

Original Article

Simplified Criteria for Selecting Patients for Vertebral Fracture Assessment

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Abstract

The 2013 Position Development Conference of the International Society for Clinical Densitometry (ISCD) has adopted simplified indications for vertebral fracture assessment (VFA) based on an analysis of the Study of Osteoporotic Fractures (SOF). This showed that a simpler regression model, which included only age, bone mineral density (BMD), and height loss, was able to differentiate women with vertebral fractures from those without vertebral fractures almost as well as more complex models. We aimed to verify these findings in 1228 women referred for BMD testing and determine if the 2013 ISCD indications for VFA would perform as well the 2007 indications. The simple and complex SOF-based models were similar in terms of sensitivity (88.4% vs 89.4%), specificity (44.4% vs 45.5%), positive (25.9% vs 26.5%) and negative (94.5% vs 95.1%) predictive values, and area under the receiver operating characteristics curve (AUROC) (0.664 vs 0.674). The 2013 and 2007 ISCD VFA indications did not differ significantly in terms of sensitivity (88.2% vs 91.3%), specificity (41.3% vs 37.5%), positive (25.3% vs 22.9%) and negative (93.9% vs 95.5%) predictive values, and AUROC (0.648 vs 0.644). Our study provides support for the use of the simplified 2013 ISCD VFA indications as a practical approach to VFA testing.

Key Words: Screening; vertebral fracture; vertebral fracture assessment.

Introduction

Vertebral fractures are the most common osteoporotic fracture with an estimated prevalence of 10%–15% among women aged 50–59 yr and up to 50% for women aged ≥ 80 yr (1,2). These fractures are important to detect because they are associated with increased morbidity and mortality (3,4) and are highly predictive of future fractures, including vertebral, hip, and other nonvertebral fractures (5). However, only about one third of vertebral fractures are clinically apparent (6), and imaging is required for their detection.

Currently, it is not clear how to best select patients for spine imaging to identify the majority of those with prevalent vertebral fractures while avoiding the additional cost and radiation exposure to those who are very unlikely to have a fracture. Several studies using either spine radiographs or vertebral fracture assessment (VFA) concluded that this is best accomplished using a combination of risk factors known to be associated with vertebral fractures (7–11). Consistent with that, the 2007 Position Development Conference (PDC) of the International Society for Clinical Densitometry (ISCD) recommended indications for VFA based on multiple risk factors and their combinations (12). Although this approach is highly evidence based and proves to be robust (12), it is cumbersome to apply in clinical practice.

To determine whether a simpler set of criteria could also identify patients with vertebral fractures, Schousboe et al (13) analyzed the data from the Study of Osteoporotic

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Fractures (SOF) and found that a simple model with fewer risk factors performed almost as well as more complex models. Based on this analysis, the 2013 ISCD PDC updated the indications for VFA with an aim to simplify the criteria to allow for easier and more widespread implementation.

However, it is not clear that the conclusions from SOF analysis are directly applicable to patients who are considered for VFA when referred for bone mineral density (BMD) testing because SOF was a population-based cohort of individuals aged ≥ 68 yr. In addition, Schousboe et al used regression-based prediction models that are more difficult to implement in clinical practice than decision-making rules based on individual risk factors. Finally, the simplified 2013 VFA indications have never been tested in an actual patient population. The aim of the present study was to compare the ability of these different approaches to separate women with and without prevalent vertebral fractures in a sample of patients referred for BMD testing. The comparisons of models that we present here include the following: (1) the simple vs the complex regression models identified by SOF analysis, (2) the 2013 vs the 2007 ISCD indications for VFA, and (3) the 2013 ISCD indications vs the simple regression model from SOF.

Methods

Study Subjects

This was a convenience sample recruited when patients presented for BMD testing ordered as part of their clinical care, and it included 946 women who were recruited between 2001 and 2007 and previously published (7) and an additional 372 women recruited between 2007 and 2012. Eighty-six women from the first cohort and 4 women from the second had uninterpretable VFA and were excluded. There were no specific inclusion criteria; study personnel needed to be present, and the subjects consented to participate. The participants represented 14.6% of all female patients who had BMD testing during this period. The study was approved by the University of Chicago's Institutional Review Board.

Measurements

Each subject completed a questionnaire that included information on personal and family history of fractures and their circumstances, young adult height, weight, medical history, medication use, and personal habits such as tobacco use, alcohol consumption, and calcium intake. Height and weight were measured using standard clinic equipment.

BMD measurements of the lumbar spine and proximal femur and VFA were obtained by 2 technologists certified by ISCD using the Prodigy densitometer (GE Medical Systems, Madison, WI). The precision errors for the BMD measurements, derived in-house, were 1% for the lumbar spine and total hip and 1.5% for the femoral neck. Data from the third National Health and Nutrition Examination Survey (NHANES III) were used to derive T-scores (gender-adjusted Caucasian norms) and Z-scores (age-, gender-, race-, and weight-

adjusted norms). T-scores were used for analyses as ISCD recommends the use of T-scores in all postmenopausal women and men aged ≥ 50 yr for all ethnic groups (<http://www.iscd.org/official-positions/2013-iscd-official-positions-adult/>). Also, as recommended by ISCD, BMD of L1–L4 with the elimination of artifact-laden vertebrae (a vertebra with clearly visible artifact and a T-score lower by at least 1 U than the mean of the other vertebrae) was used to derive lumbar spine T-score, and the lower BMD value between left and right sides was used for femoral neck and total hip T-scores.

All VFA images were evaluated by 1 ISCD-trained clinician (TJV) using the Genant semiquantitative (SQ) approach (14), as recommended by ISCD (12,15). Fractures were assigned Grade 1 for a 20%–25% reduction in vertebral height, Grade 2 for a 26%–40% reduction, and Grade 3 for a $>40\%$ reduction. Only fractures with Grade 2 or higher were considered for analyses as Grade 1 fractures are more likely to be due to nonfracture deformities (16–18). Grade 1 fractures are not as predictive of future fractures as higher grade fractures (19) and may be more difficult to diagnose with certainty on VFA (20,21).

Definition of Variables

Race was self-reported by the patient as Caucasian, black (African-American), Asian, and Hispanic. Lowest T-score was the lowest T-score between the proximal femur and the spine. Height loss was calculated by subtracting the measured height at time of BMD testing from the self-reported young adult height. For 160 subjects who could not recall their young adult height, height loss was estimated via multiple imputation (22) using linear regression estimates based on age, current height, and race. Self-reported vertebral fractures were present if the subject reported spine or vertebral fractures, excluding those of the neck, in response to the question “have you had any broken bones.” Nonvertebral fractures referred to a fracture that occurred after the age of 50 yr in the course of usual physical activity, excluding fractures of the face, fingers, and toes. Glucocorticoid use was a binary variable defined as at least 5 mg/d of systemic prednisone use or its equivalent for at least 3 mo (23). Osteoporosis treatment was defined as the patient receiving any of the following medications: estrogen (excluding vaginal preparations), raloxifene, tamoxifen, bisphosphonates, calcitonin, or teriparatide. Vertebral fracture referred to having at least a Grade 2 fracture on VFA.

Prediction Models

Four prediction models were compared in their ability to identify women with prevalent vertebral fractures: simple SOF and complex SOF models, 2007 ISCD VFA indications, and 2013 ISCD VFA indications. In SOF, prevalent vertebral fractures were adjudicated with full quantitative morphometry, with which a moderate-to-severe fracture was defined as one or more vertebral height ratio >4 SDs below the mean height ratio for that vertebral level (13). Both the simple and the complex SOF models were derived among the subset of the cohort that attended the third SOF visit between 1989

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