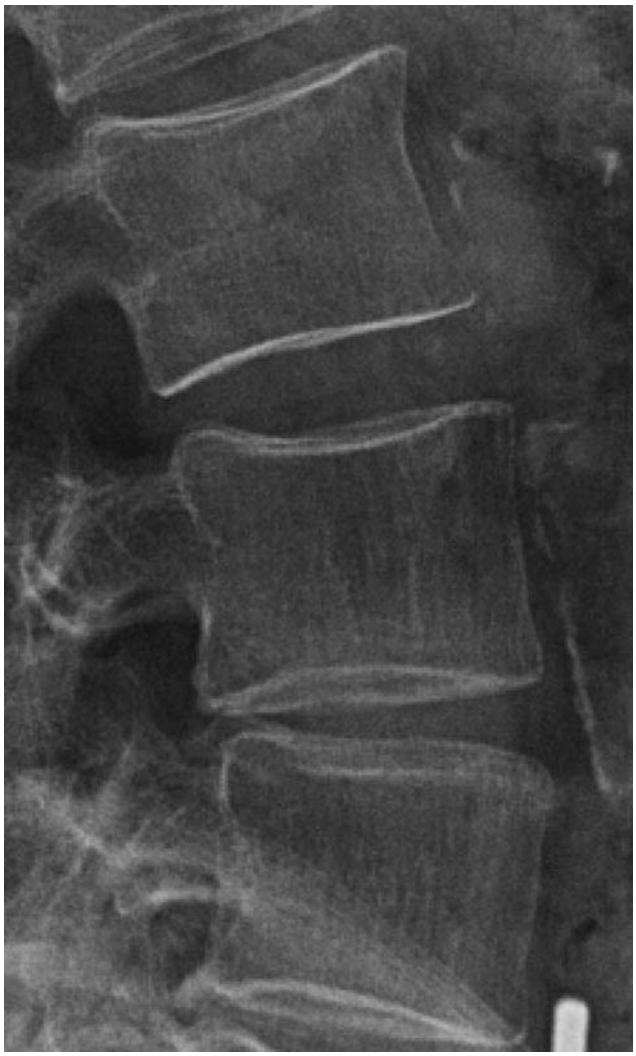

Fig. 1 Radiograph of osteoporotic lumbar vertebrae. The vertical striations of the spongiosa result from the loss of the horizontal trabeculae and preservation of remaining vertical trabeculae

radiographic vertebral deformities were clinically diagnosed as new vertebral fractures (Fink et al. 2005). Clinical recognition is better for more severe fractures (30 %) than mild fractures (15 %) (Fink et al. 2005). This low recognition rate can be attributed to the absence of specific symptoms and difficulty in determining the cause of symptoms such as pain or height loss. Less than 1 % of back pain episodes are related to vertebral fracture (Ettinger et al. 1995). Historical height loss is difficult to assess clinically. While some spinal height loss is expected with aging due to degenerative and attritional remodeling of the vertebral bodies, narrowing of intervertebral disks, and postural and scoliotic changes, loss of height can also be the result of vertebral fracture. Height loss is considered an unreliable indicator of fracture status until it exceeds 4 cm (Ettinger et al. 1992). Overall, clinical evaluation of vertebral fracture has poor sensitivity and specificity.

4 Radiographic Diagnosis of Vertebral Fracture

Although radiography of the thoracolumbar spine is the standard imaging approach for assessment of vertebral fracture, there is no agreed upon gold standard to define osteoporotic vertebral fracture. To resolve this issue, the first step is to define clearly what a "normal" vertebral body is, taking into account the wide range of intra- and inter-individual variation in vertebral body size and shape. Technical considerations, such as the oblique projection secondary to malpositioning of the patient, and the parallax effect caused by the divergent *X*-ray beam are additional factors that can create a misleading appearance (Hurxthal 1968). Once a vertebral body is recognized as "abnormal", the second step is to decide whether this abnormality actually indicates an osteoporotic fracture (Smith-Bindman et al. 1991; Cooper and Melton 1992; Herss Nielsen et al. 1991). Established methods rely mainly on the reduction of vertebral height to define a vertebral fracture. This is problematic especially for mild pre-existing (prevalent) fracture, since only a longitudinal comparison can identify true change in vertebral height (Ferrar et al. 2005).

Not every deformed vertebral body is a result of osteoporotic fracture. Radiologists should be aware of six common pitfalls that can be confused with mild vertebral fractures:

- *Physiologic wedging* is a normal feature as the spine changes from thoracic kyphosis to lumbar lordosis. All vertebrae, but particularly T5-T9, T12-L1, L4-L5 are physiologically wedged. The vertebral bodies of the lower thoracic and upper lumbar spine (T10-L2) are slightly anteriorly wedged, while the lower lumbar region is posteriorly wedged (L4 & L5) (Fig. 2) (Masharawi et al. 2008).
- *Short vertebral height (SVH)* is an important physiological feature that occurs with age and is commonly overdiagnosed as osteoporotic fracture. Differentiating SVH from a mild vertebral fracture is probably the most contentious and difficult area in vertebral fracture diagnosis. SVH is independent of osteoporosis and vertebral fracture, and is more important on the anterior aspect of the vertebrae than the middle and posterior parts, particularly with regard to thoracic kyphosis in the elderly (Diacinti et al. 1995). Women between 30 and 70 years of age show a decrease of the combined height of the anterior aspects of the vertebral bodies from T4 to L5 at a rate of about 1.5 mm/year, while the combined middle and posterior heights decline at about 1.2 mm/year (Diacinti et al. 1995). SVH refers to a reduction in vertebral height of up to 20 % of the expected height, but it is sometimes very hard to differentiate from a mild vertebral fracture

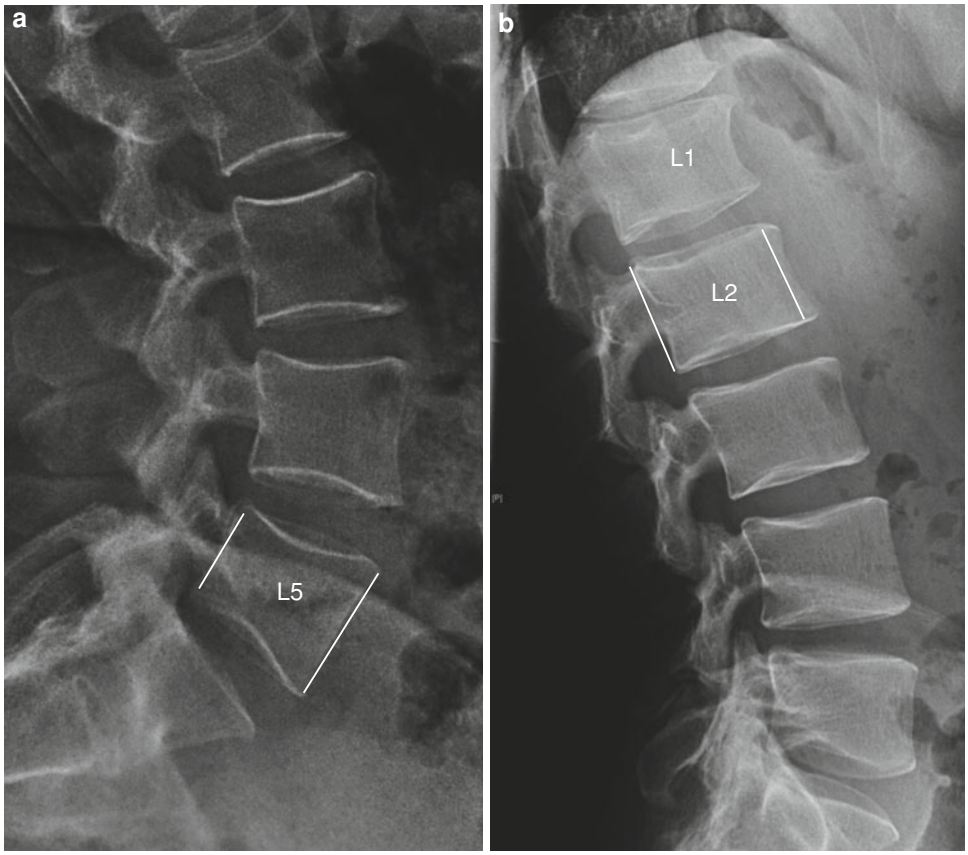

Fig. 2 Lateral *X*-rays of the lumbar spine in a 30-year-old woman and 25-year-old man, respectively. **a** Normal appearance of physiologic posterior wedging of L5. **b** Physiologic anterior wedging of L1 and L2

(20–25 % of height loss). However, the majority of evidence suggests that isolated SVH is not associated with low BMD or irregularity of the vertebral endplate (Ferrar et al. 2007). SVH, when isolated and when not associated with endplate irregularity or other features of fracture, is most likely the result of physiological wedging exacerbated by vertebral remodeling due to increasing age or spondylosis as discussed in the previous section (Fig. 3) (Griffith et al. in press).

- *Scheuermann disease* is a disorder that causes back pain in teenagers and young adults, and is likely related to compressive injuries to the cartilaginous endplates. It is identified by these criteria: (i) elongated vertebral bodies affecting at least three adjacent vertebrae; (ii) irregular wavy endplates with Schmorl nodes; (iii) accelerated degenerative changes (Ferrar et al. 2007). It can affect the thoracic or lumbar spine, mostly the former, leading to an exaggerated thoracic kyphosis and a decreased lumbar lordosis or both. An increased anteroposterior diameter of the vertebral body, small intervertebral disk, endplate irregularity, and premature disk degeneration are helpful features for diagnosing Scheuermann disease and distinguishing it from vertebral fracture.
- *Obliquity of vertebral bodies due to scoliosis* may lead to side-to-side discrepancy in vertebral body height. On the lateral projection, this obliquity gives a biconcave outline to the vertebral endplates which may be misinterpreted as a vertebral fracture. On the anteroposterior view, the vertebral body is reduced on the concave side, and of normal height, or even increased, on the convex side. Degenerative-type scoliosis is quite common, particularly in the elderly lumbar spine. With experience, one can determine whether the degree of apparent loss of vertebral height is commensurate with the degree of scoliosis. Unilateral loss of vertebral height due to scoliosis should not be considered a vertebral fracture.
- *Schmorl node* is a displacement of intervertebral disk tissue into the vertebral body. Although Schmorl node is a manifestation of Scheuermann disease, it is far more commonly encountered in isolation (Pfirrmann and Resnick 2001), present in 40–75 % of imaging studies and sometimes associated with degenerative disease of the lumbar spine (Griffith et al. in press). Schmorl node only involves a segment of the endplate, and is seen as well-defined rounded contour, with an intact sclerotic margin (Fig. 4).
- *Cupid's bow deformity* is a common developmental endplate contour abnormality, most frequently affecting the inferior endplate of the fourth and fifth lumbar vertebral bodies. The more cephalad lumbar vertebrae, as well as thoracic vertebrae, may rarely be involved (Chan et al. 1997). It results from a lack of cartilage in the

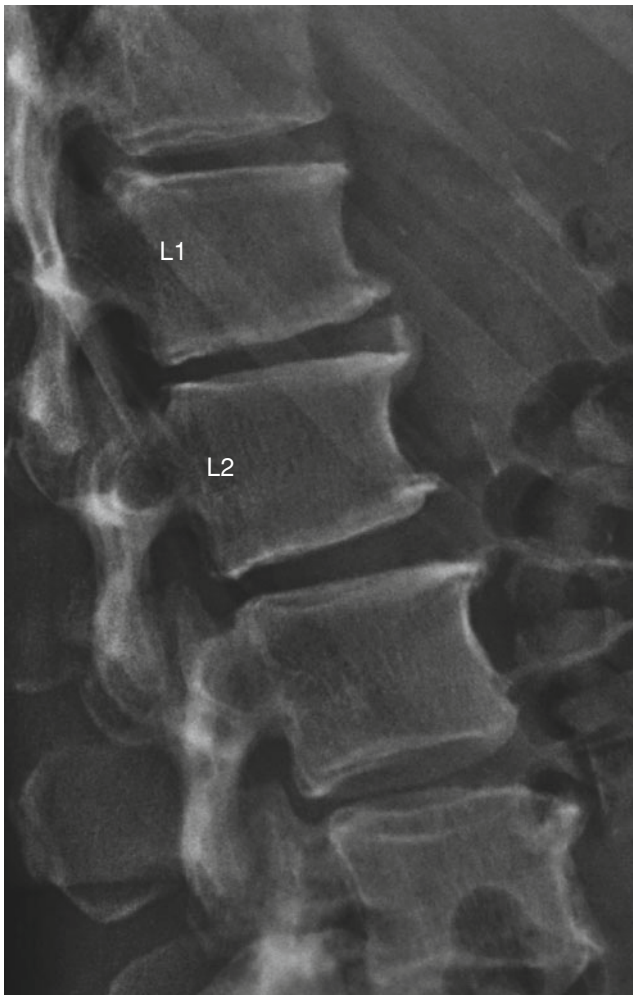

Fig. 3 SVH of L1 and L2 exaggerated by degenerative remodeling. Notice the presence of associated anterior osteophytes and L1-L2 disc space narrowing

parasagittal endplate areas leading to impaired endochondral growth of the vertebral body with concave endplate depressions, resembling Cupid's bow on the anteroposterior radiograph. The nucleus pulposis tends to be enlarged and bilobed. On the lateral projection, the posterior two-thirds of the inferior endplate are indented, simulating a depressed endplate fracture (Griffith et al. in press) (Fig. 5).

In conclusion, "while all vertebral fractures result in vertebral deformity, not all vertebral deformities represent a vertebral fracture" (Genant and Jergas 2003). Radiologists should be aware of entities other than fracture that can change vertebral body shape. The term *deformity* is appropriate when reporting such nonfracture etiologies (Link et al. 2005). With careful scrutiny of imaging features, these vertebral deformities can usually be differentiated from vertebral fractures.

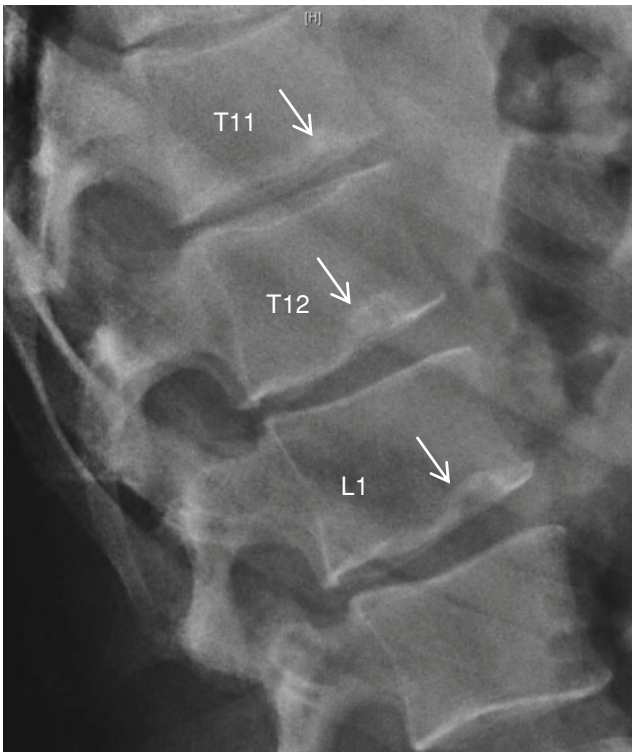

Fig. 4 Lateral *X*-ray of the lumbar spine showing Schmorl nodes of the inferior endplates of T11, T12, and L1. Notice their characteristic rounded contour with sclerotic margin (*arrows*)

5 Spinal Radiography

In clinical practice, radiographic diagnosis is the best way to identify osteoporotic vertebral fracture. The standardized radiographic protocol consists of anteroposterior (AP) and lateral views, including the C7-S1 vertebrae. A focus-film distance of 100 cm and an *X*-ray beam centered at T7 and L3, for the thoracic and lumbar spines respectively, are necessary for a good radiographic spinal examination. Because of the superimposition of the scapula and shoulder regions, the upper thoracic (T1-T3) vertebral bodies are often not clearly seen on lateral views. However, isolated osteoporotic fractures in this region are extremely uncommon. On the lateral projection, the spine must be parallel to the film so that the vertebral endplates at the level of the central *X*-ray beam are superimposed and seen as single dense, well-defined cortical lines. Since the *X*-ray beam is divergent, the endplates distant from the centering point appear concave ("bean can" effect) and must not be mistaken for vertebral fractures. Although a lateral view is usually sufficient, an AP projection may help detect scoliosis and determine the anatomical level of a vertebral fracture. For the thoracic spine, both an AP and a lateral projection are often undertaken, since the lateral view in isolation may not display the vertebral body outline as consistently as in the lumbar region. The typical effective doses

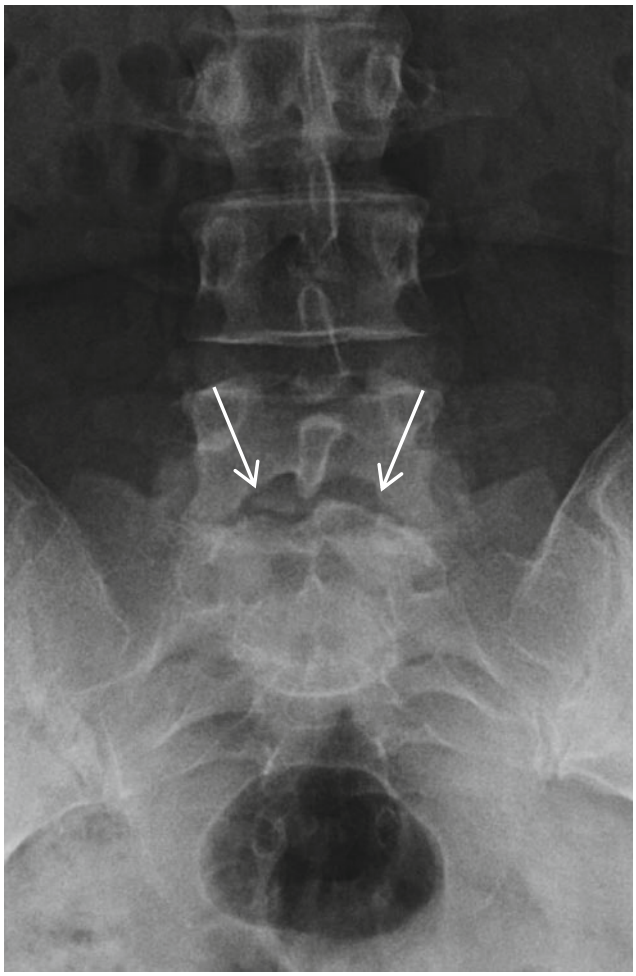

Fig. 5 AP *X*-ray of the lumbar spine in a 25-year-old woman displaying normal appearance of Cupid's bow of the inferior endplate of L5 (*arrows*)

of ionizing radiation from a single lateral and AP projection of the thoracic spine are 0.3–0.4, while for the lumbar spine they are 0.3–0.7 mSv. By comparison, a 16-hour return transatlantic flight would amount to 0.07 mSv background radiation (Griffith et al. in press; Damilakis et al. 2010).

One global prospective study (the IMPACT study (Delmas et al. 2005)), compared the results of local radiographic reports from five continents with that of subsequent central readings in more than 2,000 postmenopausal women with osteoporosis. This study pointed out the significance of radiological under-diagnosis of vertebral fractures worldwide, with false-negative rates ranging from 27 to 45 %, despite a strict radiographic protocol that provided an unambiguous vertebral fracture definition and minimized the influence of inadequate film quality. It was concluded that the failure was a global problem attributable to either or both lack of radiographic detection and use of ambiguous terminology in reports.

Radiographic examinations of the thoracolumbar spine are usually evaluated by radiologists or clinicians with experience in viewing radiographs to identify vertebral fractures. This said, there is still no universally agreed definition of vertebral fracture. The importance of radiographic evaluation in the identification of vertebral fractures, and the susceptibility of radiographic output to bias, has prompted the quest for a standardized and objective visual assessment method of vertebral fracture identification. Different approaches have been proposed to facilitate both the detection and progression of osteoporotic fracture. These methods are presented in the next section.

6 Visual Assessment of Vertebral Fracture

Since the introduction of the first standardized approach by Smith et al. (1960), which graded only the most severely deformed vertebrae on lateral radiographs, further work has attempted to bring more precision and sensitivity to reporting vertebral fractures. Meunier proposed a grading method according to the shape and deformity of the vertebrae (Meunier 1968) (normal, biconcave, endplate fracture, wedged, or crushed vertebra). A "radiological vertebral index" was calculated as the sum of the vertebral grades, or as a quotient of this sum and the number of vertebrae. Kleerekoper and Nelson (1992) modified Meunier's radiological vertebral index and introduced the so-called "vertebral deformity score" in which a score was assigned to each vertebrae from T4 to L5 based on the reduction in the anterior, middle, and posterior heights (ha, hm, and hp respectively). A vertebral deformity was defined as a reduction of ha, hm, or hp by at least 4 mm or 15 %. These methods depend on vertebral shape and an incident vertebral fracture could only be detected if vertebral shape changed significantly. Genant et al. proposed a standardized visual approach to vertebral fracture identification and grading known as the semiquantitative (SQ) method (Fig. 6) (Genant et al. 1993, 1996; Genant and Jergas 2003). This method is based on the quantification of vertebral height reduction, as well as qualitative assessment which considers the integrity of the endplate, cortical borders, and other deformities such as biconcave, wedge, and compression. The SQ method is easy to apply and is more objective and reproducible than purely qualitative methods, resulting in better interobserver agreement. These clear advantages have made it a standard in several important epidemiological studies of osteoporosis (Ferrar et al. 2005; Siris et al. 2002; Harris et al. 1999) and in most clinical trials of osteoporosis therapies (Meunier et al. 2009; Matsumoto et al. 2009; Chesnut et al. 2004).

Genant's SQ approach consists of visually grading each vertebra from T4 to L4, without direct measurements, based on the apparent degree of vertebral height loss. Relative to

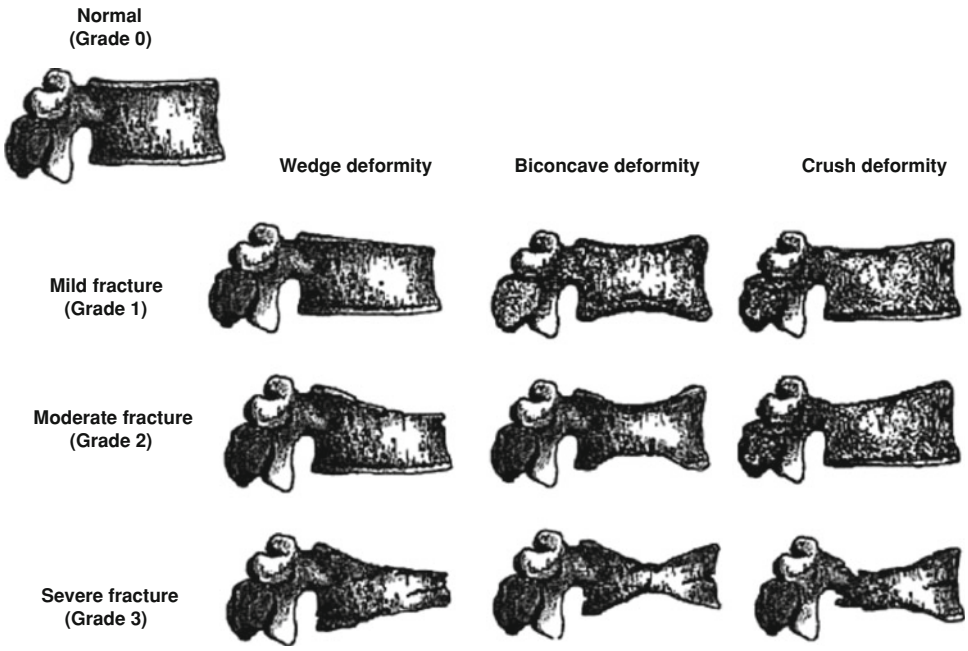

Fig. 6 Genant's grading scheme for a semiquantitative evaluation of vertebral fracture. The drawings illustrate normal vertebrae (*top row*) and mild to severe fractures (respectively in the following *rows*). The size of the reduction in the anterior, middle, or posterior height is reflected in a corresponding fracture grade, from 1 (mild) to 3 (severe) (from Genant et al. 1993)

either normal appearing adjacent vertebrae or relative to what one would normally expect vertebral height to be at that level, the vertebrae are graded as normal (grade 0), mildly deformed (grade 1, reduction of ~20–25 % of height (Fig. 7), moderately deformed (grade 2, reduction of ~25–40 % of height), and severely deformed (grade 3, reduction ~ >40 % of height). Grade 0.5 is sometimes used and designates a borderline vertebral fracture that shows deformity but cannot clearly be assigned to grade 1. In addition, when using the SQ method, it is requisite that one also considers changes of the vertebral endplate and cortical margin, and lack of consistency with adjacent vertebrae, all of which help to distinguish fracture from SVH (Genant et al. 1993).

The SQ analysis of spinal radiographs for vertebral fracture is faster than other methods of vertebral fracture assessment, easy to implement, and suited to epidemiological research studies, clinical therapeutic efficacy trials, and everyday clinical practice. Vertebral fractures detected by SQ analysis are associated with low BMD and are predictive of future fracture, regardless of BMD (Siris et al. 2002, 2007; Delmas et al. 2005; Griffith et al. in press). For longitudinal studies, serial radiographs should be viewed in chronological order to fully appreciate changes in vertebral morphology. Although visual assessment methods of vertebral fractures are potentially more subjective than morphometric analysis, they do allow the experienced reader to address critical issues such as nonosteoporotic deformity and projectional artifacts. SQ analysis is also better suited to deal with errors introduced by radiographic technique such as magnification effects, which clearly would influence serial vertebral body measurements. The SQ method is a practical and reproducible method of vertebral fracture assessment when performed by trained and experienced readers (Griffith in press; Ferrar et al. 2012; Buehring et al. 2010).

6.1 Vertebral Quantitative Morphometry

Vertebral quantitative morphometry (QM) is only used in a research setting (Guglielmi et al. 2008). The two main advantages of QM over other methods are that it can be performed by relatively inexperienced or nonmedical research staff, and it provides an objective measure of loss of vertebral height on serial images (Griffith in press). While the description and definition of the methodology is straightforward, the application in practice is often rather subjective. Vertebral QM consists of placement of six points delineating each vertebral body from T4 to L4. The four corner points and two additional points in the middle of the upper and lower endplates are used (Fig. 8). This technique was introduced in 1960 by Barnett and Nordin, who used a transparent ruler to measure vertebral heights on lateral radiographs of the thoracolumbar spine. Vertebral morphometry is performed on lateral radiographs (morphometric *X*-ray radiography or MRX) though it can also be applied to images obtained from dual *X*-ray absorptiometry (DXA) (morphometric *X*-ray absorptiometry or MXA). Currently, QM uses digital images displayed on a high-resolution workstation. Digitization allows magnification of images to a specific level, optimization of contrast and brightness levels, and digital archiving. Point placement may be done manually or automatically. Manual placement, proposed by Hurxthal (1968), excludes features such as

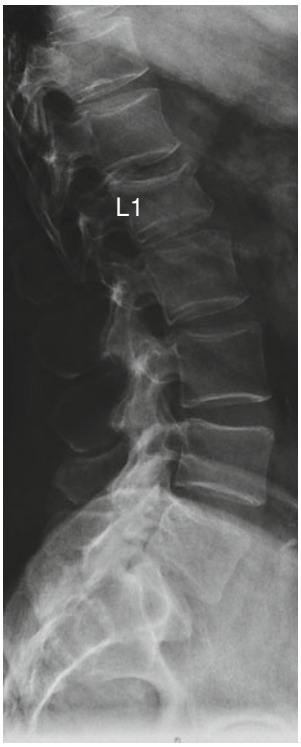

Fig. 7 Lateral *X*-ray of the lumbar spine showing a mild anterior fracture of L1 (grade 1 according to Genant's SQ assessment) in a 53-year-old man presenting with 1 week history of back pain

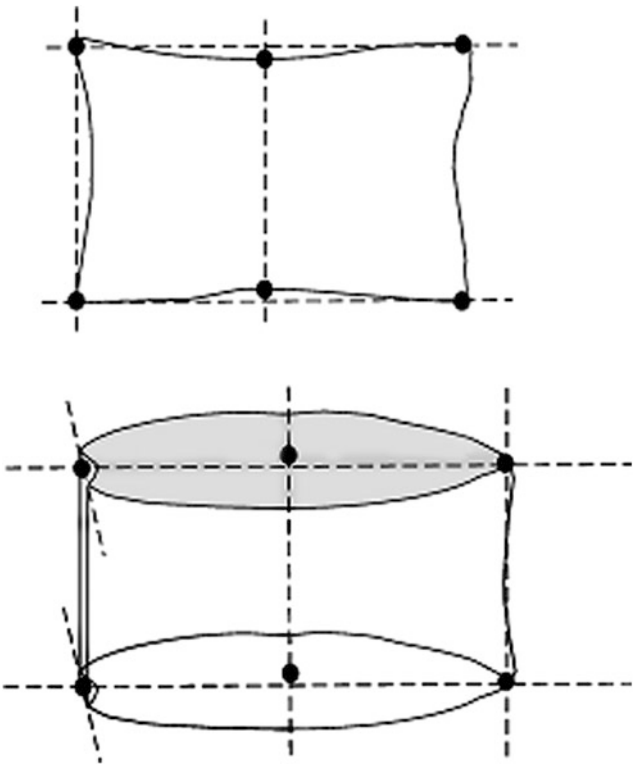

Fig. 8 Example of six-point placement for vertebral morphometry

Schmorl nodes and osteophytes from measurements. When the outer contours of the endplate are not superimposed (due to incorrect positioning or severe scoliosis), the middle point is placed centrally between the upper and the lower endplate contour (Guglielmi et al. 2008). With automatic placement, which brings more precision by reducing operator dependent errors (Nicholson et al. 1993; Kalidis et al. 1992), the endplates and the four corners of the vertebral bodies are highlighted by image post-processing. The software determines the midpoints between the posterior and anterior corner points of the upper and lower endplates, and then the reader selects the true midpoints by moving the caliper along the vertical midline joining the endplates (Guglielmi et al. 2008). Afterward, the computer calculates the posterior, anterior, and middle heights (ha, hm, and hp) of each vertebra from T4 to L5, as well as specific indices reflecting vertebral shape. These indices consist of A_H/P_H (anterior wedging), M_H/P_H (endplate concavity), and $P_H/P_{H'}$ of the adjacent normal vertebrae (posterior compression) (Griffith et al. in press; Grados et al. 2009). Prevalent vertebral fracture is defined as a reduction in one or more of the three vertebral height ratios (A_H/P_H, M_H/P_H, or $P_H/P_{H'}$) >20 % or 3 standard deviations from the mean of a reference population. Incident vertebral fracture is defined as a reduction in one of the three height ratios (A_H/P_H, M_H/P_H, or $P_H/P_{H'}$) >15–20 % or 3–4 mm compared to baseline (Griffith et al. in press; Melton et al. 1993; Eastell et al. 1991). While the reproducibility of QM is good in normal subjects, with an interobserver coefficient of variation of <2 %, it is not as good in the very elderly and in those with osteoporotic fractures where the interobserver and intraobserver coefficients of variation are 5 and 6.3 % for M_H (Grados et al. 2001). Although QM parameters are objective, the approach has some significant limitations.

However, good the radiographic technique, even a mild degree of scoliosis will invariably lead to the endplate being visualized slightly en-face. In such situations, observer experience will influence reference point placement for baseline and sequential imaging examinations. Small differences in reference point placement on follow-up radiographs can result in an erroneous diagnosis of incident vertebral fracture by QM, though readily interpreted by the expert reader. QM also does not allow distinction between vertebral fracture and nonfracture vertebral deformity (such as SVH and physiological wedging) (Griffith et al. in press), resulting in false positive diagnoses (Grados et al. 2001; Grigoryan et al. 2003).

6.2 Algorithm-Based Qualitative Assessment

The algorithm-based qualitative (ABQ) method is a modified approach to qualitative assessment. It relies on the detection of vertebral endplate abnormalities related to fracture rather than height loss. The vertebrae are classified as either (i) normal, (ii) osteoporotic fracture, or (iii) nonosteoporotic deformity or SVH. The diagnosis of an osteoporotic vertebral

fracture requires evidence of vertebral endplate fracture and/or loss of expected vertebral height but with no minimum threshold for apparent reduction in vertebral height (Jiang et al. 2004). If a fracture of the cortical margin is also visible radiographically, then there is a vertebral fracture present and it is likely to be of recent origin. Radiographically visible fracture lines in vertebral fracture are uncommon, however. When one or more vertebral heights (anterior, middle, or posterior) is shorter than expected, but without specific endplate abnormalities of fracture (altered texture adjacent to the endplate due to microfracture), it is designated as non-osteoporotic deformity (Griffith et al. in press). The ABQ method is specific but lacks sensitivity. The distinction between endplate fracture, the hallmark of the ABQ method, and other causes of endplate deformity such as Schmorl nodes and degenerative remodeling could be confounders here, especially if vertebral height loss is minimal.

6.3 Mild Vertebral Fracture

Practically, all of the current confusion in vertebral fracture identification is caused by the mild vertebral fracture. Diagnosis of moderate or severe fractures is so much more reliable that some investigators limit vertebral fracture diagnosis to these fractures alone. Such an approach clearly adds to the specificity but reduces the sensitivity of the study. Several studies have documented the clinical relevance of even mild fractures, albeit carrying less importance than moderate and severe SQ fractures (Delmas et al. 2003). When analyzing the findings of any study addressing vertebral fracture prevalence, one must pay careful attention to the criteria that were used to diagnose fracture. Over or under-diagnosing a small number of equivocal fractures will not make a great deal of difference if the population prevalence of vertebral fractures is high, such as in elderly at-risk women, but it will have a more noticeable effect if the vertebral fracture prevalence is low as in a younger population. Vertebral fracture prevalence is often the focus and point of pivotal interest in research studies and requires vigorous standardization to optimize accuracy of vertebral fracture diagnosis. Similarly, on an individual patient basis, diagnosing vertebral fracture at the earliest possible stage will have the most beneficial patient outcome. Conversely, over diagnosis of vertebral fracture may lead to the patient being incorrectly diagnosed as osteoporotic.

6.4 Standardization of Approach to Vertebral Fracture Assessment

In an effort to develop a standardized consensus protocol for the visual assessment of vertebral fracture, the United States National Osteoporosis Foundation Working Group on Vertebral Fractures suggested the following procedural requirements for qualitative (and SQ) assessment of vertebral fracture in osteoporosis research (Kiel 1995):

- Assessments should be performed by a radiologist or trained clinician with specific expertise in the radiology of osteoporosis.
- Qualitative and SQ assessments should be performed according to a written protocol of fracture definition, which is sufficiently detailed that it can be reproduced by other experts. Reference to an atlas of standard films or illustrations may be helpful. It is recommended that a standardized protocol be developed by a consensus of experts radiologists. For large clinical trials, either SQ should be employed in isolation or else QM should be used to support SQ of vertebrae with reduced height on QM assessment.
- The definition of fracture should include deformities of the endplates and anterior borders of vertebral bodies, as well as generalized collapse of the vertebral body.
- Grading of the degree of each fracture should employ discrete, mutually exclusive categories. Again, an atlas of standard film illustrations may help to assure consistency.

There is some subjectivity in each method, and segregating grading into exclusive categories may be problematic, especially for prevalent fractures. However, when assessing vertebral fractures as fracture/nonfracture, trained readers have achieved excellent results. Distinction of fracture from nonfracture is probably the most important step in the assessment, and the SQ standardized grading schemes are appropriate instruments to make this diagnosis reliable and valid. Ensuring reliability in interpretation of incident vertebral fractures on serial radiographs requires close attention to the imaging procedure. Serial radiographs of a patient should always be viewed together in chronological order to achieve a thorough and reliable analysis of all new fractures. Because a vertebral fracture is a permanent event that is not going to return to normal on follow-up radiographs, temporal blinding is not useful: most readers can identify the temporal sequence to a film series by new deformities as well as progressive degenerative changes (Grigoryan et al. 2003).

7 Dual *X*-ray Absorptiometry

Because of the difficulty in identifying vertebral fractures clinically, and the practicalities of routine radiographic assessment, vertebral fracture status is increasingly performed at the same time as the BMD evaluation by DXA. Imaging vertebral fractures using DXA is known as vertebral fracture assessment (VFA). VFA requires a fan-beam DXA scanner with appropriate software and can be performed either with the patient supine on a scanner with a rotating C arm gantry or with the patient in a lateral decubitus position

on a scanner with a fixed gantry. Modern fan-beam DXA scanners can obtain single energy images of the spine from T4 to L4 in <10 s during suspended respiration. The T4-T6 vertebral bodies can be adequately visualized in 40–70 % of patients while vertebrae from T7 and below can be adequately identified in nearly all patients (Ferrar et al. 2000).

The advantages of VFA by DXA rather than radiographs are many and include a substantial reduction in patient dose (up to 100 times), lower cost, and the ability to perform the examination at the point of standard BMD assessment (Grigoryan et al. 2003). Fan-beam *X*-ray bone densitometry systems provide modest resolution lateral spine images, offering a practical alternative to radiographs for clinical VFA. The technology of fan-beam DXA systems with VFA capability is similar to computed tomography in providing a lateral spine image in as little as 10 s (Grigoryan et al. 2003). The DXA *X*-ray beam is orthogonal, rather than divergent, with less parallax and image distortion than radiography. VFA also shows all vertebrae on a single image allowing easier recognition of which vertebral body is fractured.

Once the DXA image is obtained, manual or automated vertebral morphometry known as MXA can be performed (Diacinti and Guglielmi 2010). Morphometric assessment of DXA spinal images assumes progression given the need for quantitative fracture evaluation in clinical trials. Demarcation of the vertebral body by reference points allows measurement of vertebral body height, and an automatic calculation of height ratios and average height. Automated assessment of fracture status based on comparison with normative data is also available (Diacinti and Guglielmi 2010). Superimposition of these baseline reference points on follow-up VFA spine images makes it simple to compare examinations (Diacinti and Guglielmi 2010). However, MXA alone is not recommended for fracture diagnosis. Visual inspection using the Genant SQ method is recommended by the International Society of Clinical Densitometry (ISCD) for diagnosing and grading the severity of vertebral fracture on VFA [http://www.iscd.org/Visitors/positions/OfficialPositionsText.cfm]. Even with current DXA systems, image quality is poorer than radiography, raising the question of how accurately VFA can identify vertebral fracture compared to radiography. Fuerst compared VFA by DXA and radiography, and showed that VFA has only moderate sensitivity for diagnosis of mild vertebral fracture, but a much higher sensitivity/specificity (>90 %) for detecting moderate or severe vertebral fractures (Fuerst et al. 2009). VFA will, certainly, have an increasingly important role in the diagnosis of vertebral fractures and in osteoporosis evaluation. In one DXA-based study, VFA detected unknown vertebral fractures in 1 of 5 patients (Jager et al. 2010).

While DXA-measured BMD is predictive of absolute risk and relative vertebral fracture risk, the degree of risk is difficult to apply on an individual patient basis in clinical practice. FRAX is a computer-based algorithm (http://www.shef.ac.uk/FRAX) developed by the World Health Organization Collaborating Centre for Metabolic Bone Diseases. The algorithm is mainly designed for primary care and calculates the fracture probability from easily obtained clinical risk factors (Kanis et al. 2008). The output of FRAX is the 10-year probability of a major osteoporotic fracture (hip, clinical spine, humerus, or wrist) and the 10-year probability of a hip fracture (Kanis et al. 2011). FRAX aids fracture prediction and such an assessment is needed to make rational treatment decisions, although it does not define any particular interventional threshold, which can vary from country to country.

8 Computed Tomography

Computed tomography (CT) technology includes from multidetector spiral whole-body CT (MDCT) to high-resolution peripheral quantitative CT to microCT. Thanks to its wide availability and ease of midline sagittal reformation, MDCT allows the thoracic/lumbar spine to be evaluated on all CT studies of the thorax/abdomen regardless of clinical indications. This allows the fortuitous detection of vertebral fracture (Fig. 9). In a recent study of patients older than 55 years who had thoracic CT, one-fifth had a moderate or severe thoracic vertebral fracture but less than one-fifth of these fractures had been reported. This same study showed a higher sensitivity of sagittal reformation for the detection of vertebral fracture compared with axial images (Williams et al. 2009). The CT scout views should also be scrutinized routinely for vertebral fractures, since these usually will include more of the spine than is covered by axial sections (Samelson et al. 2011). The major limitation to more widespread primary use and evaluation of CT in vertebral fracture diagnosis is the cost and radiation dose. The effective dose for DXA examination is 0.01–0.05, for 2D QCT of the lumbar spine it is 0.06–0.3 mSv, and for high-resolution volumetric CT to examine vertebral microarchitecture is 3 mSv (equivalent to 1.5 years of background radiation) (Krug et al. 2010).

9 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) has several advantages for assessing bone compared to CT, such as the lack of ionizing radiation, direct orthogonal plane imaging, and the ability to investigate aspects of bone physiology beyond structure, such as marrow fat content, marrow diffusion, and marrow perfusion. Its known disadvantages include the cost and complexity of the MRI equipment and analyses. While a vertebral fracture is generally diagnosed on radiography

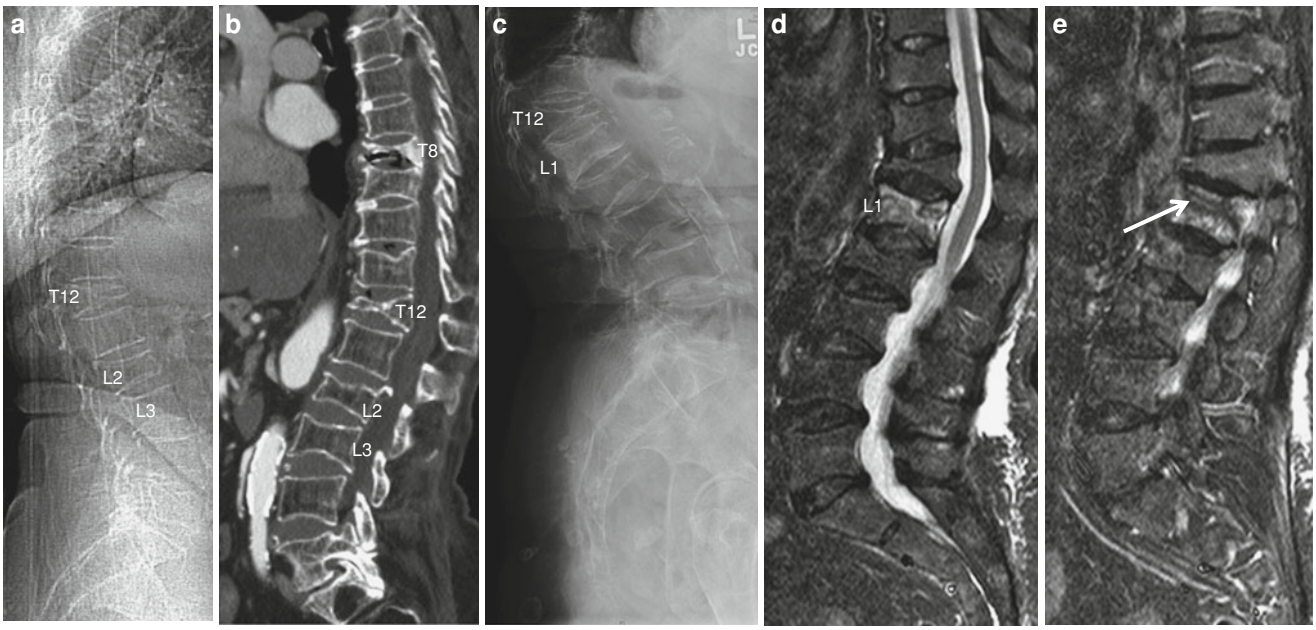

Fig. 9 Osteoporotic fractures in an 85-year-old woman presenting with a new onset of back pain. **a** and **b** Scout view and sagittal reformation of angio CT in 2006 fortuitously show vertebral fracture in T8 (Grade 3), T12 (Grade 3), L2 (Grade 2), and L3 (Grade 1) according to Genant's SQ assessment. Note the nonunion of T8 fracture with intravertebral vacuum and the normal appearance and height of L1. **c** Lateral *X*-ray of the lumbar spine, 5 years later, performed for a new onset of back pain showing a new vertebral fracture of L1 (Grade 2). **d** and **e** Sagittal T2-weighted images with fat suppression displaying diffuse high signal intensity of the vertebral body of L1. No hyperintensity in the fractured vertebrae T12 and L2, indicates older fractures. **e** Linear hypointense fracture line parallel to the superior endplate of L1 (*arrow*)

when there is more than 20 % loss of vertebral height, MRI allows detection of true vertebral fracture without significant height loss, by demonstrating marrow edema in even mild fractures. This is particularly helpful in symptomatic patients without evidence of vertebral fracture on radiography. As MRI scanners have become more widely available, the use of MRI in the assessment of acute vertebral fractures has increased (Griffith et al. in press). Moreover, MRI is an important tool in determining the age of vertebral fracture by detecting marrow edema on fat-suppressed MRI. The presence and degree of edema on T2-weighted fat-suppressed MRI is a reliable guide to the age of a vertebral fracture (Fig. 9). Conversely, vertebral fractures which lack marrow edema are not recent fractures, and unlikely to be symptomatic. These old fractures are much less likely to respond to percutaneous vertebroplasty or balloon kyphoplasty (Griffith et al. in press).

Metastatic vertebral fracture is often the first manifestation of malignancy. Conversely, up to one-third of vertebral fractures in patients with known malignancy are osteoporotic rather than metastatic (Fornasier and Czitrom 1978). Accurate distinction between acute/subacute vertebral fracture and metastatic fracture is often not easy radiographically. The high contrast resolution of MRI makes it very useful in clinical practice for differentiating between osteoporotic and malignant vertebral fracture. By applying a variety of imaging criteria, the distinction can be made with a high degree of accuracy, avoiding any need for percutaneous biopsy (Griffith and Guglielmi 2010).

Nonunion affects about 10 % of acute osteoporotic vertebral fractures. Nonunion is particularly prevalent in the T12 and L1 vertebrae and is evident radiographically as a vacuum cleft extending horizontally across the vertebral body (Fig. 9). These nonunited vertebral fractures are associated with more severe back pain than united fractures (Tsujio et al. 1976). Risk of nonunion is increased significantly if there is retropulsion of the posterior vertebral cortex, with areas of localized high intensity on T2-weighted images or diffuse low intensity within the vertebral body on T2-weighted images (Tsujio et al. 1976). MRI may have the potential to distinguish acute vertebral fractures particularly susceptible to progression or nonunion, which are more likely to benefit from aggressive treatment such as vertebroplasty (Griffith et al. in press).

10 Conclusion

Vertebral fracture is the most common consequence of osteoporosis, occurring in a substantial number of the elderly population. Most vertebral fracture, however, remains clinically unrecognized. The presence, number, and severity of vertebral fracture are strong risk factors for the development

of subsequent osteoporotic fracture. Large-scale clinical trials have demonstrated that osteoporosis therapy can reverse bone loss and reduce the fracture rate, and that these benefits are most pronounced in patients with low BMD and pre-existing vertebral fracture. Clinical guidelines published by the National Osteoporosis Foundation, International Osteoporosis Foundation, and others recognize the importance of vertebral fracture along with BMD as key risk factors for evaluating osteoporosis. Although BMD is widely used in patient evaluation, radiological assessment of vertebral fracture is much less common, or if it is used, it is not well standardized and interpreted. Good radiographic technique and a high level of observer experience in image interpretation are important for the reliable diagnosis of vertebral fracture. VFA by DXA is increasingly being used for vertebral fracture identification. Vertebral fracture diagnosis may be made fortuitously from any imaging method in which the spine is included. In the future, virtual estimation of vertebral body strength with high-resolution imaging techniques may enable patients at risk of vertebral fracture to be identified more effectively. MRI can detect relatively minor acute or subacute vertebral fracture or re-fracture, assess fracture age, and distinguish between osteoporotic and neoplastic fracture with greater sensitivity than other imaging techniques.

References

Adams JE, Lenchik L, Roux C, Genant HK (2010) Radiological assessment of vertebral fracture. International osteoporosis foundation vertebral fracture initiative resource document part II 2010, pp 1–49. http://www.iofbonehealth.org/health-professionals/educational-tools-and-slide-kits/vertebral-fracture-teaching-program.html

Banse X, Devogelaer JP, Grynpas M (2002) Patient-specific microarchitecture of vertebral cancellous bone: a peripheral quantitative computed tomographic and histological study. Bone 30(6):829–835

Black DM, Arden NK, Palermo L, Pearson J, Cummings SR (1999a) Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures. Study of osteoporotic fractures research group. J Bone Miner Res 14(5):821–828

Black DM, Palermo L, Nevitt MC, Genant HK, Christensen L, Cummings SR (1999b) Defining incident vertebral deformity: a prospective comparison of several approaches. the study of osteoporotic fractures research group. J Bone Miner Res 14(1):90–101

Buehring B, Krueger D, Checovich M, Gemar D, Vallarta-Ast N, Genant HK et al (2010) Vertebral fracture assessment: impact of instrument and reader. Osteoporos Int 21(3):487–494

Chan KK, Sartoris DJ, Haghighi P, Sledge P, Barrett-Connor E, Trudell DT et al (1997) Cupid's bow contour of the vertebral body: evaluation of pathogenesis with bone densitometry and imaging-histopathologic correlation. Radiology 202(1):253–256

Chesnut IC, Skag A, Christiansen C, Recker R, Stakkestad JA, Hoiseth A et al (2004) Effects of oral ibandronate administered daily or intermittently on fracture risk in postmenopausal osteoporosis. J Bone Miner Res 19(8):1241–1249

Christiansen BA, Bouxsein ML (2010) Biomechanics of vertebral fractures and the vertebral fracture cascade. Curr Osteoporos Rep 8(4):198–204

Clark P, Cons-Molina F, Deleze M, Ragi S, Haddock L, Zanchetta JR et al (2009) The prevalence of radiographic vertebral fractures in Latin American countries: the Latin American vertebral osteoporosis study (LAVOS). Osteoporos Int 20(2):275–282

Cooper C, Melton LJ 3rd (1992) Vertebral fractures. BMJ 304(6842): 1634–1635

Cooper C, Atkinson EJ, O'Fallon WM, Melton LJ 3rd (1992) Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985–1989. J Bone Miner Res 7(2):221–227

Damilakis J, Adams JE, Guglielmi G, Link TM (2010) Radiation exposure in *X*-ray-based imaging techniques used in osteoporosis. Eur Radiol 20(11):2707–2714

Delmas PD, Genant HK, Crans GG, Stock JL, Wong M, Siris E et al (2003) Severity of prevalent vertebral fractures and the risk of subsequent vertebral and nonvertebral fractures: results from the MORE trial. Bone 33(4):522–532

Delmas PD, Van de Langerijt L, Watts NB, Eastell R, Genant H, Grauer A, Cahall DL (2005) Underdiagnosis of vertebral fractures is a worldwide problem: The IMPACT study. J Bone Miner Res 20(4):557–563

Diacinti D, Guglielmi G (2010) Vertebral morphometry. Radiol Clin North Am 48(3):561–575

Diacinti D, Acca M, D'Erasmo E, Tomei E, Mazzuoli GF (1995) Aging changes in vertebral morphometry. Calcif Tissue Int 57(6): 426–429

Diamond TH, Clark WA, Kumar SV (2007) Histomorphometric analysis of fracture healing cascade in acute osteoporotic vertebral body fractures. Bone 40(3):775–780

Eastell R, Cedel SL, Wahner HW, Riggs BL, Melton LJ 3rd (1991) Classification of vertebral fractures. J Bone Miner Res 6(3):207–215

Ensrud KE, Schousboe JT (2011) Clinical practice. Vertebral fractures. N Engl J Med 364(17):1634–1642

Ensrud KE, Thompson DE, Cauley JA, Nevitt MC, Kado DM, Hochberg MC et al (2000) Prevalent vertebral deformities predict mortality and hospitalization in older women with low bone mass. Fracture intervention trial research group. J Am Geriatr Soc 48(3): 241–249

Ettinger B, Cooper C (1995) Clinical assessment of osteoporotic vertebral fractures. In: Genant HK, Jergas M, van Kuijk C (ed.) Vertebral fracture in osteoporosis. Radiology Research and Education Foundation Publishers, San Francisco, pp 15–20

Ettinger B, Black DM, Nevitt MC, Rundle AC, Cauley JA, Cummings SR et al (1992) Contribution of vertebral deformities to chronic back pain and disability. The study of osteoporotic fractures research group. J Bone Miner Res 7(4):449–456

Ferrar L, Jiang G, Barrington NA, Eastell R (2000) Identification of vertebral deformities in women: comparison of radiological assessment and quantitative morphometry using morphometric radiography and morphometric *X*-ray absorptiometry. J Bone Miner Res 15(3):575–585

Ferrar L, Jiang G, Adams J, Eastell R (2005) Identification of vertebral fractures: an update. Osteoporos Int 16(7):717–728

Ferrar L, Jiang G, Armbrecht G, Reid DM, Roux C, Gluer CC et al (2007) Is short vertebral height always an osteoporotic fracture? The osteoporosis and ultrasound study (OPUS). Bone 41(1):5–12

Ferrar L, Roux C, Reid DM, Felsenberg D, Gluer CC, Eastell R (2012) Prevalence of non-fracture short vertebral height is similar in premenopausal and postmenopausal women: the osteoporosis and ultrasound study. Osteoporos Int 23(3):1035–1040

Fink HA, Milavetz DL, Palermo L, Nevitt MC, Cauley JA, Genant HK et al (2005) What proportion of incident radiographic vertebral deformities is clinically diagnosed and vice versa? J Bone Miner Res 20(7):1216–1222

Fornasier VL, Czitrom AA (1978) Collapsed vertebrae: a review of 659 autopsies. Clin Orthop Relat Res 131:261–265

Foundation NO (2010) Clinician's guide to prevention and treatment of osteoporosis. National Osteoporosis Foundation, Washington

Fuerst T, Wu C, Genant HK, von Ingersleben G, Chen Y, Johnston C et al (2009) Evaluation of vertebral fracture assessment by dual *X*-ray absorptiometry in a multicenter setting. Osteoporos Int 20(7):1199–1205

Genant HK, Jergas M (2003) Assessment of prevalent and incident vertebral fractures in osteoporosis research. Osteoporos Int 14(Suppl 3):S43–S55

Genant HK, Wu CY, van Kuijk C, Nevitt MC (1993) Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res 8(9):1137–1148

Genant HK, Jergas M, Palermo L, Nevitt M, Valentin RS, Black D et al (1996) Comparison of semiquantitative visual and quantitative morphometric assessment of prevalent and incident vertebral fractures in osteoporosis. The study of osteoporotic fractures research group. J Bone Miner Res 11(7):984–996

Gold DT (2001) The nonskeletal consequences of osteoporotic fractures. Psychologic and social outcomes. Rheum Dis Clin North Am 27(1):255–262

Grados F, Roux C, de Vernejoul MC, Utard G, Sebert JL, Fardellone P (2001) Comparison of four morphometric definitions and a semiquantitative consensus reading for assessing prevalent vertebral fractures. Osteoporos Int 12(9):716–722

Grados F, Fechtenbaum J, Flipon E, Kolta S, Roux C, Fardellone P (2009) Radiographic methods for evaluating osteoporotic vertebral fractures. Jt Bone Spine 76(3):241–247

Griffith JF, Guglielmi G (2010) Vertebral fracture. Radiol Clin North Am 48(3):519–529

Griffith JF, Adams JE, Genant HK Diagnosis and classification of vertebral fracture. Primer metabolic bone disease and disorders of mineral metabolism, 8th edn. in press

Grigoryan M, Guermazi A, Roemer FW, Delmas PD, Genant HK (2003) Recognizing and reporting osteoporotic vertebral fractures. Eur Spine J 12(Suppl 2):S104–S112

Guermazi A, Mohr A, Grigorian M, Taouli B, Genant HK (2002) Identification of vertebral fractures in osteoporosis. Semin Musculoskelet Radiol 6(3):241–252

Guglielmi G, Diacinti D, van Kuijk C, Aparisi F, Krestan C, Adams JE et al (2008) Vertebral morphometry: current methods and recent advances. Eur Radiol 18(7):1484–1496

Harris ST, Watts NB, Genant HK, McKeever CD, Hangartner T, Keller M et al (1999) Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis: a randomized controlled trial. Vertebral efficacy with risedronate therapy (VERT) study group. JAMA 282(14):1344–1352

Herss Nielsen VA, Podenphant J, Martens S, Gotfredsen A, Riis BJ (1991) Precision in assessment of osteoporosis from spine radiographs. Eur J Radiol 13(1):11–14

Hurxthal LM (1968) Measurement of anterior vertebral compressions and biconcave vertebrae. Am J Roentgenol Radium Ther Nucl Med. 103(3):635–644

Jager PL, Slart RH, Webber CL, Adachi JD, Papaioannou AL, Gulenchyn KY (2010) Combined vertebral fracture assessment and bone mineral density measurement: a patient-friendly new tool with an important impact on the Canadian risk fracture classification. Can Assoc Radiol J 61(4):194–200

Jiang G, Eastell R, Barrington NA, Ferrar L (2004) Comparison of methods for the visual identification of prevalent vertebral fracture in osteoporosis. Osteoporos Int 15(11):887–896

Johnell O, O'Neill T, Felsenberg D, Kanis J, Cooper C, Silman AJ (1997) Anthropometric measurements and vertebral deformities. European vertebral osteoporosis study (EVOS) group. Am J Epidemiol 146(4):287–293

Kadowaki E, Tamaki J, Iki M, Sato Y, Chiba Y, Kajita E et al (2010) Prevalent vertebral deformity independently increases incident vertebral fracture risk in middle-aged and elderly Japanese women: the Japanese population-based osteoporosis (JPOS) cohort study. Osteoporos Int 21(9):1513–1522

Kalidis L, Felsenberg D, Kalender WA, et al. (1992) Morphometric analysis of digitized radiographs: description of automatic evaluation. In: EFJ R (ed.) Current research in osteoporosis and bone mineral measurement II. British Institute of Radiology, London, pp 4–16

Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E (2008) FRAX and the assessment of fracture probability in men and women from the UK. Osteoporos Int 19(4):385–397

Kanis JA, Hans D, Cooper C, Baim S, Bilezikian JP, Binkley N et al (2011) Interpretation and use of FRAX in clinical practice. Osteoporos Int 22(9):2395–2411

Kiel D (1995) Assessing vertebral fractures. national osteoporosis foundation working group on vertebral fractures. J Bone Miner Res 10(4):518–523

Kleerekoper M, Nelson DA (1992) Vertebral fracture or vertebral deformity. Calcif Tissue Int 50(1):5–6

Krug R, Burghardt AJ, Majumdar S, Link TM (2010) High-resolution imaging techniques for the assessment of osteoporosis. Radiol Clin North Am 48(3):601–621

Kwok AWL, Gong J-S, Wang Y-X J, Leung JCS, Kwok T, Griffith JF, Leung PC (2012) Prevalence and risk factors of radiographic vertebral fractures in elderly Chinese men and women: results of Mr. OS (Hong Kong) and Ms. OS (Hong Kong) studies. Osteoporos Int In press doi: 10.1007/s00198-012-2040-8

Lenchik L, Rogers LF, Delmas PD, Genant HK (2004) Diagnosis of osteoporotic vertebral fractures: importance of recognition and description by radiologists. AJR Am J Roentgenol 183(4):949–958

Lindsay R, Silverman SL, Cooper C, Hanley DA, Barton I, Broy SB et al (2001) Risk of new vertebral fracture in the year following a fracture. JAMA 285(3):320–323

Link TM, Guglielmi G, van Kuijk C, Adams JE (2005) Radiologic assessment of osteoporotic vertebral fractures: diagnostic and prognostic implications. Eur Radiol 15(8):1521–1532

Masharawi Y, Salame K, Mirovsky Y, Peleg S, Dar G, Steinberg N et al (2008) Vertebral body shape variation in the thoracic and lumbar spine: characterization of its asymmetry and wedging. Clin Anat 21(1):46–54

Matsumoto T, Hagino H, Shiraki M, Fukunaga M, Nakano T, Takaoka K et al (2009) Effect of daily oral minodronate on vertebral fractures in Japanese postmenopausal women with established osteoporosis: a randomized placebo-controlled double-blind study. Osteoporos Int 20(8):1429–1437

Mc Donnell P, Harrison N, Liebschner MA, Mc Hugh PE (2009) Simulation of vertebral trabecular bone loss using voxel finite element analysis. J Biomech 42(16):2789–2796

Melton LJ 3rd, Lane AW, Cooper C, Eastell R, O'Fallon WM, Riggs BL (1993) Prevalence and incidence of vertebral deformities. Osteoporos Int 3(3):113–119

Meunier P (1968) La dynamique du remaniement osseux humain, etudiee par lecture quantitative de la biopsie osseuse. Lyon

Meunier PJ, Roux C, Ortolani S, Diaz-Curiel M, Compston J, Marquis P et al (2009) Effects of long-term strontium ranelate treatment on vertebral fracture risk in postmenopausal women with osteoporosis. Osteoporos Int 20(10):1663–1673

Nicholson PH, Haddaway MJ, Davie MW, Evans SF (1993) A computerized technique for vertebral morphometry. Physiol Meas 14(2):195–204

Pfirrmann CW, Resnick D (2001) Schmorl nodes of the thoracic and lumbar spine: radiographic-pathologic study of prevalence, characterization, and correlation with degenerative changes of 1,650 spinal levels in 100 cadavers. Radiology 219(2):368–374

Riggs BL, Melton III LJ, 3rd, Robb RA, Camp JJ, Atkinson EJ, Peterson JM et al. (2004) Population-based study of age and sex differences in

bone volumetric density, size, geometry, and structure at different skeletal sites. J Bone Miner Res 19(12):1945–1954

Samelson EJ, Christiansen BA, Demissie S, Broe KE, Zhou Y, Meng CA et al (2011) Reliability of vertebral fracture assessment using multidetector CT lateral scout views: the framingham osteoporosis study. Osteoporos Int 22(4):1123–1131

Sanders KM, Nicholson GC, Watts JJ, Pasco JA, Henry MJ, Kotowicz MA et al (2006) Half the burden of fragility fractures in the community occur in women without osteoporosis. When is fracture prevention cost-effective? Bone 38(5):694–700

US Department of Health and Human Services (2004). Bone health and osteoporosis: a report of the surgeon general. In: Rockville MD (ed.)

Siris ES, Miller PD, Barrett-Connor E, Faulkner KG, Wehren LE, Abbott TA et al (2001) Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the national osteoporosis risk assessment. JAMA 286(22):2815–2822

Siris E, Adachi JD, Lu Y, Fuerst T, Crans GG, Wong M et al (2002) Effects of raloxifene on fracture severity in postmenopausal women with osteoporosis: results from the MORE study. multiple outcomes of raloxifene evaluation. Osteoporos Int 13(11):907–913

Siris ES, Genant HK, Laster AJ, Chen P, Misurski DA, Krege JH (2007) Enhanced prediction of fracture risk combining vertebral fracture status and BMD. Osteoporos Int 18(6):761–770

Siris ES, Boonen S, Mitchell PJ, Bilezikian J, Silverman S (2012) What's in a name? What constitutes the clinical diagnosis of osteoporosis? Osteoporos Int In press doi:10.1007/s00198-012-1991-0

Smith RW, Eyler WR, Mellinger RC (1960) On the incidence of osteoporosis. Ann Intern Med 52:773–781

Smith-Bindman R, Cummings SR, Steiger P, Genant HK (1991) A comparison of morphometric definitions of vertebral fracture. J Bone Miner Res 6(1):25–34

Thomsen JS, Ebbesen EN, Mosekilde LI (2002) Age-related differences between thinning of horizontal and vertical trabeculae in human lumbar bone as assessed by a new computerized method. Bone 31(1):136–142

Tsujio T, Nakamura H, Terai H, Hoshino M, Namikawa T, Matsumura A, et al. (2011) Characteristic radiographic or magnetic resonance images of fresh osteoporotic vertebral fractures predicting potential risk for nonunion: a prospective multicenter study. Spine (Phila Pa 1976) 36(15):1229–1235

Williams AL, Al-Busaidi A, Sparrow PJ, Adams JE, Whitehouse RW (2009) Under-reporting of osteoporotic vertebral fractures on computed tomography. Eur J Radiol 69(1):179–183