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Original Article

Prediction Models of Prevalent Radiographic Vertebral Fractures Among Older Women

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Abstract

It is unknown how well prediction models incorporating multiple risk factors identify women with radiographic prevalent vertebral fracture (PVFx) compared with simpler models and what their value might be in clinical practice to select older women for lateral spine imaging. We compared 4 regression models for predicting PVFx in women aged 68 y and older enrolled in the Study of Osteoporotic Fractures with a femoral neck T-score ≤ -1.0, using area under receiving operator characteristic curves (AUROC) and a net reclassification index. The AUROC for a model with age, femoral neck bone mineral density, historical height loss (HHL), prior nonspine fracture, body mass index, back pain, and grip strength was only minimally better than that of a more parsimonious model with age, femoral neck bone mineral density, and historical height loss (AUROC 0.689 vs 0.679, p values for difference in 5 bootstrapped samples $<0.001-0.35$). The prevalence of PVFx among this older population of Caucasian women remained more than 20% even when women with low probability of PVFx, as estimated by the prediction models, were included in the screened population. These results suggest that lateral spine imaging is appropriate to consider for all Caucasian women aged 70 y and older with low bone mass to identify those with PVFx.

Key Words: Bone densitometry; model discrimination; prediction models; prevalent vertebral fracture; vertebral fracture assessment.

Introduction

Prevalent vertebral fractures (PVFxs) are common among older persons *(1,2)*, are a marker of bone fragility and high fracture risk *(3−5)*, but frequently remain unrecognized in clinical practice *(6)*. Vertebral fracture assessment either with densitometric lateral spine images *(7)* or standard spine radiographs *(8)* is a cost-effective method to identify those with PVFx. A barrier to identifying those with PVFx may be the complexity of existing guidelines *(9)*. Although many risk factors have been shown to be independently associated with PVFx in multivariable-adjusted regression models

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(1,10–19), it is unknown if prediction models incorporating these additional risk factors identify those with radiographic PVFx better than more parsimonious models. We had 2 objectives: (1) to examine how well simple regression-based vs complex models discriminate those who have radiographic PVFx from those who do not in women aged 68 y or older enrolled in the Study of Osteoporotic Fractures (SOF), using area under receiving operator characteristic curves (AUROC) and the net reclassification improvement (NRI) method of Pencina (20); and (2) to establish the simplest, most parsimonious model that might be used in clinical practice to detect previously undiagnosed PVFx in older women.

Materials and Methods

The SOF enrolled 9704 Caucasian women in 1986–1988 in 4 metropolitan areas of the United States (Baltimore, MD; Minneapolis, MN; Pittsburgh, PA; and Portland, OR). Methods of study recruitment have been described previously (21). Lateral lumbar and thoracic spine radiographs were obtained at the first (1986–1988) and third (1990–1991) SOF study visits. Bone mineral density (BMD) was measured at the hip at the second and subsequent SOF visits, but only calcaneal BMD was measured at the first study visit. Because BMD is more often measured at the hip in clinical practice, we used data from the second and third SOF visits for our analyses.

Identification of Prevalent Radiographic Vertebral Fractures

The parent study population consisted of 7233 women who attended the third SOF visit and had technically adequate lateral lumbar and thoracic spine X-rays. As previously described, 6-point digitations of each vertebra from T4 through L4 inclusive were done, so anterior (H_a), middle (H_m), and posterior (H_p) vertebral heights could be accurately measured for quantitative morphometry (3). A vertebral body was considered deformed if either of 2 height ratios within the vertebra (H_a/H_p, H_m/H_p) was >3 standard deviation (SD) below the mean for that vertebral level or if both the anterior and posterior heights relative to the vertebra immediately inferior ($H_a/H_a + 1$ and $H_p/H_p + 1$) or superior ($H_a/H_a - 1$ and $H_p/H_p - 1$) were >3 SD below the mean for that level. Mild vertebral deformities and moderate to severe vertebral deformities, respectively, were defined as those with height ratios >3 SD but ≤ 4 SD and >4 SD below the expected value for that vertebral level based on normative SOF data (22).

Detection of a previously undiagnosed vertebral fracture is based on the supposition that such identification would alter therapy. Therefore, we restricted our analyses to the population with a femoral neck T-score ≤ -1.0 (n = 5560) because there is no published evidence regarding the efficacy of currently available fracture prevention therapies in those with normal BMD.

Measurement of BMD

BMD was measured at the femoral neck and total hip with QDR-1000 scanners (Hologic, Bedford, MA), at each study site for every fifth person (a total of 1506) who attended the third SOF study visit, whereas 94% of the 7223 third visit attendees had femoral neck and total hip BMD measured at the second SOF visit. In vivo coefficient of variation was 1.2% at the femoral neck. Further details of densitometry quality control methods in SOF have been published previously (23).

One thousand two hundred sixty-four women (1264) had hip BMD measured at both visits. We imputed missing femoral neck and total hip bone density values among the 5531 women with hip BMD only measured at visit 2 in 2 steps using a validated statistical method (24,25), as detailed in the Appendix.

Measurement of Other Covariates

At the baseline visit, all SOF participants were asked their height at age 25 and if they had had any fractures since age 50. Participants were subsequently mailed postcards every 4 mo and asked if they had had any fractures and their skeletal locations. They were asked whether they were currently smoking cigarettes, taking estrogen replacement therapy, and/or systemic glucocorticoid therapy at the baseline and all subsequent visits. Current height and weight were measured at each study visit, respectively, using a Harpenden stadiometer and a balance beam scale. Historical height loss (HHL) was defined as the difference between recalled height at age 25 minus measured height at the third SOF visit. Body mass index (BMI) was defined as weight (kg) divided by height (m) squared.

Selection of Covariate Predictors

The positive predictive value of a positive self-report of vertebral fracture has been reported to be as high as 85% (26). If our analyses confirmed this estimate, we planned to develop models in the subset of the SOF population who had neither a self-reported prior vertebral fracture at the baseline visit nor an incident clinical vertebral fracture between the first and third visits.

We chose age and femoral neck BMD as our simplest model. HHL is an independent risk factor for PVFx (12,14,16) and a stand-alone indication for vertebral fracture assessment in the 2007 International Society for Clinical Densitometry Position Statement for Vertebral Fracture Assessment (VFA) indications (9). Hence, our second model for comparison included age, femoral neck BMD, and HHL as predictors. Prior nonvertebral fracture, BMI, grip strength, and self-reported back pain were included in a third, more complex model. Prior fracture is a secondary indication (when combined with age) in the 2007 International Society for Clinical Densitometry indications for VFA (9), and BMI has been identified in some studies (10,12,14,17) but not others (15,18,19) as a risk factor for vertebral fracture. Other studies have identified back pain to be associated with PVFxs in women (19,27,28), and 2 have identified grip strength as to be associated with PVFx (1,19). The fourth, most complex model included the covariates of the third model, glucocorticoid use, estrogen replacement therapy, and current smoking.