Assessment of Vertebral Fractures in Osteoporosis Research

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ABSTRACT. The evaluation of conventional radiographs of the spine for vertebral fractures is an important component of clinical practice and research in osteoporosis. Aside from the traditional approach of qualitative assessment of spinal radiographs 2 additional approaches have evolved, particularly for applications in clinical research and epidemiological studies. The first is quantitative morphometry (QM), which is based upon measurement of 4–10 points on the lateral projection of the vertebral body and determination of vertebral heights and ratios of heights. QM is a definable, describable, and relatively reproducible method for detecting both prevalent and incident fractures. However, projectional effects substantially influence the reliability of these measures performed in isolation. Therefore, there has been renewed interest in the visual assessment of fractures using a semiquantitative assessment (SQ) grading scale with definable, morphological and morphometric criteria. This second approach, while perhaps not as objective as QM, makes use of all the information regarding vertebral size and shape and is fundamentally more complex. When performed with adequate training, however, it provided good reproducibility and reliability. This overview provides a brief analysis of the methodologies and the advantages and disadvantages of the QM and SQ approaches, and compares their relative performance, alone or combined, in a large prospective population based study. (*J Rheumatol 1997;24:1212–4*)

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The assessment of spinal radiographs for prevalent or incident vertebral fractures is important in the clinical evaluation of patients with osteoporosis, in the epidemiological evaluation of populations at risk for osteoporosis, and in the management of clinical drug trials for osteoporosis treatment[1–8]. Traditionally, conventional radiographs of the thoraco-lumbar region in lateral projection have been analyzed qualitatively by radiologists or experienced clinicians to identify vertebral fractures in patients with clinical indications.

In the context of conducting epidemiologic studies or clinical drug trials in osteoporosis research, however, the requirement and expectations differ considerably from the clinical environment. Examinations are frequently performed without specific clinical indications and without specific therapeutic ramifications. In an effort to reduce potential subjectivity in qualitative readings and to provide definable, reproducible, and objective methods to detect vertebral fracture, and to accommodate the assessment of large numbers of radiographs by technicians (in the absence of radiologists or experienced clinicians), various morphometric approaches have been explored and employed.

Early studies using direct measurements of vertebral dimensions on lateral radiographs were described by a number of investigators[9–13] with the rationale to reduce potential subjectivity intrinsic to qualitative assessment of spinal radiographs. In more recent years, increasingly sophisticated morphometric approaches have been derived, all measuring 4 to 10 points on a vertebral body to define its geometry and applying various empirical or statistical approaches to derive morphometric data[2,14–23].

Several comprehensive studies have compared the various methods or cutoff criteria in the same populations to examine the effect of methodology on estimates of vertebral prevalence and on identification of individual patients or individual vertebrae as fractured. In these studies by Sauer[22], Smith-Bindman[16], Hansen[24], Adami[6], and Wu[25] the expected tradeoffs between sensitivity and specificity were observed and 2 to 4-fold differences in estimates of fracture prevalence were reported, as well as only fair kappa scores ($\kappa = 0.40–0.60$) between the different algorithms for defining fractures. Therefore, despite having developed sophisticated, describable, and objective methods, the application and interpretation of results have been complicated by large differences observed from one technique to the next. Additionally, factors including the normal variations in configuration of vertebral bodies, vagaries of posterior uncinate processes and anterior degenerative remodeling, and consid-

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erable projectional and parallax variations, all contribute to substantial subjectivity in the placement of points during digitization. Although strict guidelines are provided in an effort to reduce or at least standardize the decision process, subjective point placements are still frequently necessary. In particularly difficult cases, specific vertebral levels are excluded or decisions on measurements deferred to a radiologist. In serial studies, reference is carefully made to previous radiographs as is done in bone densitometry.

Because of some of the potential deficiencies in morphometry, there is renewed interest in exploring qualitative visual approaches for defining vertebral fractures in an effort to determine whether visual criteria can be standardized and quantified in a manner that could be defined and reproduced[3,23,25]. Since the semiquantitative approach makes use of all the information regarding vertebral body size, shape, and projection, as well as uniformity and consistency with adjacent vertebrae, it is fundamentally more complex than morphometry, requiring an understanding of anatomy, pathology, and the geometric factors intrinsic to the radiographic procedure. Clearly, the early experience[12] with qualitative readings indicated that considerable variability in fracture identification existed, perhaps because the radiologists or clinicians interpreted radiographs without specific training, standardization, reference to an atlas, or prior consensus readings. Two recent studies[3,25], however, have shown that semiquantitative interpretation, after careful centralized training and standardization, can produce results with excellent intra and interobserver reproducibility.

Unfortunately, there is no gold standard for defining fractures by which to judge methods or their variable cutoff criteria. However, as a first approximation, there is some rationale for comparing visual assessment and morphometric data on a per vertebra basis to develop a consensus interpretation based upon the expertise of experienced radiologists and highly trained research assistants. To examine this approach and to provide perspective and understanding to these complex issues, a recent study[26] of vertebral fracture assessment is briefly reviewed below.

The aims of this study were to provide a comprehensive analysis of qualitative or semiquantitative approaches and quantitative or morphometric approaches to the assessment of prevalent and incident vertebral fractures, to examine the comparability of these 2 fundamental approaches, and to determine how combinations of these 2 methods could be applied to advantage in epidemiologic studies or clinical trials. To accomplish these aims, a random sample of postmenopausal women from the Study of Osteoporotic Fractures[8] was examined, and the expertise of experienced radiologists and trained technicians was used.

Lateral thoraco-lumbar spine radiographs (baseline and ~3.5 year followup) of 503 women (age ≥ 65) randomly selected from the Study of Osteoporotic Fractures population were analyzed. Semiquantitative assessment (SQ) by an experienced radiologist visually graded vertebral fractures from 0 (normal) to 3 (severe) based upon altered size and shape of the vertebral bodies. Incident fractures by SQ were defined as an increase of ≥ 1 grade on followup radiographs. Trained research assistants visually triaged women as normal, uncertain, or probably fractured, and visually flagged vertebrae with moderate or severe (grade ≥ 2) prevalent fractures or with any (grade ≥ 1 change) incident fracture. The radiographs were also digitized by research assistants, and quantitative morphometry (QM) was used to classify vertebral deformities at several cutoffs based on standard deviation (SD) reductions in height ratios from normal means, e.g., QM ≥ 3 SD. Incident fractures by QM were defined as a decrease in height of more than 15% (QM 15) on followup radiographs. Finally, a combination of these methods was used to detect moderate or severe prevalent fractures and any grade of incident fractures.

In the overall analysis, prevalence of fractures varied from 14 to 33% and incidence from 5 to 10% in this population depending upon the method and cutoff criteria. In the detailed analysis, considering those cases visually triaged uncertain as abnormal, triage by research assistants detected 97.0% (163/168) of women with SQ grade ≥ 1 fracture and 100% (70/70) with SQ grade ≥ 2 fractures. Visual flagging by research assistants detected 88.5% (108/122) of SQ ≥ 2 prevalent fractures (κ = 0.82), and 85.2% (52/61) of SQ incident fractures (κ = 0.79). QM ≥ 3 SD detected 37.9% (141/372) of SQ ≥ 1 prevalent fractures (κ = 0.51) and 79.5% (97/122) of SQ ≥ 2 prevalent fractures (κ = 0.68), plus 18 vertebrae without SQ fractures. QM 15 detected 59% (36/61) of SQ incident fractures (κ = 0.70), plus 5 vertebrae without SQ incident fractures. The combination assessment detected 92% (112/122) of SQ ≥ 2 prevalent fractures (κ = 0.76), and 84% (51/61) of SQ incident fractures (κ = 0.91). The precision errors of QM vertebral height measurements (baseline vs followup) ranged from 2.71 to 2.92%. Nevertheless, excluding the 5719 vertebrae that were clearly normal by morphometry, i.e., within 2 SD of the normal means at both baseline and followup, two-thirds (358/556) of the remaining vertebrae changed classification by at least 1 SD category.

From this comprehensive study it can be concluded that visual triage and visual flagging by research assistants appear to be highly effective methods for vertebral fracture assessment in osteoporosis, potentially reducing the number of false positive and false negative fractures detected by QM, at least relative to SQ, by the radiologists. There is higher concordance among the visual approaches studied than between the visual, or semiquantitative, and the quantitative morphometric approaches, with QM having limited ability to detect mild fractures but good ability to detect moderate or severe fractures, as classified by SQ. Using a combination of sensitive qualitative and quantitative criteria, with adjudication by an experienced radiologist, is fea-

sible, and draws upon the relative strengths of each of the methods. QM should not be performed in isolation, particularly when applying highly sensitive morphometric criteria at low threshold levels, without visual assessment to confirm the detected prevalent or incident vertebral deformities as probable fractures.

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