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Ensrud, Kristine E
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What Proportion of Incident Radiographic Vertebral Fractures in Older Men Is Clinically Diagnosed and Vice Versa: A Prospective Study

Kristine E Ensrud[1,2,3], **Terri L Blackwell**[4], **Howard A Fink**[1,2,3,5], **Jie Zhang**[6], **Jane A Cauley**[7], **Peggy M Cawthon**[4,8], **Dennis M Black**[8], **Douglas C Bauer**[9], **Jeffrey R Curtis**[10], **Eric S Orwoll**[11], **Elizabeth Barrett-Connor**[12], **Deborah M Kado**[12], **Lynn M Marshall**[13], **James M Shikany**[14], and **John T Schousboe**[15,16] **for the Osteoporotic Fractures in Men (MrOS) Research Group**

[1]Department of Medicine, School of Public Health, University of Minnesota, Minneapolis, MN, USA

[2]Division of Epidemiology & Community Health, School of Public Health, University of Minnesota, Minneapolis, MN, USA

[3]Center for Chronic Disease Outcomes Research, VA Health Care System, Minneapolis, MN, USA

[4]California Pacific Medical Center Research Institute, San Francisco, CA, USA

[5]Geriatric Research Education & Clinical Center, VA Health Care System, Minneapolis, MN, USA

[6]Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL, USA

[7]Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, USA

[8]Department of Epidemiology & Biostatistics, University of California, San Francisco, CA, USA

[9]Department of Medicine, University of California, San Francisco, CA, USA

[10]Deparment of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

[11]Bone and Mineral Unit, Oregon Health & Science University, Portland, OR, USA

[12]Department of Family Medicine and Public Health, University of California, San Diego, La Jolla, CA, USA

[13]Department of Orthopaedics and Rehabilitation, Oregon Health & Science University, Portland, OR, USA

[14]Division of Preventive Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

15Park Nicollet Clinic, St. Louis Park, MN, USA

16Division of Health Policy & Management, School of Public Health, University of Minnesota, Minneapolis, MN, USA

Abstract

To determine the proportion of incident radiographic vertebral fractures (vfx) also diagnosed as incident clinical vfx in older men and vice-versa, we used data from 4398 community-dwelling men age 65 years enrolled in the Osteoporotic Fractures in Men (MrOS) study. Incident radiographic vfx were identified by comparing baseline and follow-up lateral thoracic and lumbar spine study films (average 4.6 years between films) using a semiquantitative (SQ) method and defined as a change in SQ reading of 1 at a given vertebral level from baseline to follow-up study radiograph. Participants were contacted triannually to ascertain incident clinical vfx; community spinal imaging studies were obtained and clinical vfx were confirmed when the study radiologist determined that the community imaging study showed a new deformity of higher grade than was present in the same vertebra on the baseline study radiograph. A total of 237 incident radiographic vfx were identified in 197 men, whereas 31 men experienced 37 confirmed incident clinical vfx. Of incident radiographic vfx, 13.5% were also clinically diagnosed as incident fractures, with clinical diagnoses made for 16.3% of the radiographic vfx with SQ grade change 2. Of incident clinical vfx, 86.5% were identified as incident radiographic vfx, most of them with SQ grade change 2. In summary, less than 15% of incident radiographic vfx were also clinically diagnosed, whereas the majority of incident clinical vfx were identified as severe radiographic vfx. These results in men supplement those previously published for women and suggest a complex relationship between clinical and radiographic vfx in older adults.

Keywords

VERTEBRAL FRACTURES; RADIOGRAPHS; CLINICAL DIAGNOSIS; OLDER MEN

Introduction

Vertebral fractures (vfx) are the most common manifestation of osteoporosis. In the United States, fractures of the vertebral bodies in the thoracic and lumbar spine account for an estimated 700,000 of the 1.5 million osteoporotic fractures that occur on an annual basis.[1] Vfx diagnosed in the clinical setting (clinical vfx) are most commonly identified when a patient presents with back pain, and a spinal imaging study is interpreted to show a fracture of a vertebral body (usually in the thoracolumbar transition zone or midthoracic region).[2] However, most vfx do not come to medical attention at the time of their occurrence and are identified solely on the basis of radiographic findings alone. Although prior studies limited primarily to older women suggest that only one-quarter to one-third of incident vfx[3,4] identified on the basis of radiographs alone (radiographic vfx) are also clinically diagnosed as fracture events, there is a paucity of data in men.

To determine the proportion of incident radiographic vfx in community-dwelling older men that are also diagnosed as incident clinical vfx (and vice-versa), we used systematically

collected data on both incident clinical vfx and incident radiographic vfx in 4398 men aged 65 years enrolled in the prospective Osteoporotic Fractures in Men (MrOS) study.

Materials and Methods

Study population

A total of 5994 men (from 2000 to 2002) 65 years old were enrolled in the prospective MrOS study.[5] Participants were recruited from population-based listings in six regions of the United States.[6] A history of bilateral hip replacement or the inability to walk without the assistance of another person excluded individuals from study participation. The institutional review board at each participating institution approved the study protocol and written informed consent was obtained from all participants. This analysis is limited to 4398 men who completed technically adequate baseline and follow-up spine films (Supporting Fig. 1).

Ascertainment of incident radiographic vfx

Incident radiographic vfx were identified by comparing baseline and follow-up (obtained at the second examination) lateral and thoracic spine study films (average 4.6 years between films). First, all follow-up films underwent a triage process by trained technicians ($n = 2$) in order to eliminate grossly normal images from further review. Once triage was complete, baseline and follow-up films from participants with a possible fracture or other abnormality (triage positive) were evaluated by a single physician reader using the semiquantitative (SQ) method of Genant.[7] The physician reader evaluated baseline and follow-up images independently and was blinded to the order in which they were obtained. Incident radiographic vfx were defined as those with a change in SQ reading of 1 at a given vertebral level from the baseline to the follow-up radiograph. For incident radiographic vfx with grade 1 severity, endplate depression was also required to distinguish wedged vertebrae from nonfracture deformities (eg, short vertebral height) and degenerative changes.[8] Triage-negative films were assumed to be fracture-free and the SQ score was set to 0 for all levels.

The same physician reader evaluated films (up to 4 images) from a randomly selected sample of 494 men to calculate the sensitivity and specificity of the triage process; the process had a sensitivity of 96.8% (few false negatives) and its specificity was 46.3%. In addition, the SQ scoring had excellent reproducibility (intrareader kappa statistics ranged from 0.79 to 0.91 on a series of quality assurance readings).[9]

Ascertainment of incident clinical vfx

Participants were contacted by mail or phone every 4 months after baseline (>99% of follow-up contacts were completed) and queried about fractures. Information regarding the circumstances of fracture events was collected using a standardized questionnaire. For any self-reported spine fracture, a copy of the community spinal imaging study (X-rays, CT, and/or MRI studies) was obtained. Clinical vfx were confirmed by the study radiologist who used the SQ method to establish that the community imaging study showed a new deformity of higher grade than was present in the same vertebra on the baseline study film. For this

study, clinical vfx identified in T_4 to T_{12} and L_1 to L_4 were included in the analyses. The follow-up period for incident clinical vfx was identical to that for incident radiographic vfx.

Measurements

At baseline, questionnaires were administered and examinations were performed to assess potential fracture risk factors.[10] Proximal femur bone mineral density (BMD) was measured using Hologic QDR 4500W densitometers (Hologic, Inc., Waltham, MA, USA). Details regarding BMD measurement protocol and quality assurance procedures have been published elsewhere.[11]

Statistical analysis

Because individual men may have had multiple incident radiographic vfx and/or incident clinical vfx, we calculated the proportion of men with incident radiographic vfx that were also diagnosed with incident clinical vfx at any vertebral level and vice-versa.

For the primary analysis, the proportion (along with its 95% confidence interval) of incident radiographic vfx also diagnosed as clinical vfx at the corresponding vertebral level ± 1 level was then calculated. We allowed for this variability because radiographic review of lateral spine images alone may result in some mislabeling of individual vertebral bodies. This was performed first for all incident radiographic vfx considered as a group and then separately according to severity category (SQ grade change = 1, SQ grade change 2) of radiographic vfx. Likewise, the proportion of incident clinical vfx also identified as incident radiographic vfx at same vertebral level ±1 level was determined along with its 95% confidence interval. This was performed for all incident radiographic vfx considered as a group, after which the proportion of clinical vfx that fell into each radiographic vfx severity category was determined.

Sensitivity analyses were performed using an alternative stricter definition of concordance (fractures identified at the same vertebral level).

Results

Among the 4398 men, mean age at baseline was 72.9 years, 90.5% were white, and 11.1% had at least a mild prevalent radiographic vfx (Table 1). A total of 197 men (4.5%) had 237 incident radiographic vfx identified by the comparison of baseline and follow-up study films an average of 4.6 years later. During this same time period, 51 men (1.2%) self-reported spine fracture events. Of these, no community spinal imaging study could be obtained for 2 men. Among the remaining 49 men who self-reported a spine fracture event within the study period and had baseline and follow-up study spine radiographs and a community imaging study performed, 31 (63.3%) experienced 37 incident clinical vertebral fractures that were confirmed by the study radiologist's comparison of the participant's MrOS baseline spine radiographs with his community spinal imaging study. For the 31 men with confirmed clinical vfx, back pain was the presenting complaint in 83.9% cases and a fall was reported in 71.0% of cases. Among the 18 men who self-reported a spine fracture event that was not confirmed by the study radiologist, 15 men had a radiologist report from the imaging study obtained in the community noting the presence of at least one radiographic vfx, but a new

vfx(s) was not adjudicated by the study radiologist upon comparison of the baseline study films with the community spinal imaging study.

Of the 197 men with incident radiographic vfx, 28 (14.2%) had an incident clinical vfx diagnosed at any vertebral level. Among all 51 men who self-reported a spine fracture event, 38 (74.5%) had an incident radiographic vfx identified at any vertebral level. Of the 31 men with confirmed incident clinical vfx, 28 (90.3%) had an incident radiographic vfx identified at any vertebral level. Among the 3 men with no confirmed radiographic vfx but with a confirmed incident clinical vfx (one with new grade 1 fracture at L_1, one with a new grade 1 fracture at L_3, and one with a new grade 2 fracture at L_2), imaging studies obtained in the community were lateral spine radiographs in all cases (one case had a CT scan of the lumbosacral spine in addition to radiographs).

Of the 237 incident radiographic vfx, 32 (13.5%) were also clinically diagnosed at the same vertebral level ±1 level, with clinical diagnoses made for 8.3% of the radiographic vfx with SQ change = 1 and 16.3% of the radiographic vfx with SQ grade change   2 (Table 2*A*). Using the alternative stricter definition of concordance (ie, fractures identified at same vertebral level), 12.2% of the incident radiographic vfx were also clinically diagnosed.

Of the 37 incident confirmed clinical vfx, 32 (86.5%) were identified as incident radiographic vfx at the corresponding vertebral level ±1 level, with nearly all of them (30) with SQ grade change   2 (Table 2*B*). Using the alternative stricter definition of concordance (fractures identified at same vertebral level), 78.4% of the incident confirmed clinical vfx were also identified as incident radiographic vfx.

Discussion

In this prospective study of community-dwelling older men, less than 15% of incident radiographic vfx were also clinically diagnosed as new vfx, whereas the majority of incident clinical vfx were also identified as incident radiographic vfx.

Our findings suggest the proportion of vfx that come to medical attention at the time of their occurrence may be lower in men than in women. We found that about 14% of incident radiographic vfx were also clinically diagnosed at the corresponding vertebral level ±1 level, with the proportion somewhat higher for more severe radiographic vfx. In contrast, a study[3] in postmenopausal women (mean age 68.1 years, femoral neck BMD *T*-score   1.6) with a similar design reported that about 25% of incident radiographic vfx (defined at a given vertebral level by a reduction between baseline and follow-up radiographs of   20% and 4 mm in any vertebral height) were also diagnosed as clinical vfx at the same corresponding vertebral level. Other studies[4,12–14] in women have estimated that approximately one-third of incident radiographic vfx are also clinically diagnosed, but most did not compare baseline and follow-up radiographs to confirm a new clinical fracture but relied on diagnoses made by community physicians who did not adhere to standardized criteria. Thus, the discrepancy in findings between sexes may be due in part to differences in study design and choice of fracture definitions. However, it may also reflect a greater

difficulty in distinguishing radiographic vfx from non-osteoporotic vertebral deformities[2] in men and a greater reluctance of men to seek medical attention for health problems.[15]

Our results indicate that about 85% of incident clinical vfx in men are also identified as incident radiographic vfx, with nearly all of them being identified as more severe (grade 2) radiographic vfx. The study[3] in postmenopausal women with a similar design reported that approximately 75% of incident clinical vfx were also identified as incident morphometric deformities at the same vertebral level, the majority of which were severe deformities. Incident clinical vfx not identified as incident radiographic vfx may result from inconsistencies in radiographs obtained in study centers versus community settings and less than perfect interrater reliability, even among expert readers.

This study has several strengths. It was comprised of a large cohort of community-dwelling men with prospective fracture follow-up every 4 months. A validated approach for defining incident radiographic vfx was utilized along with confirmation of self-reported incident clinical vfx. However, this study also has several limitations. The cohort was predominantly older, white, community-dwelling men, so results may not be generalizable to other male populations. Participants in this study were contacted every 4 months and queried about fracture events, but they were not queried in a standardized manner about acute episodes of back pain. Data about these episodes including obtaining medical records for participants who sought medical attention for these symptoms may have provided more insight into the relationship between clinical and radiographic vfx. In addition, there is a lack of gold standards for identifying radiographic vfx and defining clinical vfx.

In conclusion, the majority of incident clinically diagnosed vfx in community-dwelling older men were identified as severe radiographic vfx. However, less than 15% of incident radiographic vfx were also clinically diagnosed. These findings in men supplement those in women and suggest a complex relationship between clinical and radiographic vfx in aged populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Characteristics of 4398 Participants

Characteristic	Overall cohort (*n*=4398)
Age (years), mean±SD	72.9±5.5
White, *n* (%)	3978 (90.5)
Self-reported health status, *n* (%)	
Poor/very poor/fair	493 (11.2)
Good/excellent	3905 (88.8)
Smoking status, *n* (%)	
Past	2554 (58.1)
Current	132 (3.0)
Selected medical conditions, *n* (%)[a]	
0–1	2272 (51.8)
2–3	1724 (39.3)
4+	394 (9.0)
Any fracture since age 50 years, *n* (%)	947 (21.6)
Body mass index (kg/m²), mean±SD	27.4±3.8
Femoral neck BMD (g/cm²), mean±SD	0.79±0.13
Femoral neck BMD T-score, female white norms, mean±SD	–0.58±1.05
Radiographic vfx at baseline, SQ 1, *n* (%)	487 (11.1)

BMD=bone mineral density; vfx=vertebral fracture; SQ=semiquantitative.

[a]Selected medical conditions include prior fracture after age 50 years, arthritis, hyper/hypothyroidism, stroke, diabetes, myocardial infarction, angina, congestive heart failure, chronic obstructive pulmonary disease, Parkinsonism, hypertension, and non-skin cancer.

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Table 2

Incident Radiographic Vfx Versus Clinically Diagnosed Vfx

(*A*) Proportion of incident radiographic vfx also diagnosed as incident clinical vfx			
Category of radiographic vfx	*n*	% (95% CI) with clinical vfx at ±1 vertebral level	% (95% CI) with clinical vfx at same vertebral level
Any (SQ grade change ≥1)	237	13.5 (9.4–18.5)	12.2 (8.3–17.1)
SQ grade change=1	84	8.3 (3.4–16.42)	8.3 (3.4–16.4)
SQ grade change ≥2	153	16.3 (10.9–23.2)	14.4 (9.2–21.0)

(*B*) Proportion of incident clinical vfx also identified as incident radiographic vfx			
Category of clinical vfx	*n*	% (95% CI) with radiographic vfx at ±1 vertebral level	% (95% CI) with radiographic vfx at same vertebral level
Any (SQ grade change ≥1)	37	86.5 (71.2–95.5)	78.4 (61.8–90.2)
SQ grade change=1	6	33.3 (4.3–77.7)	33.3 (4.3–77.7)
SQ grade change ≥2	31	96.8 (83.3–99.9)	87.1 (70.2–96.4)

vfx=vertebral fracture; SQ=semiquantitative.