

Detection of Vertebral Fractures

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Despite the importance of vertebral compression fractures, there is much that remains uncertain. There is no “gold standard” for the definition which has led to epidemiologic and study differences. Height loss is a way to suspect vertebral fractures but it has its own issues. There are multiple radiographic systems for defining vertebral fractures, both prevalent and incident; risk factors for prevalent fractures have already been delineated. Recent studies have elucidated the risk factors for incident vertebral fractures including age, low weight, late menarche, lower bone mineral density, history of vertebral and nonvertebral fractures, smoking, and use of a walking aid. Fan beam densitometers have had improving ability to image the spine, a procedure now known as vertebral fracture assessment (VFA). Recently (in the United States) a CPT code and reimbursement was established. Yet, many vertebral fractures go undiagnosed, diagnosed but unreported, or reported but not utilized in patient care. Because of this, the International Osteoporosis Foundation developed a Vertebral Fracture Initiative for radiologists and the International Society for Clinical Densitometry began a VFA course. Both teaching programs use the semi-quantitative assessment of Genant to aid the radiologists and clinicians in detecting vertebral fractures.

Introduction

The detection of vertebral fractures has assumed increasing importance in the past decade because of the realization that such fractures are not incidental abnormalities but rather key findings that bear on the diagnosis, prognosis, and need for and response to treatment in individuals who have sustained them whether they occur asymptotically or symptomatically.

The detection of vertebral fractures can come about in two ways, clinically or radiographically. Clinically, their detection is based on a thorough history relative to the back and its symptoms and the performance of a good physical examination with reference to the back and height. Radiographically, imaging whether it be a radio-

graphic spine series, MRI, or CT of the spine or of other areas that include incidental visualization of the spine (eg, a chest x-ray or an abdominal x-ray) may be utilized to assess the presence of vertebral fractures. In addition, the availability of vertebral fracture assessment (VFA) as a point-of-service modality is expected to increase our recognition of vertebral fractures in the general population.

Definition of a Vertebral Fracture

It is usually clear clinically and radiographically when an individual has a long bone fracture. We are not usually confronted by the problem of silent fractures of a long bone. Unfortunately, the statement that “there is no gold standard for the diagnosis or definition of a vertebral fracture” is repeated throughout the literature and complicates the ability to make a diagnosis. However, this is not helpful to clinicians, radiologists, or those undertaking clinical trials or epidemiologic studies [1,2,3•,4,5].

A Working Group on Vertebral Fractures of the National Osteoporosis Foundation issued a 1995 Report on Assessing Vertebral Fractures [3•] to try to begin standardizations in this area. At that time, it was felt that x-rays of the spine were the best method for assessing the presence of vertebral fractures. Ten years later, the developments in imaging by fan beam dual-energy x-ray absorptiometry (DXA) VFA may represent an alternative procedure.

The Working Group suggested five standards for taking the radiographs [3•]: 1) Technologists should be trained and follow a written protocol; 2) Standards for taking the radiographs need to be developed so that there are normal values and fracture criteria; 3) Films should include lateral views of the thoracic and lumbar spine; 4) Antero-posterior (AP) views can be helpful; and 5) Vertebral levels should be numbered according to a written protocol.

They also suggested criteria for longitudinal studies [3•]. Identical methods should be utilized for obtaining, locating, and identifying the vertebrae for all x-rays from a single patient. All radiographs from a single patient should be assessed at the same time. In clinical trials, those who prepare, read, or make measurements must be blinded to the treatment of the subjects. Occasionally, patients may have such severe deformity of the spine, severe scoliosis, osteoarthritis, or other conditions, that it is impossible to assess the presence or progression of vertebral deformity.

They reviewed issues concerning prevalent fractures through different approaches such as qualitative visual or semi-quantitative assessments versus quantitative assessment

(morphometry). In clinical trials involving community populations, prevalent vertebral fractures were defined as a reduction of three standard deviations (SD) or more from normal mean ratios of dimensions for that particular vertebral level [6]. Incident fractures showed significant reductions in vertebral body height over a short period of time when reviewing serial x-rays of the spine. The occurrence of prevalent fractures could be approached through the qualitative visual, (semi-quantitative) or quantitative (morphometric) assessments; incident fractures by the latter two methods.

In the alendronate trials [7], for example, a woman was classified as having a prevalent fracture if any of the ratios of anterior, middle, and posterior heights, as marked with a translucent digitizer and cursor, was more than three SDs below the mean population normative value for each vertebral level. A new vertebral fracture was defined as a decrease of 20% and at least 4 mm in any vertebral height from the baseline radiograph to that taken at the end of the study. Each fracture was confirmed by repeat digitization and review of the morphometry by the study radiologist (Genant HK).

In the risedronate trials, new incident vertebral fractures were defined as a loss of 15% or more in the anterior, middle, or posterior height in a vertebra that was normal at baseline and semi-quantitatively as a change from grade 0 (normal) to grades 1 (mild), 2 (moderate), or 3 (severe). A worsening vertebral fracture was recorded if there was a change of 4 mm or more in vertebral height since the previous radiograph or a change in grade in a previously fractured vertebra. Again, a blinded independent radiologist reviewed discrepancies between the morphometric and semi-quantitative methods [8].

Height Loss

Historically, one of the ways to suspect the silent occurrence of vertebral fractures is through height loss. This is important clinically since, from early studies, it has been recognized that many vertebral fractures do not come to clinical attention and are found incidentally [9]. Early on, the best data showed that each complete compression fracture caused the loss of about 1 cm in height [10].

Subsequently, it has become clear that there are two aspects of importance when evaluating height loss—historical height loss so that this can be estimated at the time of initial clinical evaluation and prospective height loss so that this can be evaluated in follow-up of the patient [11•]. “Historical height loss” is calculated as the difference between current measured height and self recalled tallest height. Some studies refer to “height at age 25” but this is not always known. In addition, self recalled tallest height is fraught with errors in measurement (which methods, in the physicians’ offices, are not always standardized) and errors in recall. In addition, because of the length of time from the measurement of tallest height (if accomplished) and the next measurement at age 60 and 70 or older, the timing of occurrence of a fracture can not be

pinpointed. “Prospective monitoring of height” where height loss is measured as the difference in height between several height measurements done as part of serial medical examinations [9] is not dependent on patient recall and may be able to identify the time period (eg, the last 6 months) in which a fracture occurred.

Thereafter, this issue began to be looked at in population-based prospective studies. In the Hawaii Osteoporosis Study (HOS), a total of 1379 men and 1105 wives participated in the first examination during 1981 and 1982 [12]. Of these, 504 postmenopausal Japanese-American women aged 54 and 88 had baseline and repeated full spine radiographs and had longitudinal measurements of stature. Over a 7.7 year follow-up period, women without incident fractures lost only 0.4 cm. Women with at least one incident vertebral fracture lost an average of 2.1 cm in height and lost height at an average rate of 2.6 mm per year versus 0.5 mm per year for women without new fractures. Individual vertebral bodies were measured for anterior, middle, and posterior heights. Incident vertebral fractures were defined as a decrease of more than 15% in one of these dimensions on follow-up x-ray films. Upon analysis, it turned out that only total anterior vertebral body height loss was significant. The number of incident wedge and crush fractures, but not endplate fractures, was a strong predictor of height loss.

The European Vertebral Osteoporosis Study (EVOS) [13] found all types of deformity were associated with height loss which was greatest for individuals with crush deformity and smallest for those with wedge deformities. The number of wedge and crush fractures was positively and significantly associated with height loss. The majority of deformities were wedge, followed-up by biconcave and crush. The majority of subjects with vertebral deformity (> 80%) had only one type of deformity present.

The geographic distribution of the three different deformity types by vertebral level was similar in men and women. Wedge deformities tended to occur in the mid-thoracic vertebral bodies (T6-T8) and the thoraco-lumbar junctions (T12-L1). Biconcave deformities were highest in the lumbar area. For each deformity, the degree of height loss was more marked in women. In women, the mean height loss was 5.9 cm for those with two or more wedge deformities and 7.9 cm for those with two or more crush deformities; in men, 3.7 cm and 5.1 cm, respectively.

In the Vertebral Efficacy with Risedronate Therapy (VERT) [11•] studies analysis, height loss was categorized into six groups over the 3-year period of the trials; new fractures occurred in 20.3% of the 985 subjects. Forty-one percent of those who sustained an incident fracture experienced more than one fracture. The more vertebral fractures one developed the greater the height loss: one fracture, 1.1 cm loss; two fractures, average of 2.3 cm loss; three fractures, 6.1%; four fractures, 2.3 cm; those with five or more new fractures lost an average of 5.9 cm. When height loss was greater than 4.0 cm the positive predictive value was 63.9% (23/36) the highest value reached when utilizing receiver

operating characteristics curves for the ability of height loss to detect the development of incident vertebral fractures.

There was, again, a difference in how height was described as being taken with Siminoski *et al.* [11•] having the most complete description and the most rigorous protocol for measuring the height including breathing; the HOS study having an intermediate description of the height taking process but had a crude hand built stadiometer for their initial heights. In the EVOS study, no mention is made of how height was taken.

In the HOS study, there was no apparent attempt to define historic height loss but only height monitoring. In the EVOS study, historic height loss was obtained but not reported nor were there actual millimeter or centimeter changes in height. From Siminoski *et al.* [11•], both historic height and monitoring of height loss were undertaken and prevalent fractures and incident fractures defined.

Each of these representative studies (HOS, EVOS, VERT) utilized a different definition of a vertebral fracture. HOS used a decrease of more than 15% in anterior, medial, or posterior height; EVOS used the McCloskey-Kanis method [14]; and VERT used a definition of 3 SD decrease for heights for a prevalent fracture and 15% or 4 mm for an incident fracture.

In developing indications for VFA the International Society of Clinical Densitometry (ISCD) felt that documented height loss of 2 cm (0.75") or greater and a historic height loss of 4 cm (1.5") were the key deficits in height that might cause one to consider ordering a VFA [15].

However, in clinical practice, height is usually not measured with as close attention to detail as in these prospective population-based or clinical trials from which the data is derived. Most likely, the height is measured by non-stadiometer devices.

Incident Vertebral Fractures

Definition of incident vertebral fracture

If the 1980s and 1990s were the decade of the prevalent fracture, then the present decade has been one of the incident fracture. Black *et al.* [16] from the Study of Osteoporotic Fractures Research Group evaluated different methods for defining prevalent vertebral fractures. In a similar way, they reviewed the various techniques that have been proposed for detecting incident vertebral fractures [17].

The methods for defining incident deformities involve two approaches: changes in vertebral heights of the same vertebral body from a baseline or other in the series of radiographs to a second or later radiograph and defines a fracture as a decrease in height of 15% or 20% or 4 mm [6,7,17–20]; changes in indices of vertebral area [21] or change in the number or presence of prevalent deformities [22].

Black *et al.* [17] proposed that the definition that showed the best relationship to height, back pain, and other predictors would result in the best estimate of true deformity occurrence. After evaluating these systems, they

decided that none of these methods was consistently better than any other method. They used a decrease of 20% or a 3 mm decrease in vertebral height. They determined that using a decrease of 20% to 25% as a standard would allow studies to use smaller sample sizes.

Again, the lack of a gold standard in defining an incident vertebral deformity required the Study of Osteoporotic Fractures (SOF) group to utilize clinical criteria to help validate the presence of a fracture—height loss, presence of a baseline vertebral deformity, and bone mass in the lowest quartile.

Numerous studies have reviewed the risk factors for prevalent vertebral fractures—older age, low bone mass, smoking, alcohol intake, a shorter reproductive span, and long-term use of corticosteroids [4,23].

Risk factors for incident fractures

The conduct of large epidemiologic studies (the European Prospective Osteoporosis Study [EPOS] [24], 14,011 men and women, the Rotterdam Study [25], 3001 men and women, the Canadian Multicentre Osteoporosis Study [CaMos] [26], 5143 postmenopausal women, SOF [27••], 9677 white women > 65 years of age) and clinical trials (Multiple Outcomes of Raloxifene Evaluation [MORE] [28] study, 7705 postmenopausal women with osteoporosis, and the placebo populations from three large 3 year clinical trials of risedronate [Vertebral Efficacy with Risedronate Therapy Multinational trial [VERT-MN], Vertebral Efficacy with Risedronate Therapy North America [VERT-NA] and the Hip Intervention Program [HIP], 2326 subjects) [29] has allowed the observation of the occurrence of numerous incident fractures including their characteristics and risk factors.

In the EPOS, Roy *et al.* [30] reviewed the radiographs on 3173 men (mean age 63.1 years) and 3402 women (mean age 62.2 years). At least one incident morphometric vertebral fracture developed in 67 men and 126 women during 3 to 8 years of follow-up and 80 men and 144 women developed at least one qualitative radiologist diagnosed vertebral fracture. Forty-eight men and 116 women were identified as having an incident vertebral fracture by both techniques. A variety of risk factors were elucidated including increasing age, the lowest quartile of body mass index (BMI), a late menarche (16 years and older), and lack of taking hormone therapy (HT). There was no relation to lifestyle risk factors. Neither smoking, alcohol consumption, regular walking, nor cycling were associated with incident vertebral fractures.

In the Rotterdam Study [25], 3001 subjects (1624 women, 1377 men) older than 55 years of age were evaluated initially with baseline spine radiographs and then at 6.3 years with follow-up spine radiographs. An incident fracture was said to have occurred if there was a minimum decrease of 4.6 mm or 15% in absolute height at the anterior, central, or posterior vertebral heights. Forty-four men and 113 women had at least one incident vertebral fracture. Individuals with an incident vertebral fracture had lower

bone mineral density (BMD) at the spine and hip, were more likely to have had a vertebral or nonvertebral fracture, and smoked more. Women with incident fractures were older, thinner, and more often, used a walking aid, and had an earlier natural menopause. In men, only a history of nonvertebral fractures turned out to be a significant independent risk factor.

The SOF Research Group [27••] reviewed spine x-rays on 5822 women about 65 years of age or older who had no fracture on baseline radiographs. A new incident fracture was defined as a decrease of vertebral body height ratios of 20% or 4 mm in any of the three vertebral heights. Baseline calcaneal and distal radius BMD was measured; subsequently, proximal femur and lumbar spine BMD were also measured.

One hundred eighty-one (3.1%) women had had a first annual incident vertebral fracture at follow-up 3.7 years later. Thirty-three of these women (18.2%) had two or more new fractures. One thousand four hundred sixteen (19.6%) of the 7238 women with follow-up x-rays and 499 (20.4%) of the 2444 women without a follow-up study had prevalent vertebral fractures at baseline. There was a more than three-fold increase of first vertebral fractures in women between the ages of 65 to 69 and older than 80 years. Among women aged 65 to 74, there were 118 first fractures and, in women older than 75 years of age, there were 60 new fractures. In multivariate analyses, independent risk factors for a first incident fracture included older age, previous non-spine and hip fracture, low BMD at all sites (hip, spine and distal radius, a low BMI [$< 24 \text{ kg/m}^2$]), current smoking, low milk consumption during pregnancy, low levels of daily physical activity, falling, and regular use of aluminum-containing antacids.

The CaMos evaluated risk factors associated with incident clinical vertebral fractures [26]. CaMos is a prospective population-based cohort study involving 5143 postmenopausal women 25 years of age and older. Spinal radiographs were obtained at baseline to evaluate individuals 50 years of age and older to document the presence of prevalent vertebral fractures. Clinically recognized incident vertebral fractures were based on self-reports as documented in annually mailed questionnaires during the 3-year study period. Reported fractures were followed-up by contacting the treating physician or hospital for additional information.

During the follow-up period, 34 women developed a clinically recognized incident vertebral fracture. The relative risks for sustaining an incident vertebral fracture increased by 2.16 and 1.23 for each one SD decrease in femoral neck BMD (SD = 0.12) and five-point decrease in the Short Form 36 (SF-36) physical component summary (PCS) score. A prevalent vertebral fracture and height loss may also be associated with fracture risk. Those with new deformities were much more likely to have at least a 2 cm height loss than those without a new deformity regardless of the method or cutpoint used [31]. Vertebral fractures that are more severe seem to have a larger adverse effect than do other less severe ones [31].

In an analysis of the EPOS, the authors cite Euler's buckling theory that loss of horizontal trabeculae not only increases the risk for vertebral fracture but also indicates that severity of the collapse will be greater when a fracture happens [32].

Of the original 7340 subjects with baseline x-rays enrolled in the EVOS, 7273 subjects had follow-up x-rays taken at a mean of 3.8 years (1.4 to 8 years). Each of the 94,549 vertebral bodies from T4 to L4 were evaluated after being scanned and digitized. Criteria for an incident fracture were a loss of 4 mm in height at the anterior, middle, or posterior heights and at least one dimension had to have decreased by 20% or more. An incident fracture occurred in an unfractured vertebra in 3.1% of subjects. One hundred forty-four subjects had one incident fracture which met the above definition, 37 subjects had two incident fractures, 14 had three incident fractures, and 12 had four or more [31].

Prevalent baseline biconcave and crush deformities predicted the loss of an additional 9.4% + 2.9% of vertebral body size. The authors created a number of factors to review the incident fractures: Max% size reduction (SR) for the largest fracture defined by percent reduction, Cum% SR where the percent size reductions were summed to generate a cumulative vertebral size reduction, and Res% SR which denotes the size reduction attributable to incident fractures except the largest.

Basically, the larger the previous fracture the larger the future fracture. In multivariate modeling, age and the type of baseline deformity (crush > biconcave > uniconcave > wedge) were the best determinants of more severe and cumulative height loss. With biconcave or complete crush prevalent fractures, the loss of height by the next incident fracture will be double of what would be expected. Thus, the role of the expert radiologist was emphasized for their ability to call the clinical shape over the morphologic changes. Age was also an important predictor of size of collapse.

The EPOS approach may be somewhat complicated to apply clinically and so a simpler approach, the semi-quantitative spinal deformity index (SDI) has been proposed by Crans *et al.* [34] using the Genant semi-quantitative assessment, the fracture number, and severity are brought into play by adding their numbers into a measure that reflects the total burden of fractures in the spine [33••,34].

As described, the index is the sum of the fracture grading for each vertebrae from T4-L4. Therefore, a patient with no vertebral fractures would have an SDI of 0 and a patient with one Grade 1 fracture and one Grade 3 fracture would have an SDI of 1+3=4. In a validation evaluation, involving the MORE study, the SDI correlated very closely with future vertebral fracture risk up to an SDI score of 5. The authors concluded that the SDI should be incorporated along with BMD and demographics in the assessment of future fracture risk.

In an analysis of the placebo population from 3 year risedronate trials (VERT-MN, VERT-NA, and the Hip Intervention Program [HIP]), the authors modeled the fracture distribution over time. Of the 2336 patients randomized to placebo who had osteoporosis by BMD criteria (T-score

< -2.5 at the lumbar spine or femoral neck and/or prevalent vertebral fractures at baseline, 703 patients had no fractures). For a woman with no vertebral fractures at baseline, there is a 7.7% (1 in 13) chance that such a woman given calcium and vitamin D will have at least one vertebral fracture within 1 year [29]. There is an 88.2% chance that they will not fracture again; they have a 10.4% chance of having a second fracture; and a 1.4% chance that they will have a third or fourth fracture. For an osteoporotic woman with two vertebral fractures; within the next year, there is an 85.3% chance that she won't fracture; a 12% chance of having a third fracture, a 1.7% chance of a fourth fracture and a 9.5% chance of a fifth or sixth fracture. The yearly fracture risk increases with increasing number of existing vertebral fractures from 8% if the woman had zero vertebral fractures to about 50% if a woman has six to eight spine fractures. Over 5 years, a woman with no vertebral fractures taking calcium and vitamin D has a one in three chance of having vertebral fractures; 11% will have two or more fractures; in 10 years, 55% will have vertebral fractures, and 29% will have two or more fractures.

In an analysis of data from the Fracture Interventional Trial, Fink *et al.* [35] prospectively examined 6084 postmenopausal women to determine what proportions of incident radiographic vertebral deformities is clinically diagnosed and what proportion of clinically diagnosed vertebral fractures have radiographic findings at the same vertebral levels in the same women [35]. For this study, incident vertebral abnormalities were defined as a reduction between baseline and closeout x-rays, at each vertebral body, of 20% or more in anterior, middle, or posterior vertebral height(s) with at least a 4 mm decrease in that height(s). To assess severity, the incident vertebral deformities were divided into those greater than 20% but less than 30% loss in any vertebral height and those with greater than 30% loss in any vertebral height. Those with at least a 15% height loss were reviewed in a secondary analysis. The semi quantitative (SQ) assessment methodology was also applied [33••].

Four hundred forty six incident vertebral fractures were present in 330 women among the 6084 eligible subjects using the 20% and 4 mm definition of a new fracture; 453 women had 659 incident fractures using the 15% loss criteria. One hundred seventy (2.8%) self reported a clinical vertebral fracture; of these 49 were excluded from the analysis because 10 had no community radiograph and 39 had no fracture when the x-rays were centrally reviewed. In addition, 12 cases were not diagnosed in the community until after the study closeout radiograph was taken and 12 others had no closeout radiograph completed. Thus, the final analysis consisted of 97 women with 139 confirmed incident fractures. More than 90% presented with complaints of back pain [35].

Approximately one-fourth ($101/446 = 22.6\%$) of the incident fractures involving a height loss of at least 20% and 4 mm were clinically diagnosed as vertebral fractures at the same level. The more severe the incident deformities the more likely an event was to be diagnosed clinically. In those

with more than a 30% and 4 mm height loss had a clinical diagnosis made 28.4% of the time; only 14.3% of subjects had a clinical diagnosis made where the height loss of the deformity was more than 20% and 4 mm but less than 30%. Only 4.7% of deformities that showed height loss of at least 15% but less than 20% were clinically diagnosed.

In those with an incident deformity, 23% had a clinically diagnosed incident vertebral fracture diagnosed at the same vertebral level; if the height loss was at least 30% and 4 mm, 28.9% of subjects had a clinical diagnosis of a vertebral fracture at the same level while only 11.6% of those with height loss of at least 20% and 4 mm but less than 30% height loss had a clinical diagnosis.

Of all the confirmed incident clinical vertebral fractures, 72.7% were also identified by morphometry at the same vertebral level. When the deformity was classified as severe (height loss of at least 30% and 4 mm), 54% of new clinical spine fractures were identified by morphometry at the same vertebral level. Morphometry identified 18.7% of the clinical vertebral fractures with at least 20% and 4 mm height loss but less than 30%. So, 78.3% of women with clinical vertebral fractures also had a morphometric vertebral deformity at the same level; 64.9% of women with clinical fractures had a severe deformity while 13.4% had a mild deformity. Therefore, about one fourth of incident radiographic vertebral deformities were clinically diagnosed at the same vertebral level if they had a height loss of at least 20% and 4 mm height loss. Significantly one fourth of the new clinical fractures did not meet even the most liberal (at least 15% and 4 mm height loss) morphometric deformity criteria.

Underdiagnosis of Vertebral Fractures

Despite the importance of vertebral fractures, there is significant under-diagnosis of compression fractures. Gehlbach *et al.* [36] reported on the phenomenon in 2000 in a clinical as opposed to a research setting. They used the lateral chest radiograph to identify cases receiving medical care in a population of hospitalized older women. Fractures seen on the chest x-ray films were reviewed in conjunction with the film reports, medical record charts and discharge diagnoses. Readers were instructed to evaluate all vertebral bodies from T2 to L2. The vertebrae were classified as could not be assessed or by a system similar to the Genant semi quantitative assessment system [33••] which also included an assessment of area of the vertebral body.

All white women aged 60 years or older admitted to a single hospital between October 1, 1993 and March 31, 1997, who had a lateral chest radiograph taken during an admission were eligible to participate. Of those eligible to participate (2450), a sample of 934 individuals were selected for the final analysis. Mean age for study subjects was 75.9 years (range 60 to 97 years). The study found that most thoracic vertebrae were well visualized in the lateral chest radiographs. Vertebral deformities not related to osteoporosis were excluded (Table 1).

Table 1. Vertebral deformities related to conditions other than osteoporosis

Scheruermann's disease [2]
Metastatic tumors [2,3•]
Anemia and hematopoietic disorders [2]
Chronic renal disease
Ankylosing spondylitis
Severe osteoarthritis [2,3•]
Trauma [2]
Congenital abnormalities [2,3•]
Infectious disease [2]
Pagets' disease

Results indicated that 132 moderate-to-severe compression fractures based on the Genant semi quantitative assessment system were found in the 934 patients. Eighty-one patients had single moderate-to-severe fracture; 51 had two or more fractures; of the 63 who had severe fractures 49 had single fractures, and 14 had two or more fractures. Of the 132 patients with fractures on their films, only 126 (95%) had radiology reports which could be reviewed. Of these, 65 (52%) mentioned the finding of a vertebral fracture in the narrative body of the report and 29 (23%) had fracture mentioned in the summary impression. Of the 132 patients with moderate-to-severe (grade 2 or grade 3) fractures, 19 (14%) were mentioned in the medical record notes, 11 (8%) were mentioned in the discharge summary, three were the primary diagnosis. Of the 63 with only severe (grade 3) fractures, 13 (21%) were mentioned in the medical record notes, seven (11%) in the discharge summary and only two were the primary diagnosis. Of these severe fractures, only 42 were mentioned in the descriptive radiology report and only 22 (36%) in the summary impression.

In conclusion, the authors noted that only one in every 12 hospitalized women over 60 years of age who had radiographic evidence of a thoracic vertebral compression fracture had such mentioned as one of the discharge diagnoses. Thus, it was apparent that a gap was present in recognition and application of the significance of vertebral fractures to patient care. The study also confirmed that careful evaluation of hospital admission lateral chest x-rays in older white women would be a good way to screen for and detect vertebral fractures.

More recent studies have expanded upon the under-diagnosis of prevalent vertebral fractures on x-rays from clinical settings rather than research settings.

Majumdar *et al.* [37] reviewed prevalent vertebral fractures discovered on chest radiographs taken in an emergency room setting. They selected an approximate 10% (500) sample of the 5083 people older than 60 years who had chest x-rays taken. The x-rays were reviewed for the presence or absence of a moderate-to-severe vertebral fracture (based on the Genant SQ assessment) [33••].

The x-ray files, radiographic reports, emergency room and hospital medical records were reviewed. A fracture was considered present if the word fracture, deformity, com-

pression, wedging, or if loss of height was mentioned. A prevalence of 16% of moderate-to-severe fractures was found. Vertebral fractures were found in 72 patients but only 18 (25%) had a history of osteoporosis. When a vertebral fracture was mentioned in a radiology report, a diagnosis of osteoporosis was made more often than when no fracture was noted. Forty percent of fractures (19) were not described in the final x-ray reports. There was no documentation in the emergency room or in-hospital charts of 75% of the patients with vertebral fractures. They concluded that under-diagnosis of vertebral fractures was a major finding on chest x-rays taken in the emergency room.

Not only are vertebral fractures underdetected in chest x-rays but also in spine films themselves. The Improving Measurements of Persistence of Actonel Treatment (IMPACT) Study is a multi-center multi-country study of ambulatory women aged 65 to 80 years of age [38]. Baseline spinal radiographs were taken according to a standardized protocol. The radiologists and technologists reviewed a quality assurance manual. The worldwide radiologists were directed to use the Genant semi-quantitative technique of Genant but no additional training regarding the interpretation of vertebral fractures was provided [33••]. The central reading results served as the "reference standards" and false-negative rates (%) and false-positive rates (%) were calculated based on the adjudicated discrepancies between the local and central readings.

Of the 2451 study participants who had spinal radiographs that were examined both locally and centrally, there were 496 discrepancies noted (336 false-negative, 160 false-positive). There were 789 participants with one or more prevalent fractures read centrally: of these 266 were not classified as a fracture by the local radiologist for a false-negative rate of 34%; and 523 classified as a fracture for a true-positive rate of 66%.

On the other hand, there were 1662 participants without a prevalent fracture per the central adjudication; 84 had been classified as a fracture locally for a false-positive rate of 5%; 1511 did not have a fracture when read locally for a true-negative rate of 95%.

There were significant differences in regional reporting: the false-negative rate was highest in Latin America (46.5%) and North America (45.2%) compared with Europe/South Africa/Australia (29.5%). Despite an attempt to strive for uniformity of description, 72 (27%) of the local reports contained ambiguity in their description utilizing terms such as "biconcavity", "end plate compression", "wedge deformity", and "slight reduction in vertebral height." Of those with false-negative reports (266 subjects), 134 (50.4%) were diagnosed centrally with one prevalent vertebral fracture and 132 (49.6%) had more than one fracture. A total of 537 vertebral fractures were found in the false-negative radiographs. Per the Genant SQ assessment scale; grade 1–299 (55.7%), grade 2–191 (35.6%), and grade 3–47 (8.8%). For those with true-positive radiographs (523 subjects), 272 (52.0%)

were diagnosed with one prevalent fracture and 251 (48.0%) had more than one fracture (fracture total 1105 in 523 subjects). Of these 1105 fractures, 568 (51.4%) were grade 1, 399 (36.1%) grade 2, and 138 (12.5%) grade 3. For all the women with centrally validated locally interpreted diagnosed fractures (789 subjects), there were 1642 vertebral fractures of which 867 (52.8%) were grade 1, 590 (35.9%) grade 2, and 185 (11.3%) grade 3. Of the 1662 women without vertebral fracture per the central reading, 84 had been said to have a vertebral fracture on local radiologist reading, a 5% false-positive rate.

Thus, this analysis of the radiographs from the IMPACT trial demonstrated that local radiologists worldwide showed a significant gap in the accuracy of their ability to diagnose vertebral fractures resulting in a worldwide problem of underdiagnosis. The majority of fractures that were missed were grade 1 fractures. This is the most difficult grade to assess [39].

In order to improve these problems of under diagnosis and over diagnosis of vertebral fractures and the reporting issues, especially by radiologists, the International Osteoporosis Foundation (IOF) and the European Society of Musculoskeletal Radiology (ESSR) developed the Vertebral Fracture Initiative (VFI) which includes a Resource Document in two parts. Part 1 contains information on "Osteoporosis and Related Fractures" coauthored by Szule P and Delmas PD. Part 2 entitled "Radiological Assessment of Vertebral Fractures" is coauthored by Genant HK, Jergas M, van Kuijk C [1,2].

The VFI Resource Document (RD) states that "the radiographic diagnosis is considered the best way to identify and confirm the presence of vertebral fractures in clinical practice."

Historically starting in 1947, and progressing into the 1970's Fletcher [40] and, subsequently, other authors [41–43] developed various descriptive terms of vertebral deformities [44,45••]. Subsequently, in the mid 1980s [46] to the early 1990s, a number of epidemiologists and other investigators created systems for the analysis of vertebral fracture. These are reviewed in the Vertebral Fracture Initiative Resource Document (VFIRD) [1,2].

There are two major factors in diagnosing a vertebral fracture—standardization of the radiographic techniques and factors and standardization of the interpretations. A review of the standardization of radiographic techniques is beyond the scope of this paper. Within the IMPACT study central radiologists emphasized one of the major problems was the ambiguity of some of the terms used to describe a deformity or fracture and emphasized the need to call a fracture a fracture.

Despite this review of multiple systems of analysis that have been proposed over the years, again, as in the ISCD VFA Course, the preferred system of analysis appears to be the Genant semi-quantitative fracture assessment [33••,47].

Genant's semi quantitative assessment

The semi quantitative system of assessment proposed by Genant [33••,48] and others has lately come to be accepted almost as a pseudo-standard in the IOF/European Society of Skeletal Radiology [ESSR] Vertebral Fracture Ini-

tative [1,2] and the ISCD VFA Course [15] as a clinical model to aid in diagnosing prevalent and incident vertebral fractures.

As this system was described vertebrae from T4 to L4 were graded on visual inspection without direct measurement of the anterior, middle, or posterior heights as normal (Grade 0), a borderline deformed vertebra (Grade 0.5), mildly deformed (Grade 1, a 20%–25% reduction in one of the three heights and a reduction of area 10%–20%), moderately deformed (Grade 2, a 25%–40% reduction in any height and a reduction in area of 20–40%) and severely deformed (Grade 3, a 40% or more reduction in height and area). Over the years, the area reduction requirement was dropped from the analysis. The initial description above was for prevalent fractures. An incident fracture was defined as a change in a vertebral body leading to a higher deformity Grade in a follow-up x-ray (eg, Grade 0 to Grade 1 or Grade 1 to Grade 2). Thus, a prevalent fracture at baseline could become an incident fracture on a follow-up x-ray if the deformity was more severe.

According to the ISCD course and Dr. Genant (personal communication Sanford Baim), the first step in the process is to visually determine whether a fracture or a non-fracture deformity exists (Table 2). The next steps include determining whether endplate deformities (horizontal edges) are present; lack of parallelism of endplates exists, buckling of cortices (on the vertical edges) and, finally, whether there is loss of vertical continuity with adjacent vertebrae.

Algorithm-based qualitative assessment

Eastell *et al.* continue to try to improve the identification of vertebral fractures [5,49]. In 2005, there is still no "gold standard" for the definition of an osteoporotic vertebral fracture and no single technique that meets all the needs of an ideal system of a standardized reproducible approach that differentiates a fracture from normal changes or non-fracture deformity. Using an intensive review of incident fractures so that changes in vertebral body anatomy can be perceived, they developed a modified visual approach—the algorithm-based qualitative assessment (ABQ). The ABQ system differs from the SQ assessment in two ways—the focus is on depression of the central endplate and emphasis on a short vertebral height with changes at vertical anterior vertebral endplate. In ABQ, the reader uses a decision making algorithm for vertebral classification as normal, non-fracture deformity, and osteoporotic fracture. There are also differences between the SQ assessment and the ABQ method in identifying incident fractures.

Vertebral Fracture Assessment

The development and clinical appearance of the fan beam densitometers by a number of manufacturers in the mid 1990s has led to the ability to capture the entire vertebral spine from T4 to L4 in one image. The development of this technique and the software and image improvements of

Table 2. Official position of the 2005 ISCD

<p>Indications for VFA*</p> <p>Consider VFA when the results may influence clinical management</p> <p>When BMD measurement is indicated, performance of VFA should be considered in clinical situations that may be associated with vertebral fractures</p> <p>Documented height loss of > 2 cm (0.75") or historical height loss > 4 cm (1.5") since young adult</p> <p>History of fracture after age 50</p> <p>Commitment to long term oral or parenteral glucocorticoid therapy</p> <p>History and/or findings suggestive of vertebral fracture not documented by prior radiologic study</p> <p>VFA contraindications</p> <p>"Recent" imaging of spine that can be reviewed for incident fractures (eg, CXR, CT, or MRI of spine or nuclear medicine bone scans).</p> <p>Pregnancy</p> <p>When it will not alter therapeutic-clinical course</p> <p>Indications for following VFA with another imaging modality</p> <p>The decision to perform additional imaging must be based on each patient's overall clinical picture including the VFA result</p> <p>Consider additional imaging when there are equivocal fractures, unidentifiable vertebrae between T7-L4, and sclerotic or lytic changes or findings suggestive of conditions other than osteoporosis</p>
<p>*VFA is designed to detect vertebral fractures and not other abnormalities.</p> <p>BMD—bone mineral density; CT—computed tomography; CXR—chest x-ray; ISCD—International Society for Clinical Densitometry; MRI—magnetic resonance imaging; VFA—vertebral fracture assessment.</p>

Table 3. Comparison of x-ray and VFA

	X-ray	VFA
Radiation dose	600 uSv	3 uSv
Access	Separate visit	Point of service
Cost	Higher (\$92*)	Lower (\$45*)
Resolution	Higher	Lower
Visualization	Superior above T7	Often superior in LS
Obliquity	Common in LS	Less parallax effect
Automated morphometry	No	Yes

*Medicare reimbursement
VFA—vertebral fracture assessment.

the past several years have brought this modality to a level of maturity to allow widespread usage. A technical description of the aspects of the various devices are beyond the scope of this paper, but a recent review is available [44].

Although the manufacturers have various proprietary names and abbreviations, the ISCD has proposed that VFA be the official term for this procedure and this has been accepted by the American Medical Association Coding Committee and Centers for Medicare and Medicaid Services. Some of the advantages and disadvantages of VFA versus radiography are given in Table 3.

As mentioned previously, the ISCD has adopted the SQ assessment of Genant as the basis of their teaching course on VFA [33••].

At its recent Position Development Conference, held in Vancouver, Canada in July, 2005, the ISCD created its official Positions concerning VFA including contraindications and, indications for following VFA [45••] with another imaging modality.

A major outcome of efforts by the ISCD was the assignment (in the United States) of a CPT Code (76077) and

reimbursement through Medicare and other insurers so that we can add VFA to the clinical armamentarium of the battle to detect and reduce vertebral fractures and their risk.

Conclusions

Despite the continued refrain of the past 15 years that there is no "gold standard" for the definition of a vertebral fracture (prevalent or incident); a tremendous amount of work has been done in this area. Perhaps, the use of newer imaging techniques such as CT and MRI scanning will help to further focus the definitions available. Methodologies such as SQ assessment and ABQ have produced clinically useful systems to make major improvements. Worldwide initiatives such as the IOF VFI and the ISCD VFA course attest to the importance now attached to vertebral fractures and clinical efforts to improve their detection. The advent of new reimbursement mechanisms (in the United States which can serve as a global model) indicate that even the payers are getting the message.

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