Mini-review

Diagnosis of osteoporotic vertebral fractures

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Summary

Vertebral fractures are the hallmark of osteoporosis, and are associated with increased morbidity and mortality. Because a majority of vertebral fractures often occur in absence of specific trauma and are asymptomatic, their identification is radiographic. The two most widely used methods to determine the severity of vertebral fractures are the visual semiquantitative assessment and the morphometric quantitative approach, involving the measurements of vertebral body heights. Actually the measurements may be made on conventional spinal radiographs (MRX: morphometric X-ray radiography) or on absorptiometric images (MXA: morphometric X-ray absorptiometry). The main advantage of MXA is that the effective dose-equivalent to the patient is considerably lower than for conventional radiography. It also allows combined evaluation of vertebral fracture status and bone mass density, improving selection of candidates for therapeutic intervention.

KEY WORDS: osteoporosis, vertebral fractures, semiquantitative vertebral assessment, quantitative vertebral morphometry, morphometric X-ray radiography, dual X-ray absorptiometry, morphometric X-ray absorptiometry.

Introduction

Vertebral fractures are the most common of all osteoporotic fractures and are present in a significant percentage (25%) of the population over the age of 50, especially in Caucasian women and men in Europe and the United States (1-6). Vertebral fractures are associated with increased mortality rate and loss of independence and impaired quality of life (7-12). Even asymptomatic vertebral fractures could have clinical consequences for the patient because of the increased, approximately five fold, risk of future fractures that may be symptomatic (13). For these reasons the prevention of future fractures for patients with vertebral fractures has been considered the endpoint in clinical trials on osteoporosis therapy (14-18). Because a majority of vertebral fractures often occur in absence of specific trauma and are asymptomatic, they are often difficult to identify clinically. It is in the accurate diagnosis of asymptomatic vertebral fractures that radiologists make perhaps the most significant contribution to osteoporotic patient care. In everyday clinical practice, the qualitative reading of spinal radiographs is still the standard tool to identify vertebral fractures. The assessment by radiologists of conventional radiographs of the thoracic and lumbar spine in lateral and anterior-posterior (AP) projections generally is uncomplicated, allowing the identification of moderate and severe vertebral fractures, *as wedge, end-plate (mono- or biconcave), and crush fractures* (Fig. 1). However, the osteoporotic vertebral fractures often appear such as mild vertebral deformities, without the visible discontinuity of bone architecture. So the visual radiological approach may cause disagreement about whether a vertebra is fractured (19). In an effort to improve the accuracy of the diagnosis of vertebral fractures the semiquantitative assessment (SQ) and the quantitative measurement of vertebral heights (e.g., vertebral morphometry) for the definition of vertebral fractures were introduced more than a decade ago.

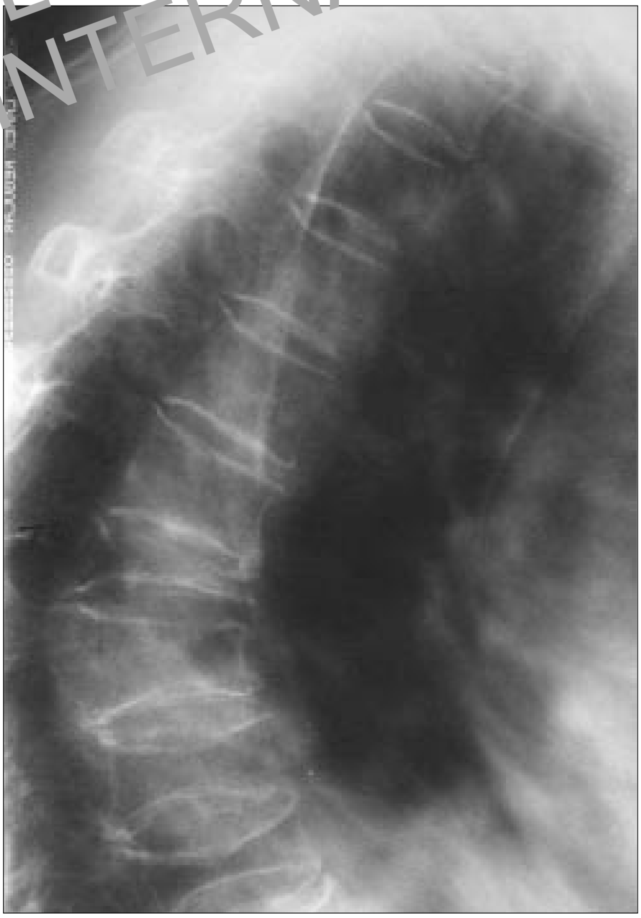

Figure 1 - Lateral thoracic radiograph shows crushing of T9, wedging of T8, T10 and biconcavity of T11, T12.

Visual Semiquantitative (SQ) method

In this approach the conventional radiographs are evaluated by skeletal radiologists or experienced clinicians in order to identify and to classify the vertebral fractures (20). Vertebrae T4-L4 are graded by visual inspection and without direct vertebral measurement as *normal* (grade 0), *mild* but "definite" fracture (grade 1 with approximately 20-25% reduction in anterior, middle, and/or posterior height and 10-20% reduction in area), *moderate* fracture (grade 2 with approximately 25-40% reduction in any height and 20-40% reduction in area), and *severe* fracture (grade 3 with approximately 40% or greater reduction in any height and area). Additionally, a grade 0.5 was used to designate a borderline deformed vertebra that is not considered to be a definite fracture (Tab. I).

Incident fractures are defined as those vertebrae that show a higher deformity grade on the follow-up radiographs. The SQ method is a simple but standardized approach that provides reasonable reproducibility, sensitivity, and specificity, allowing excellent agreement for the diagnosis of prevalent and incident vertebral fractures to be achieved among trained observers (21).

However, this method has some limitations. In cases of subtle deformities (some mild wedges in the midthoracic region and bowed endplates in the lumbar region) the distinction between borderline deformity (grade 0.5) and definite mild (grade 1) fracture can be difficult and sometimes arbitrary (Fig. 2). Another limitation, relatively unimportant, of visual SQ assessment is the poor reproducibility or concordance in distinguishing the three grades of prevalent fractures.

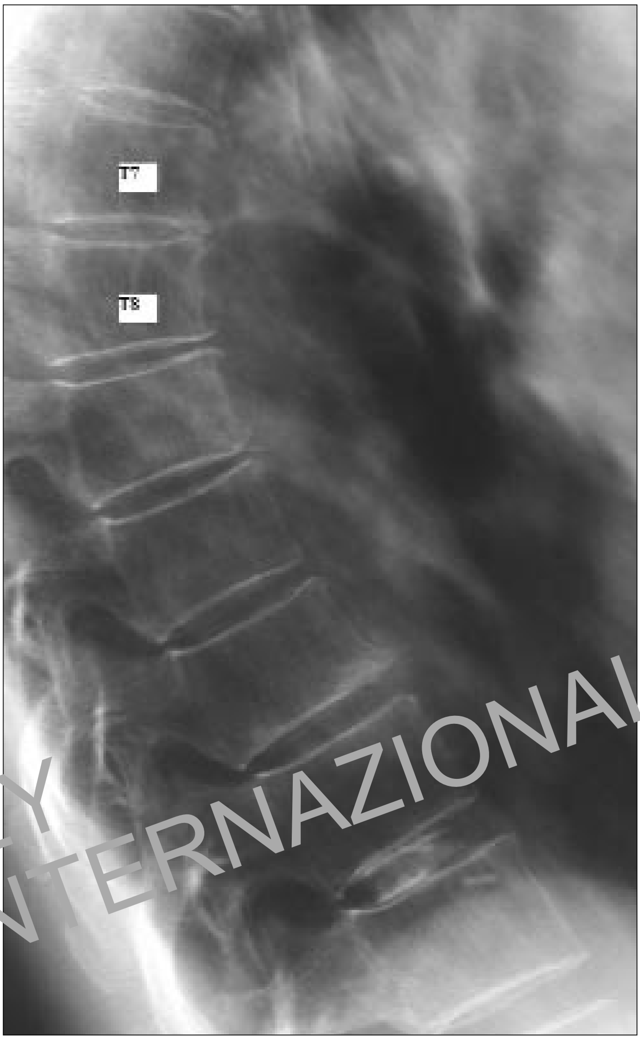

Figure 2 - Visual SQ assessment of T7 and T8: borderline deformities (grade 0.5) or definite mild (grade 1) fractures?

Vertebral morphometry

Quantitative vertebral morphometry involves making measurements of vertebral body heights. Actually the measurements may be made on conventional spinal radiographs (MRX: morphometric X-ray radiography) or on absorptiometric images (MXA: morphometric X-ray absorptiometry).

a) Morphometric X-ray Radiography (MRX)

This technique was introduced as early as 1960 by Barnett and Nordin (22), who used a transparent rule to measure vertebral heights on conventional lateral radiographs of the thoracolumbar spine. Before performing the measurement of vertebral heights, the reader has to identify the vertebral levels; to make this easier, T12 and L1 should be seen on both the lateral thoracic and lumbar radiographs. The vertebral bodies should be marked so that they can be more easily identified in other reading sessions or when compared with follow-up radiographs. On lateral radiographs, with six-point digitization – the most widely used technique – the four corner points of each vertebral body from T4 to L5 (or L4, because of the highly variable shape of L5) and additional point in the middle of the upper and lower endplates are marked (Fig. 2). The manual point placement is done according to Hurxthal (23), who proposed excluding the uncinate process at the posterosuperior border of the thoracic vertebrae from vertebral height measurement and discussed extensively the projection geometry of vertebral bodies. Schmorl's nodes and osteophytes should be ignored in the placement of the vertebral points.

Some investigators (24-27) have assessed the vertebral dimensions from digital images of spine radiographs captured by

Table I - Semiquantitative (SQ) grading scheme (ref. 20).

Fractures	Grading	Vertebral heights	Area
Absent	0	Normal	Normal
Uncertain	0.5	"Borderline"	"Borderline"
Mild	1	Reduction of 20-25%	Reduction of 10-20%
Moderate	2	Reduction of 25-40%	Reduction of 20-40%
Severe	3	Reduction > 40%	Reduction > 40%

means of a video camera or scanner. Post-processing of the digital images can highlight the endplate and the four corners of vertebral bodies allowing points to be placed more precisely. After the radiographs have been digitized, the operator manually selects the four corners of each vertebra. The software then automatically determines the midpoints between the anterior and posterior corner points of the upper and lower endplates and calculates the posterior, middle and anterior heights (Hp, Hm, Ha) of each vertebra and specific indices derived from height measurements for defining vertebral deformities (Fig. 3).

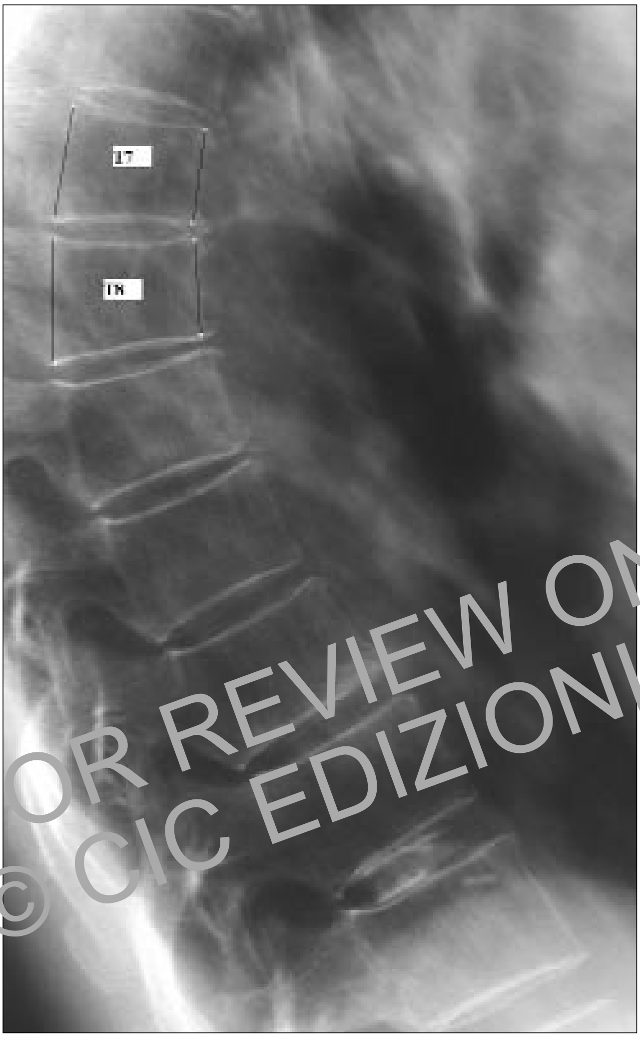

Figure 3 - Useful of MRX: measurement of vertebral heights showed mild wedging of T7 (ha/hp=0.80) and T8 (ha/hp=0.76).

b) Morphometric X-ray Absorptiometry (MXA)

The MXA has been developed by the two major manufacturers of dual-energy X-ray absorptiometry (DXA) equipment: Hologic, Inc. (Waltham, Mass.) and General Electric/Lunar (Madison, Wis.) (28, 29). In Hologic systems, two views of the thoracic and lumbar spine are acquired: a posteroanterior (PA) scan and a lateral scan. The PA image is acquired in order to visualize spinal anatomy such as scoliosis, to determine the centerline of the spine. This information is used in subsequent lateral scan to maintain a constant distance between the center of the spine and the x-ray tube for all subjects at all visits, regardless of patient position or degree of scoliosis, thus eliminating the geometric distortion. Each lateral scan covers a distance of 46 cm, imaging the vertebrae from L4 to T4. The GE /Lunar scanner determines the starting position of the lateral morphometry scan by positioning a laser spot 1 cm above the iliac crest. The scan range for the GE-Lunar systems is determined by measuring the lenght between the iliac crest and the armpit. The lateral scan can be acquired using a single-energy X-ray beam with the scan time very short (12 s). However the analysis may be affected by soft tissue artifacts in the image caused by the prominent imaging of lung structures. These artifacts are absent from the dual-energy scans, that, however, take between 6 minutes (array mode) and 12 minutes (fast and high definiton modes). After the scan, the program automatically identifies vertebral levels and indicates the centers of the vertebrae. The six-point placement for the determination of the vertebral heights is semiautomated. The operator uses a mouse pointing device to specify the 13 locations of the anterior inferior corner of the vertebrae L4 to T4. Then the MXA software computes the positions of the remaining five vertebral points for each. To guide the operator during image analysis of follow-up scans the vertebral endplate markers from the previous scan are superimposed on the current scan improving long-term precision. After the analysis is finished, a final report is displayed. It gives information on the measured vertebral body heights and their ratios, and includes an assessment of the patient's fracture status based on normative data and different models for fracture assessment using quantitative morphometry (Fig. 4).

Comparison between MRX with MXA

The coefficients of variability (CV) of MXR and MXA are similar, the CV ranging from 1.2 to 3.4% (intraoperator CV) and from 1.9 to 5.3% (interoperator CV) according to various authors (30-32). For MXA the precision obtained with two systems, Hologic and GE/Lunar, is similar (33). For MRX it is important that the radiographs are performed very carefully according to standardized procedures in order to achieve good quality images. First, it is important that the films are exposed properly, because the image quality may have a substantial impact on the manual point placement process. Then, because of the vertebral distortion due to the cone beam geometry, the same centering of the X-ray beam should be used (e.g., T7 and L3) (34, 35). MXA overcome some of the patient-positioning and exposure factor problems inherent in conventional radiography. In fact the scanner arm of some models of densitometers can be rotated 90°, so that lateral scans can be obtained with the patient in the supine position without repositioning. A further advantage of MXA when using the scanning fan-beam geometry of DXA devices is the absence of distorsions and magnification effects inherent in the standard X-ray technique (36). The main attraction of MXA is that the effective dose-equivalent to the patient is considerably lower than for conventional radiography (37, 38). While MXA is able to assess the entire spine in a single image, in conventional radiography radiographs of the lumbar and thoracic spine have to be taken separately, so the identification of the vertebral levels to perform MRX may be difficult at times. The principal source of error for MXA is the relatively limited spatial resolution of the lateral spine scans that in the new DXA scanners, Discovery (Hologic, Inc.) and Prodigy (GE/Lunar, Inc.) has been improved by a factor of two, achieved by doubling the number of detectors and by even finer collimation of the x-ray beam. This

Vertebral Assessment

Label	Height (mm) Post	Mid	Ant	Deformity (Grade)	Percent Deformation Wedge	Biconcave	Crush
T4	17.5	16.7	19.3	Normal	0.0%	4.8%	9.2%
T5	19.4	17.8	15.5	Wedge (Mild)	20.0%	8.3%	0.0%
T6	19.1	16.0	17.4	Normal	8.1%	12.0%	0.0%
T7	20.8	18.4	15.8	Wedge (Mild)	24.1%	11.3%	0.0%
T8	18.4	18.7	16.7	Normal	9.3%	9.0%	0.0%
T9	18.9	17.4	18.1	Normal	4.1%	8.0%	0.0%
T10	20.5	18.5	18.5	Normal	9.9%	9.9%	0.0%
T11	22.0	20.5	21.8	Normal	0.9%	7.0%	[illegible]
T12	20.7	16.3	13.8	Wedge (Moderate)	33.6%	[illegible]	[illegible]
L1	25.6	23.2	22.7	Normal	[illegible]	[illegible]	0.0%
L2	26.8	[illegible]	26.2	Normal	2.4%	7.8%	0.0%
L3	[illegible]	[illegible]	[illegible]	Normal	8.6%	15.2%	0.0%
L4	25.8	21.9	25.1	Normal	2.8%	15.2%	0.0%
StdDev	1.0	1.0	1.0		5.0%	5.0%	5.0%

* denotes automatic assessment update

Figure 4 - The final MXA scan report contains data on the vertebral height measurements and on percent vertebral deformation.

improved image spatial resolution allows a better vertebral morphometry (39). Another limitation of the MXA is the limited visualization in the single-energy images of the upper thoracic spine (T4 and T6) and thoracolumbar junction as a result of overlying soft-tissue and bony (ribs, shoulder blade) structures. Dual-energy images is able to visualize the entire spine, but may result in very noisy images that do not allow a clear distinction of anatomic structures. In adipose patients the MXA images may result very noisy because the increased soft-tissue thickness reduces the photon flux significantly. In Table II are summarized advantages and limits of MRX and MXA. So far various comparative studies exist (40-43) that have found excellent agreement with qualitative and quantitative radiographic assessment using fan-beam dual-energy DXA images, particularly for moderate and severe deformities. A large proportion of vertebrae are not visualized sufficiently for analysis on MXA scans and this reduces the number of vertebral fractures identified, particularly in the upper thoracic spine.

Table II - Comparative characteristics of radiographs *vs* fan-beam DXA in spine imaging.

Parameter	Radiographs	Fan-beam DXA
Image resolution	5 lp/mm	0.5-1 lp/mm
Radiation dose	800 μSv	< 10 μSv
Lateral images required	2	1
Imaging geometry	Cone-beam	Fan-beam
Cone beam distortion	Yes	No
Patient positioning	Lateral	Supine
Patient anatomy (scoliosis, obesity)	Possible compensation	Not possible compensation
Vertebrae visualized	All from T4 to L5	Poor visualization of T4-T6

Morphometric definition of vertebral fractures

Because there is no “gold standard” of deformity, it may sometimes be difficult to discriminate the osteoporotic vertebral fracture from a normal variant of vertebral shape or from a vertebral deformation that may have occurred long ago (44). Furthermore, there is variation in vertebral size and shape at different levels of the spine; the anterior and posterior vertebral height increases from T3 to L2, but for L3-L5 the posterior height is lower than the anterior height (45). Vertebral size also varies between individuals: large people tend to have larger vertebrae (46). For these reasons the morphometric diagnosis of vertebral fractures requires the establishment of first the normal values for vertebral heights and then the threshold for separating vertebral deformities from vertebral fractures.

a) Morphometric reference data

Several approaches have been developed to determine the reference values of vertebral bodies heights. Some authors have used a sample of premenopausal women, assuming that the prevalence of vertebral fractures is very low in this population (47-49). This approach may not be feasible for many studies because it involves radiation exposure for fertile women. Moreover it has been demonstrated that vertebral heights change significantly with age, showing rates of loss of 1.2-1.3 mm/year (50-52). Age-related decrease of vertebral heights influences the definition of the normal range of vertebral shape, since a deformity which may be in excess of 2SD from the mean in younger subjects may be well within this limit 20 years later. Other authors (53, 54) have selected a subsample of postmenopausal women in which all vertebrae have been judged to be normal (unfractured) on the radiographs by an expert reader. This approach assumes that qualitative readings are a gold standard, whereas expert readers often disagree about vertebral fractures (19). A third approach for defining normal vertebral dimensions uses the values of a population that includes postmenopausal women with and without vertebral fractures (55).

Also, in a large study (39) the authors have shown that reference ranges of vertebral heights derived from MRX studies may not be applicable to MXA, in view of the observed differences between their MXA mean values when compared with MRX values reported in the earlier studies (47-55). The differences observed led to a tendency for lower MXA critical values for detection of vertebral deformities, suggesting the use of technique-specific reference ranges. However, reference ranges are not generally applicable to different populations, genders, or ages, because the differences in vertebral size are too large (56) and some true fractures may be found within the normal range for the population. For this reason reference ranges should be established in the population under study, using the same technique, and derived from "normal" subjects or by "data trimming" of a population-based-sample.

b) When a vertebral deformity is a vertebral fracture?

There is still disagreement about establishing a threshold of height reduction which would allow unequivocal discrimination between vertebral fractures, deformities, and normal shape (57). Various morphometric algorithms to define vertebral fractures have therefore been developed. Melton et al. (54) introduced an "adjusted algorithm" based on analysis of vertebral height ratios corrected by an adjustment factor. A vertebral body was fractured if any of three height ratios – anterior to posterior height (H_a/H_p for wedge), middle to posterior height (H_m/H_p for biconcavity) and posterior to posterior height of adjacent vertebra (rH_p for crush) – was reduced by more than 15% compared to the normal ratio for that level. The method developed by Eastell et al. (58) classified vertebral fractures by type of deformity (wedge, biconcavity, or crush) and further by degree of deformity as grade 1 or grade 2 based on vertebral height ratios below 3SD or 4SD of a respective normal range for that vertebral level. This approach fails when three or more consecutive posterior deformities are present, and for this reason McCloskey et al. (59) suggested using a predicted posterior height (H_{pp}) that represents for each vertebra the mean of up to four individual predicted posterior heights.

Thus, it is not possible to measure accurately the true and false positive rates of various morphometric definitions of vertebral fractures because there is no "gold standard" for defining a vertebral fracture. In fact, results wide discordances between the studies on the prevalence of vertebral fractures, ranging from 33 to 85% (48, 54, 60, 61) and clinical trials have also shown that the estimated incidence of new vertebral fractures in postmenopausal osteoporosis varies markedly, from 6 to 83 fractures per 100 patient-years (62-65). In particular, less stringent criteria (e.g., -2SD) result in too many false positive results, because they identify as fractures some deformities that may represent developmental abnormalities. By contrast, a more stringent cutoff level, such as 4SD, results in a lower false positive rate (66).

c) Can vertebral morphometry predict a vertebral fracture?

The number of vertebral fractures may not be representative of the severity of spinal osteoporosis, especially in the case of biconcavity fractures, which represent deformations of only the endplate. For this reason, some methods have been developed to estimate the deformity of overall thoracic and lumbar spine. Minne et al. (67) developed the Spine Deformity Index (SDI) to quantify spinal deformity and assess progression of vertebral deformation during follow-up. Other authors (68) introduced new morphometric indices to quantify the spinal deformity, namely, sums of anterior, middle and posterior heights (AHS, MHS, PHS) defined as the sums of the respective 14 vertebral body heights from T4 to L5. It is shown a strongly correlation between these indices and the lumbar bone mineral density (L-BMD), suggesting their use as fracture risk indices.

Comparison of semiquantitative (SQ) visual and quantitative morphometric assessment of vertebral fractures

A vertebral deformity is not always a vertebral fracture, but a vertebral fracture is always a vertebral deformity. There are many causes of vertebral deformities and the correct differential diagnoses for them can be achieved only by visual inspection and expert interpretation of a radiograph. The quantitative morphometry is unable to distinguish osteoporotic vertebral fractures by vertebral deformities due to other factors, such as degenerative spine and disc disease. This limitation is a characteristic of any method of quantitative morphometry, but the limited spatial resolution of the DXA images in MXA may increase this problem (69). On the other hand, MRX, with its superior image quality, has the potential for qualitative reading of the radiographs to aid the differential diagnosis. In fact, although it is recognized that the visual interpretation of radiographs is subjective, it is also true that an expert eye can better distinguish between true fractures and vertebral anomalies than can quantitative morphometry. For example, the distinction between a fractured endplate and the deformity associated with Schmorl's nodes can only be made visually by an experienced observer; as is the case for the diagnosis of the wedge-shaped appearance caused by remodeling of the vertebral bodies in degenerative disc disease (70).

Some comparative studies (21, 71, 72) found a high concordance between different quantitative morphometric approaches and visual semiquantitative evaluation for prevalent vertebral fractures defined as moderate or severe. In this cases there was a strong association with clinical parameters (bone mineral density, height loss, back pain, incidence of subsequent deformities).

Recently the visual semiquantitative method for identification of vertebral fractures has applied to images of the spine acquired by fan-beam DXA devices, and called "instant vertebral assessment" (IVA) by Hologic and "vertebral fracture assessment" (VFA) by GE/Lunar (Fig. 5). IVA has been compared with SQ evaluation of spinal radiographs demonstrating good agreement (96.3%, k=0.79) in classifying vertebrae as normal or deformed in the 1978 of 2093 vertebrae deemed analyzable on both the DXA scans and conventional radiographs (73). IVA showed good sensitivity (91.9%) in the identification of moder-

Figure 5 - Combining BMD & Instant Vertebral Assessment: a new approach to improve the diagnosis rate of vertebral fracture.

ate/severe SQ deformities and an excellent negative predictive value (98%) to distinguish subjects with very low risk of vertebral fractures from those with possible fractures. The disagreement between IVA and SQ method resulted from the poor image quality, particularly in the upper thoracic vertebrae that were not visualized sufficiently for analysis. Although some vertebral fractures were missed by IVA, all patients with prevalent vertebral fractures were identified; therefore, for the identification of patients with fracture, visual assessment of DXA scans had 100% sensitivity and specificity (74). This means that if IVA had been used as a diagnostic pre-screening tool at the first assessment, all the patients with prevalent vertebral fracture would have been correctly referred for radiography to confirm the diagnosis. Also the “normal” subjects can then be excluded prior to performing conventional radiographs and further time-consuming and costly methods of vertebral deformity assessment such as SQ by an experienced radiologist and/or quantitative morphometry.

Conclusions

A combination of semiquantitative visual and quantitative morphometric methods may be the best approach to fracture definition, as suggested by National Osteoporosis Foundation (75) and by the International Osteoporosis Foundation (76). Currently there is no consensus on which morphometric technique should be used, or how, to evaluate patients at risk of osteoporosis. MRX, based upon assessment of conventional radiographs, has unlike MXA the potential for qualitative reading of the radiographs by a trained radiologist or highly experienced clinician who can distinguish between vertebral anomalies and true fractures and detect technical artifacts on the films which might increase the errors on quantitative morphometry. However, in view of the relatively low radiation dose to the patient and the excellent agreement with visual SQ method for the identification of vertebral deformities, the visual or morphometric assessment of lateral DXA spine images may have the potential for use as a prescreening tool. If all vertebrae are visualized adequately by lateral DXA images and classified as normal by IVA or MXA, the patient could be classified as normal. If all vertebrae are not visualized by DXA and if one or more deformities are detected by IVA or MXA, it will be necessary to acquire conventional radiography to check for further prevalent deformities and to identify the nature of the deformity. The availability of a rapid, low-dose, method for assessment of vertebral fractures, using advanced fan-beam DXA devices, provides a practical means for integrated assessment of BMD and vertebral fracture status. This approach allows the identification of most osteoporotic vertebral fractures, even asymptomatic, in patients with low BMD improving selection of candidates for therapeutic intervention.

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