

Osteoporosis as a Risk Factor for Distal Radial Fractures

A Case-Control Study

By Jannike Øyen, MSc, Christina Brudvik, PhD, MD, Clara Gram Gjesdal, PhD, MD, Grethe S. Tell, PhD, MPH, Stein Atle Lie, PhD, MSc, and Leiv M. Hove, PhD, MD

Investigation performed at the Departments of Orthopedic Surgery and Rheumatology, Haukeland University Hospital, Bergen, and the Bergen Accident and Emergency Department, Bergen, Norway

Background: Distal radial fractures occur earlier in life than hip and spinal fractures and may be the first sign of osteoporosis. The aims of this case-control study were to compare the prevalence of osteopenia and osteoporosis between female and male patients with low-energy distal radial fractures and matched controls and to investigate whether observed differences in bone mineral density between patients and controls could be explained by potential confounders.

Methods: Six hundred and sixty-four female and eighty-five male patients who sustained a distal radial fracture, and 554 female and fifty-four male controls, were included in the study. All distal radial fractures were radiographically confirmed. Bone mineral density was assessed with use of dual x-ray absorptiometry at the femoral neck, total hip (femoral neck, trochanter, and intertrochanteric area), and lumbar spine (L2-L4). A self-administered questionnaire provided information on health and lifestyle factors.

Results: The prevalence of osteoporosis was 34% in female patients and 10% in female controls. The corresponding values were 17% in male patients and 13% in male controls. In the age group of fifty to fifty-nine years, 18% of female patients and 5% of female controls had osteoporosis. In the age group of sixty to sixty-nine years, the corresponding values were 25% and 7%, respectively. In adjusted conditional logistic regression analyses, osteopenia and osteoporosis were significantly associated with distal radial fractures in women. Osteoporosis was significantly associated with distal radial fractures in men.

Conclusions: The prevalence of osteoporosis in patients with distal radial fractures is high compared with that in control subjects, and osteoporosis is a risk factor for distal radial fractures in both women and men. Thus, patients of both sexes with an age of fifty years or older who have a distal radial fracture should be evaluated with bone densitometry for the possible treatment of osteoporosis.

Level of Evidence: Prognostic Level III. See Instructions to Authors for a complete description of levels of evidence.

The incidence of distal radial fractures in Norway is among the highest in the world¹⁻³, and the prevalence of low bone mineral density and osteoporosis in these patients is high⁴.

Patients with low-energy distal radial fractures are at increased risk for subsequent hip and spinal fractures^{5,6}. Known risk factors for distal radial fractures include previous low-energy fracture⁷⁻⁹ and a family history of fracture¹⁰. The use of estrogen-replacement therapy^{7,10-14} and high body-mass index^{8,11,15} seem to have protective effects. Distal radial fractures occur earlier in life than hip and spinal fractures do⁵, although

studies have demonstrated that low bone mineral density exists in a high proportion of patients with a distal radial fracture^{7,11}, indicating that this type of fracture might be the first presentation of osteoporosis. Currently, such patients are often not evaluated and treated for osteoporosis¹⁶⁻¹⁸.

How the prevalence of low bone mineral density and osteoporosis in patients with low-energy distal radial fractures^{4,19-21} compares with that of individuals without such fractures is not well known. We are not aware of any large published studies comparing the bone mineral density in patients who have distal radial fractures with that in comparable controls of both sexes.

Disclosure: In support of their research for or preparation of this work, one or more of the authors received, in any one year, outside funding or grants in excess of \$10,000 from The Research Council of Norway, the University of Bergen, and The Western Norway Health Authority. Neither they nor a member of their immediate families received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity.

The aim of this case-control study was to compare the prevalence of osteopenia and osteoporosis in female and male patients who had low-energy distal radial fractures with that in sex and age-matched controls. Furthermore, we wanted to examine whether observed differences between patients and controls with regard to bone mineral density could be explained by potential confounders.

Materials and Methods

Study Design and Study Population

Participants in the present case-control study included middle-aged and elderly women and men with low-energy distal radial fractures and control subjects who were randomly selected from the general population in the same area. Patients were recruited from the Bergen Accident and Emergency Department and Haukeland University Hospital, located in the city of Bergen, Norway. The hospital's osteoporosis clinic is organized according to the Fracture Liaison Service model^{4,20,22}. According to a standard protocol, all patients with an age of fifty years or older who had a low-energy distal radial fracture from October 2003 until October 2007 were invited, at the time of the fracture, to the osteoporosis clinic for the assessment of osteoporosis with use of dual x-ray absorptiometry and the determination of a clinical risk score with use of a self-administered questionnaire. The attending physician at the Bergen Accident and Emergency Department received automatic reminders through the electronic medical record. In the case of emergency treatment at the Department of Orthopedic Surgery at Haukeland University Hospital, diagnoses and patient data were made available on the twenty-four-hour shift lists and patients received the invitation after the treatment. Patients were informed that osteoporosis could be a possible diagnosis given the nature of the fracture, and they were offered a referral to the osteoporosis clinic for the measurement of bone mineral density.

Patients

During the four-year period from October 2003 until October 2007, 1252 female and 185 male patients with an age of fifty years or older who had a low-energy distal radial fracture were registered and evaluated for the study at the Bergen Accident and Emergency Department and Haukeland University Hospital. Of these, 117 female and four male patients were unwilling to participate because they had previously been evaluated for osteoporosis. Another 230 female and sixty-one male patients did not want to participate, for unknown reasons. Thirty-five women and seven men were not included because they were tourists. Furthermore, 194 women and twenty-seven men were not able to participate because of confusion, dementia, serious illness, or hospitalization. We chose to exclude five female patients who were more than ninety years old because no controls were more than ninety years old. Seven women and one man who had the examination at the osteoporosis clinic more than six months after the current distal radial fracture were also excluded. Thus, the final study sample comprised 664 female and eighty-five male patients with an age of fifty to ninety years. Ninety percent of the patients were referred from the Bergen

Accident and Emergency Department and 10% were referred from Haukeland University Hospital. The average time between the fracture and the examination at the osteoporosis clinic was sixty-six days (range, six to 169 days) for female patients and sixty-three days (range, eighteen to 156 days) for male patients.

A low-energy fracture was defined as a fracture that was sustained after minor trauma, such as falling from standing height or lower²³. All distal radial fractures were confirmed on radiographs.

Controls

Controls were randomly selected by Statistics Norway with use of the Norwegian Population Register and were matched on the basis of the town of residency, age (plus or minus two years), sex, and the month of examination. These subjects were invited by mail to participate and were included from April 2008 until June 2009. We invited twice as many controls as there were patients. Specifically, 1352 women and 172 men were invited, and, of these, 612 women and fifty-five men agreed to participate. Control subjects with a previous low-energy distal radial fracture after the age of fifty years (including fifty-four women and one man) were excluded. In the cases of four female controls, neither hip nor spine scans could be used because of a bilateral hip fracture, surgery, or degenerative changes in the spine. Thus, 554 female and fifty-four male control subjects were included.

The study was approved by the National Data Inspectorate (10117) and the Regional Committee for Medical Research Ethics (122.03). Each participant signed an informed consent form.

Demographic and Clinical Data

Weight and height were measured at the osteoporosis clinic. A self-administered questionnaire provided information regarding previous and current smoking and medical illness, including rheumatoid arthritis, endocrine diseases, and cardiovascular diseases. Information about the use of glucocorticoids and bisphosphonates, history of hip fracture in a parent, and previous fractures also were included in the questionnaire. Previous fractures were defined as fractures of the proximal part of the arm, rib, spine, hip, distal part of the femur, or leg resulting from low-energy trauma after the age of fifty years. The difference between the examined height and the self-reported maximum adult height was calculated. In addition, for women, the age at menopause, the use of selective estrogen receptor modulators, and the use of postmenopausal estrogen therapy were recorded. Natural loss of regular menstruation before the age of forty-five years was defined as early menopause (Table I).

Bone Mineral Density Measurements

Bone mineral density was measured at the femoral neck, total hip (femoral neck, trochanter, and intertrochanteric area), and lumbar spine (L2-L4). All scans and analyses were conducted by two trained nurses with use of the same protocol. The same dual x-ray absorptiometry equipment (GE Prodigy; Lunar Corporation, Madison, Wisconsin) was used during the entire

TABLE I Demographic Variables, Clinical Characteristics, and Bone Mineral Density Measurements in Patients with Distal Radial Fractures and Controls*

	Female			Male†		
	Patients (N = 664)	Controls (N = 554)	P Value	Patients (N = 85)	Controls (N = 54)	P Value
Demographic Variables						
Age‡ (yr)	66 ± 10	65 ± 8	0.032	65 ± 10	67 ± 8	0.199
Height‡ (cm)	163 ± 6	164 ± 6	0.012	178 ± 8	178 ± 7	0.690
Weight‡ (kg)	68 ± 12	71 ± 13	<0.001	82 ± 14	86 ± 16	0.167
BMI‡§ (kg/m ²)	25 ± 4	27 ± 5	<0.001	26 ± 4	27 ± 4	0.093
BMI§ <22 kg/m ² (no. of patients or controls)	140 (21%)	93 (17%)	0.067	13 (15%)	4 (7%)	0.194
Smoking (no. of patients or controls)						
Previous	170 (26%)	142 (26%)	1.000	28 (33%)	28 (52%)	0.034
Current	105 (16%)	97 (18%)	0.440	23 (27%)	7 (13%)	0.058
Clinical characteristics (no. of patients or controls)						
Rheumatoid arthritis	12 (2%)	8 (1%)	0.658	0	3 (6%)	—
Endocrine diseases	63 (10%)	42 (8%)	0.260	1 (1%)	1 (2%)	1.000
Cardiovascular diseases	33 (5%)	15 (3%)	0.054	12 (14%)	7 (13%)	1.000
Diabetes						
Type I	1 (<1%)	8 (1%)	0.014	—	—	—
Type II	21 (3%)	22 (4%)	0.553	5 (6%)	4 (7%)	0.735
Glucocorticoids						
Previous	31 (5%)	20 (4%)	0.391	—	—	—
Current	7 (1%)	10 (2%)	0.329	—	—	—
Estrogen	19 (3%)	3 (1%)	0.002	NA	NA	—
Bisphosphonates/SERM#	55 (8%)	23 (4%)	0.003	0	1 (2%)	—
Calcium supplements	141 (21%)	104 (19%)	0.315	5 (6%)	1 (2%)	0.405
Vitamin-D supplements	129 (19%)	99 (18%)	0.507	8 (9%)	6 (11%)	0.778
Loss of adult height (≥3 cm)	182 (29%)	106 (20%)	<0.001	21 (26%)	12 (25%)	1.000
Menopause <45 yr	96 (15%)	56 (10%)	0.024	NA	NA	—
Previous fracture	183 (28%)	81 (15%)	<0.001	0	7 (13%)	—
History of hip fracture in a parent	57 (9%)	70 (13%)	0.023	4 (5%)	6 (11%)	0.186
BMD**						
BMD‡ (g/cm ²)						
Femoral neck	0.78 ± 0.12	0.84 ± 0.13	<0.001	0.85 ± 0.10	0.90 ± 0.13	0.014
Total hip	0.82 ± 0.12	0.89 ± 0.14	<0.001	0.92 ± 0.12	0.98 ± 0.15	0.024
L2-L4	0.99 ± 0.17	1.08 ± 0.19	<0.001	1.08 ± 0.17	1.23 ± 0.23	<0.001
Femoral neck (no. of patients or controls)						
Normal BMD	105 (16%)	217 (40%)		17 (20%)	19 (35%)	
Osteopenia	326 (50%)	275 (50%)		54 (64%)	28 (52%)	
Osteoporosis	223 (34%)	54 (10%)		14 (17%)	7 (13%)	
Total hip (no. of patients or controls)						
Normal BMD	191 (29%)	275 (50%)	<0.001††	32 (38%)	27 (50%)	0.329††
Osteopenia	341 (52%)	230 (42%)		48 (57%)	25 (46%)	
Osteoporosis	122 (19%)	41 (8%)		5 (6%)	2 (4%)	
L2-L4 (no. of patients or controls)						
Normal BMD	179 (27%)	234 (43%)	<0.001††	29 (35%)	37 (71%)	<0.001††
Osteopenia	257 (39%)	215 (39%)		35 (42%)	10 (19%)	
Osteoporosis	223 (34%)	98 (18%)		19 (23%)	5 (10%)	

*The total numbers in the various cells may vary slightly because of missing data. †NA = not applicable. ‡The values are given as the mean and the standard deviation. §BMI = body-mass index. #SERM = selective estrogen receptor modulators. **BMD = bone mineral density. A normal BMD is defined as a T score of -1.0 or greater, osteopenia is defined as a T score of less than -1.0 or more than -2.5, and osteoporosis is defined as a T score of -2.5 or less. ††Overall p value for the actual categorized variable.

TABLE II Factors Associated with Distal Radial Fractures in Women on Unadjusted and Adjusted Conditional Logistic Regression Analyses*†

	Unadjusted		Adjusted†	
	OR (95% CI)	P Value	OR (95% CI)	P Value
BMD femoral neck§				
Normal	1		1	
Osteopenia	2.7 (1.9 to 3.9)	<0.001	2.7 (1.9 to 3.9)	<0.001
Osteoporosis	7.1 (4.3 to 11.6)	<0.001	6.8 (4.1 to 11.2)	<0.001
BMI				
≥22 kg/m ²	1		1	
<22 kg/m ²	1.34 (0.9 to 1.9)	0.098	1.0 (0.7 to 1.5)	0.954
Hip fracture in a parent				
No	1		1	
Yes	0.7 (0.5 to 1.1)	0.106	0.7 (0.4 to 1.1)	0.093
Previous low-energy fracture				
No	1		1	
Yes	1.6 (1.1 to 2.3)	0.010	1.5 (1.0 to 2.2)	0.050
Menopause				
≥45 yr	1		1	
<45 yr	1.5 (1.0 to 2.3)	0.042	1.5 (0.9 to 2.4)	0.064
Current smoking				
No	1.0			
Yes	1 (0.7 to 1.4)	1.000		

*The analysis included 664 patients and 554 controls. †OR = odds ratio, CI = confidence interval, BMD = bone mineral density, BMI = body-mass index. ‡Variables that were included in the adjusted model included osteopenia, osteoporosis, a body-mass index of <22, hip fracture in a parent, previous low-energy fracture, and menopause at an age of less than forty-five years. §A normal BMD is defined as a T score of -1.0 or greater, osteopenia is defined as a T score of less than -1.0 or more than -2.5, and osteoporosis is defined as a T score of -2.5 or less.

study period. The main results were based on measurements of femoral neck bone mineral density as this measurement site is recommended as the reference standard²⁴. The densitometer was calibrated daily and was stable during the entire measurement period. The in vitro long-term coefficient of variation was 0.9%. The in vivo short-term precision for femoral neck, total hip, and spine measurements was 1.5%, 0.8%, and 1.4%, respectively. Bone mineral density values for the left hip were used unless there was a history of previous fracture or surgery. Scans from the right hip were used for twenty-seven female and four male patients and for eight female controls and one male control. Bone mineral density scans of the hip were missing for ten female patients and eight female controls because of a previous bilateral hip fracture or a prosthesis. For five female and two male patients and for eleven female and two male controls, spine scans could not be analyzed because of massive degenerative changes. Bone mineral density was categorized according to different levels of the T score. The T score is defined as the number of standard deviations above the mean value for healthy thirty-year-old adults of the same sex and ethnicity as the patient²⁵. The T score calculations were derived from a combined European/United States reference population sup-

plied by the dual x-ray absorptiometry manufacturer Lunar^{26,27}. The T scores for men were determined from the database of young healthy men. Osteoporosis and osteopenia were defined according to World Health Organization definitions; specifically, osteoporosis was defined as a T score of -2.5 or less and osteopenia was defined as a T score of -1.0 or less but more than -2.5. Normal bone mineral density was defined as a T score of -1.0 or more²⁵.

Statistical Methods

Categorical variables are expressed as numbers and percentages. Continuous variables are expressed as means, with variation expressed as the standard deviation and/or range. Height change during adulthood was dichotomized at 3 cm. The age groups were stratified at fifty to sixty-four years and sixty-five to ninety years. We used independent-sample t tests for continuous variables and chi-square tests for categorical variables for comparisons between patients and controls and different age groups. Odds ratios (OR) and 95% confidence intervals (95% CI) for distal radial fracture were estimated in unadjusted conditional logistic regression analyses separately for the different demographic and clinical risk factors. Variables from the

TABLE III Factors Associated with Distal Radial Fractures in Men on Unadjusted and Adjusted Conditional Logistic Regression Analyses*†

	Unadjusted		Adjusted‡	
	OR (95% CI)	P Value	OR (95% CI)	P Value
BMD femoral neck§				
Normal	1		1	
Osteopenia	3.4 (1.1 to 10.5)	0.032	3.1 (1.0 to 9.8)	0.051
Osteoporosis	8.5 (1.6 to 44.7)	0.011	8.1 (1.4 to 47.4)	0.021
BMI				
≥22 kg/m ²	1		1	
<22 kg/m ²	2.5 (0.7 to 9.8)	0.183	2.6 (0.5 to 12.3)	0.238
Current smoking				
No	1		1	
Yes	2.6 (0.9 to 6.8)	0.060	1.6 (0.5 to 5.1)	0.386
Hip fracture in a parent				
No	1			
Yes	0.8 (0.1 to 2.3)	0.437		

*The analysis included eighty-five patients and fifty-four controls. †OR = odds ratio, CI = confidence interval, BMD = bone mineral density, BMI = body-mass index. ‡Variables that were included in the adjusted model included osteopenia, osteoporosis, a body-mass index of <22, and current smoking. §A normal BMD is defined as a T score of -1.0 or greater, osteopenia is defined as a T score of less than -1.0 or more than -2.5, and osteoporosis is defined as a T score of -2.5 or less.

unadjusted analyses with a p value of ≤ 0.20 were included in the adjusted analyses. Two-tailed p values of < 0.05 were considered significant.

Source of Funding

This work was supported by research grants from The Research Council of Norway, the University of Bergen, and The Western Norway Regional Health Authority. The funds were used to pay the salaries of the health personnel who conducted measurements on the recruited control group.

Results

Characteristics of Patients and Controls

Women

The female patients were significantly older and had a lower weight and height than the female control subjects (Table I). However, the age and height differences were small and probably were not clinically relevant. The use of postmenopausal estrogen therapy, bisphosphonates, and selective estrogen receptor modulators was higher among patients than controls, and more patients than controls reported early menopause (Table I). A higher proportion of patients reported previous low-energy fracture than controls (28% compared with 15%; $p < 0.001$). However, a higher proportion of controls than patients reported a history of hip fracture in a parent (13% compared with 9%; $p = 0.023$).

Men

Compared with male controls, a lower proportion of male patients reported previous smoking (Table I).

Prevalence of Osteopenia and Osteoporosis and Bone Mineral Density Measurements in Patients and Controls

Women

The female patients had significantly lower mean bone mineral density and higher prevalence of osteopenia and osteoporosis than the controls at all measurement sites. Overall, the prevalence of osteoporosis at the femoral neck measurement site was 34% in patients and 10% in controls. The prevalence of osteopenia was 50% in both patients and controls (Table I).

A total of 18% and 25% of patients in the age groups of fifty to fifty-nine years and sixty to sixty-nine years had osteoporosis at the femoral neck, compared with 5% and 7% of controls, respectively (Fig. 1). Among women who were fifty to sixty-four years old, the prevalence of osteoporosis at the femoral neck was 18% in patients and 6% in controls; the corresponding values for osteopenia were 59% and 46%, respectively. In the age group of sixty-five to ninety years, 51% of patients and 14% of controls had osteoporosis and 40% of patients and 55% of controls had osteopenia.

Men

The prevalence of osteoporosis at the femoral neck was 17% in male patients and 13% in male controls; the corresponding values for osteopenia were 64% and 52%, respectively (Table I). Male patients had lower mean bone mineral density at all measurement sites as compared with controls (Table I). The prevalence of osteopenia at L2-L4 was 42% in patients and 19% in controls; the corresponding values for osteoporosis were 23% and 10%, respectively. Among men who were fifty to sixty-four years old, 14% of patients and 11% of controls had

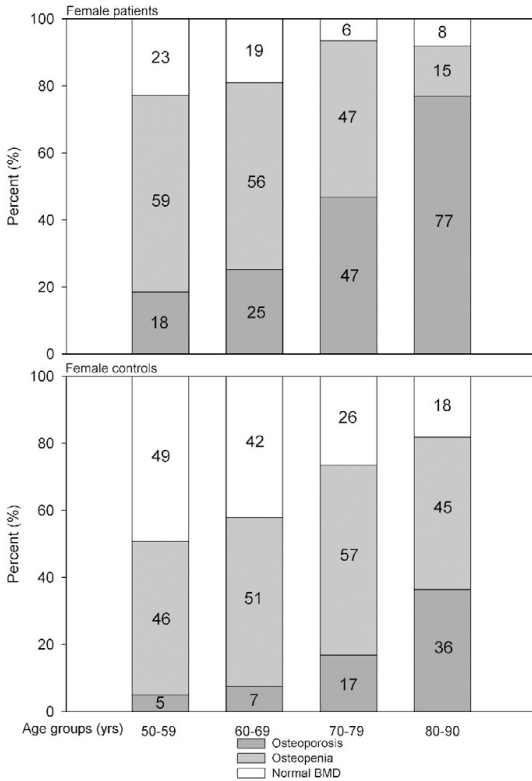


Fig. 1

Fig. 1 Graph illustrating the prevalence of normal bone mineral density, osteopenia, and osteoporosis at the femoral neck in female patients with distal radial fractures and matched controls. BMD = bone mineral density. **Fig. 2** Graph illustrating the prevalence of normal bone mineral density, osteopenia, and osteoporosis at the femoral neck in male patients with distal radial fractures and matched controls. BMD = bone mineral density.

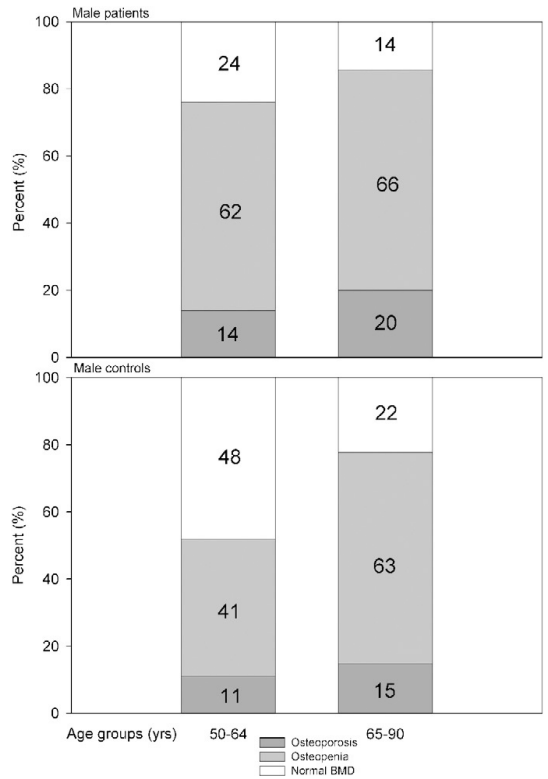


Fig. 2

osteoporosis measured at the femoral neck; the corresponding values among men who were sixty-five to ninety years old were 20% and 15%, respectively (Fig. 2).

Factors Associated with Distal Radial Fractures

Women

In unadjusted conditional logistic regression models, distal radial fractures were significantly associated with osteopenia (OR = 2.7; 95% CI, 1.9 to 3.9; $p < 0.001$), osteoporosis (OR = 7.1; 95% CI, 4.3 to 11.6; $p < 0.001$), previous low-energy fracture (OR = 1.6; 95% CI, 1.1 to 2.3; $p = 0.010$), and early menopause (OR = 1.5; 95% CI, 1.0 to 2.3; $p = 0.042$). In analyses adjusted for previous low-energy fracture, early menopause, body-mass index, and hip fracture in a parent, only osteopenia (OR = 2.7; 95% CI, 1.9 to 3.9; $p < 0.001$) and osteoporosis (OR = 6.8; 95% CI, 4.1 to 11.2; $p < 0.001$) were significantly associated with distal radial fractures (Table II).

When these analyses were repeated after stratification according to the age groups of fifty to sixty-four years and sixty-

five to ninety years, significant variables in the fully adjusted model included osteoporosis (OR = 5.9; 95% CI, 2.5 to 14.3; $p < 0.001$) and previous fracture (OR = 3.5; 95% CI, 1.8 to 6.7; $p < 0.001$) in the older group and osteopenia (OR = 3.2; 95% CI, 2.0 to 5.2; $p < 0.001$) and osteoporosis (OR = 7.1; 95% CI, 3.1 to 16.0; $p < 0.001$) in the younger group.

When the analyses were repeated after the exclusion of participants who had received bone-active drugs (bisphosphonates, selective estrogen receptor modulators, estrogen), the results did not change materially (data not shown).

Men

In unadjusted conditional logistic regression models, osteopenia (OR = 3.4; 95% CI, 1.1 to 10.5; $p = 0.032$) and osteoporosis (OR = 8.5; 95% CI, 1.6 to 44.7; $p = 0.011$) were significantly associated with distal radial fractures. In analyses adjusted for current smoking and body-mass index, only osteoporosis was significantly associated with distal radial fractures (OR = 8.1; 95% CI, 1.4 to 47.4; $p = 0.021$) (Table III).

Discussion

In the present matched case-control study, we found a higher prevalence of osteopenia and osteoporosis in female patients with distal radial fractures as compared with female controls at all measurement sites. Even female patients in the younger age group had a much higher prevalence of osteoporosis as compared with their female age-matched controls. Both osteopenia and osteoporosis were associated with distal radial fractures in women. Osteoporosis was also associated with distal radial fractures in men. These findings persisted after adjustment for body-mass index, smoking, family disposition for hip fracture, and other known risk factors for fracture. Thus, osteoporosis seems to be an independent risk factor for fracture.

To our knowledge, the present case-control study is the largest to compare the bone mineral density in female patients who had distal radial fractures with that in matched controls. Normative data supplied by the manufacturer of densitometers are based on a healthy normal population from the United States and Europe and may not be representative of members of the Norwegian population, who sustain more fragility fractures than do members of other populations^{3,28,29}. Within Norway, regional differences in hip bone mineral density have been found, with lower hip bone mineral density among women and men with an age of sixty years or more from Bergen as compared with those from Tromsø³⁰. Thus, we determined that it was important to include a control group from the same geographical area as that of the patients who had a distal radial fracture. The rationale for the inclusion of two matched controls for each patient was to minimize potential bias due to low attrition. However, despite the considerable number of female participants, selection bias still may have affected our results as the participation rate was 52% among the patients and 40% among the controls. A high proportion of female patients had previously been evaluated for osteoporosis and therefore did not consider participation in this study as meaningful. If a large proportion of those who declined to participate already were diagnosed with osteoporosis, the prevalence of osteoporosis in our study may have been underestimated; subsequently, the magnitude of the differences in bone mineral density between patients and controls might be underestimated. On the other hand, the reasons why invited control subjects did not participate are not known, and some control subjects also may have declined participation because of existing osteoporosis. If this were the case, the prevalence of osteoporosis may have been underestimated in that group as well. The latter presumption is supported by the study by Buist et al.³¹, who, in a population-based osteoporosis screening program, found that nonparticipants were postmenopausal high-risk women with previous fractures who were not receiving osteoporosis therapy. Hence, selection bias might have affected both patients and controls in our study; however, the magnitude of possible underestimation of osteoporosis and the influence on the results are unknown. Our control subjects were included six months to four years after the patients had their bone mineral density measured. However, all participants were examined at the same osteoporosis clinic, by the same personnel, in the same month of the

year as their matched patients, and with use of the same dual x-ray absorptiometry device. The densitometer was calibrated daily against a standard aluminum spine phantom, and the phantom measurements showed no drift during the study period. Thus, the results are probably not affected by the time of inclusion. Retrospective data collection may be biased by recall problems, and this may have influenced the information on some of the clinical variables, e.g., previous fractures and menopause before the age of forty-five years.

Comparisons with other studies are complicated because bone mineral density measurement sites differ between studies³²⁻³⁶. The prevalence of osteoporosis in women in our study is in accordance with the findings reported by Kanterewicz et al.³⁴, who investigated fifty-eight female patients with distal radial fractures and eighty-three controls with an age of forty-five to eighty years. In that study, bone density measurement of the hip showed that 19% of the patients and 6% of the controls had osteoporosis ($p < 0.005$). When the participants were divided into age groups (sixty-five years of age or less and more than sixty-five years of age) and the data were adjusted for age, menopausal status, and body-mass index, osteopenia and osteoporosis were found to be significantly associated with distal radial fracture only in the younger age group. In the present study, osteoporosis and previous fracture were significantly associated with distal radial fracture in the older age group and osteopenia and osteoporosis were significantly associated with distal radial fracture in the younger age group.

The prevalence of osteoporosis in our total group was not significantly different between the male patients and male controls (17% compared with 13%; $p = 0.174$). However, in adjusted conditional logistic regression analysis in which matched pairs were taken into account, osteoporosis was significantly associated with low-energy distal radial fracture (OR = 8.1; 95% confidence interval, 1.4 to 47.4; $p = 0.021$). Tuck et al.³⁷ found a higher prevalence of osteoporosis at the femoral neck in sixty-seven male patients with distal radial fractures as compared with 198 controls (37% compared with 9%; $p < 0.001$), and, in regression analyses, the authors found a lower bone mineral density in the patients with distal radial fractures than in controls after adjustment for age and body-mass index.

Unlike hip fractures, distal radial fractures are not strongly associated with increased mortality³⁸. However, in patients with low-energy distal radial fractures, low bone mineral density is associated not only with increased fracture risk but also with an increased severity of distal radial fracture³⁹. Because distal radial fractures occur an average fifteen years earlier in life than hip fractures⁴⁰, distal radial fractures may predict both subsequent vertebral and hip fractures⁵. To reduce the risk of later hip and vertebral fracture, it may be clinically appropriate to identify and monitor patients with distal radial fractures for possible indications for the treatment of osteoporosis^{5,41}. In a previous study, we found that treatment decisions had to be based on bone mineral density and not merely on clinical guidelines or the assessment of future fracture risk without the use of bone mineral density⁴.

Studies have shown that pharmacological bisphosphonate therapy reduces the fracture risk in postmenopausal women⁴²⁻⁴⁴ as well as vertebral fracture risk in middle-aged and elderly men with primary osteoporosis⁴⁵. However, only 3% to 20% of patients with distal radial fractures due to low-energy trauma are evaluated for osteoporosis with use of bone densitometry and only 8% to 30% are managed for osteoporosis with medication^{16,18,46}. Because of cognitive or functional impairments and frequent administration requirements of oral bisphosphonates, the compliance is low and the disease remains untreated⁴⁷⁻⁴⁹. However, a once-yearly intravenous infusion of zoledronic acid has been shown to be effective^{43,50,51} and safe in elderly women⁵¹.

Furthermore, today's osteoporosis treatment aims at reducing the damage after the condition is established, and the lack of a cure should lead to a focus on preventive measures and an increasing interest in a possible protective effect of nutrition and physical activity. Fall prevention to reduce the risk of fracture should also be emphasized. Hopefully, our study will add to the increasing understanding of the important role of osteoporosis, especially among clinicians who treat distal radial fractures. This large case-control study demonstrated that osteoporosis among both women and men, and osteopenia among women, are related to distal radial fractures in patients with an age of fifty to ninety years. The prevalence of osteoporosis was much higher in these patients than in matched control subjects. This finding implies that patients of both sexes with an age of fifty years and older who have a distal radial

fracture should be referred for bone mineral density assessments and evaluated for possible osteoporosis in order to receive the recommended treatment to reduce the risk of new fractures. ■

NOTE: The authors are grateful to the medical staff at Bergen Accident and Emergency Department, the Department of Orthopedic Surgery at Haukeland University Hospital, and the technicians at the osteoporosis clinic at the Department of Rheumatology at Haukeland University Hospital.

Jannike Øyen, MSc
Christina Brudvik, PhD, MD
Stein Atle Lie, PhD, MSc
Leiv M. Hove, PhD, MD

Department of Surgical Sciences, University of Bergen,
N-5021 Bergen, Norway.

E-mail address for J. Øyen: jannike.oyen@kir.uib.no.

E-mail address for C. Brudvik: Christina.brudvik@kir.uib.no.

E-mail address for S.A. Lie: stein.lie@smis.uib.no.

E-mail address for L.M. Hove: leiv.hove@kir.uib.no

Clara Gram Gjesdal, PhD, MD

Department of Rheumatology,
Haukeland University Hospital,
N-5021 Bergen, Norway.

E-mail address: clara.gjesdal@helse-bergen.no

Grethe S. Tell, PhD, MPH

Department of Public Health and Primary Health Care,
University of Bergen, N-5018 Bergen, Norway.

E-mail address: grethe.tell@isf.uib.no

References

- Falch JA. Epidemiology of fractures of the distal forearm in Oslo, Norway. *Acta Orthop Scand*. 1983;54:291-5.
- Hove LM, Fjeldsgaard K, Reitan R, Skjeie R, Sørensen FK. Fractures of the distal radius in a Norwegian city. *Scand J Plast Reconstr Surg Hand Surg*. 1995; 29:263-7.
- Lofthus CM, Frihagen F, Meyer HE, Nordsletten L, Melhuus K, Falch JA. Epidemiology of distal forearm fractures in Oslo, Norway. *Osteoporos Int*. 2008;19:781-6.
- Øyen J, Gjesdal CG, Brudvik C, Hove LM, Apalset EM, Gulseth HC, Haugeberg G. Low-energy distal radius fractures in middle-aged and elderly men and women—the burden of osteoporosis and fracture risk: a study of 1794 consecutive patients. *Osteoporos Int*. 2010;21:1257-67.
- Mallmin H, Ljunghall S, Persson I, Naessén T, Krusemo UB, Bergström R. Fracture of the distal forearm as a forecaster of subsequent hip fracture: a population-based cohort study with 24 years of follow-up. *Calcif Tissue Int*. 1993;52:269-72.
- Barrett-Connor E, Sajjan SG, Siris ES, Miller PD, Chen YT, Markson LE. Wrist fracture as a predictor of future fractures in younger versus older postmenopausal women: results from the National Osteoporosis Risk Assessment (NORA). *Osteoporos Int*. 2008;19:607-13.
- Vogt MT, Cauley JA, Tomaino MM, Stone K, Williams JR, Herndon JH. Distal radius fractures in older women: a 10-year follow-up study of descriptive characteristics and risk factors. The study of osteoporotic fractures. *J Am Geriatr Soc*. 2002;50:97-103.
- Kelsey JL, Prill MM, Keegan TH, Tanner HE, Bernstein AL, Quesenberry CP Jr, Sidney S. Reducing the risk for distal forearm fracture: preserve bone mass, slow down, and don't fall! *Osteoporos Int*. 2005;16:681-90.
- Holmberg AH, Johnell O, Nilsson PM, Nilsson J, Berglund G, Akesson K. Risk factors for fragility fracture in middle age. A prospective population-based study of 33,000 men and women. *Osteoporos Int*. 2006;17:1065-77.
- Mallmin H, Ljunghall S, Persson I, Bergström R. Risk factors for fractures of the distal forearm: a population-based case-control study. *Osteoporos Int*. 1994;4: 298-304.
- Kelsey JL, Browner WS, Seeley DG, Nevitt MC, Cummings SR. Risk factors for fractures of the distal forearm and proximal humerus. The Study of Osteoporotic Fractures Research Group. *American J Epidemiol*. 1992;135:477-89.
- Cauley JA, Seeley DG, Ensrud K, Ettinger B, Black D, Cummings SR. Estrogen replacement therapy and fractures in older women. Study of Osteoporotic Fractures Research Group. *Ann Intern Med*. 1995;122:9-16.
- Mosekilde L, Beck-Nielsen H, Sørensen OH, Nielsen SP, Charles P, Vestergaard P, Hermann AP, Gram J, Hansen TB, Abrahamson B, Ebbesen EN, Stigren L, Jensen LB, Brot C, Hansen B, Tofteng CL, Eiken P, Kolthoff N. Hormonal replacement therapy reduces forearm fracture incidence in recent postmenopausal women - results of the Danish Osteoporosis Prevention Study. *Maturitas*. 2000;36:181-93.
- Keegan TH, Gopalakrishnan G, Sidney S, Quesenberry CP Jr, Kelsey JL. Hormone replacement therapy and risk for foot, distal forearm, proximal humerus, and pelvis fractures. *Osteoporos Int*. 2003;14:469-75.
- Honkanen RJ, Honkanen K, Kröger H, Alhava E, Tuppurainen M, Saarikoski S. Risk factors for perimenopausal distal forearm fracture. *Osteoporos Int*. 2000;11: 265-70.
- Freedman BA, Potter BK, Nesti LJ, Cho T, Kuklo TR. Missed opportunities in patients with osteoporosis and distal radial fractures. *Clin Orthop Rel Res*. 2007;454:202-6.
- Khan SA, de Geus C, Holroyd B, Russell AS. Osteoporosis follow-up after wrist fractures following minor trauma. *Arch Intern Med*. 2001;161:1309-12.
- Gong HS, Oh WS, Chung MS, Oh JH, Lee YH, Baek GH. Patients with wrist fractures are less likely to be evaluated and managed for osteoporosis. *J Bone Joint Surg Am*. 2009;91:2376-80.
- Löfman O, Hallberg I, Berglund K, Wahlström O, Kartous L, Rosenqvist AM, Larsson L, Toss G. Women with low-energy fracture should be investigated for osteoporosis. *Acta Orthop*. 2007;78:813-21.
- McLellan AR, Gallacher SJ, Fraser M, McQuillan C. The fracture liaison service: success of a program for the evaluation and management of patients with osteoporotic fracture. *Osteoporos Int*. 2003;14:1028-34.

21. Sharma S, Fraser M, Lovell F, Reece A, McLellan AR. Characteristics of males over 50 years who present with a fracture: epidemiology and underlying risk factors. *J Bone Joint Surg Br.* 2008;90:72-7.
22. McLellan AR, Fraser M. Fractures in women over 50 years: implications for the secondary prevention of osteoporotic fractures of the application of the NOF and RCP London treatment guidelines. *J Bone Miner Res.* 2001;16(Suppl 1):S290.
23. Cummings SR, Nevitt MC. A hypothesis: the causes of hip fractures. *J Gerontol.* 1989;44:M107-11.
24. Kanis JA, McCloskey EV, Johansson H, Oden A, Melton LJ 3rd, Khaltaev N. A reference standard for the description of osteoporosis. *Bone.* 2008;42:467-75.
25. WHO. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Geneva: World Health Organisation; 1994.
26. Gjesdal CG, Aanderud SJ, Haga HJ, Brun JG, Tell GS. Femoral and whole-body bone mineral density in middle-aged and older Norwegian men and women: suitability of the reference values. *Osteoporos Int.* 2004;15:525-34.
27. Mazess RB, Barden H. Bone density of the spine and femur in adult white females. *Calcif Tissue Int.* 1999;65:91-9.
28. Falch JA, Meyer HE. [Osteoporosis and fractures in Norway. Occurrence and risk factors]. *Tidsskr Nor Laegeforen.* 1998;118:568-72. Norwegian.
29. Lofthus CM, Osnes EK, Falch JA, Kaastad TS, Kristiansen IS, Nordsletten L, Stensvold I, Meyer HE. Epidemiology of hip fractures in Oslo, Norway. *Bone.* 2001;29:413-8.
30. Omsland TK, Gjesdal CG, Emaus N, Tell GS, Meyer HE. Regional differences in hip bone mineral density levels in Norway: the NOREPOS study. *Osteoporos Int.* 2009;20:631-8.
31. Buist DS, LaCroix AZ, Brennen SK, Abbott T 3rd. A population-based osteoporosis screening program: who does not participate, and what are the consequences? *J Am Geriatr Soc.* 2004;52:1130-7.
32. Bahari S, Morris S, Lenehan B, McElwain JP. "Osteoporosis and orthopods" incidences of osteoporosis in distal radius fracture from low energy trauma. *Injury.* 2007;38:759-62.
33. Jutberger H, Sinclair H, Malmqvist B, Obrant K. [Screening for postmenopausal osteoporosis. Women with distal radius fractures should be evaluated for bone density]. *Lakartidningen.* 2003;100:31-4. Swedish.
34. Kanterewicz E, Yañez A, Pérez-Pons A, Codony I, Del Rio L, Díez-Pérez A. Association between Colles' fracture and low bone mass: age-based differences in postmenopausal women. *Osteoporos Int.* 2002;13:824-8.
35. Mallmin H, Ljunghall S. Distal radius fracture is an early sign of general osteoporosis: bone mass measurements in a population-based study. *Osteoporos Int.* 1994;4:357-61.
36. Peel NF, Barrington NA, Smith TW, Eastell R. Distal forearm fracture as risk factor for vertebral osteoporosis. *BMJ.* 1994;308:1543-4.
37. Tuck SP, Raj N, Summers GD. Is distal forearm fracture in men due to osteoporosis? *Osteoporos Int.* 2002;13:630-6.
38. Johnell O, Kanis JA, Odén A, Sembö I, Redlund-Johnell I, Petterson C, De Laet C, Jönsson B. Mortality after osteoporotic fractures. *Osteoporos Int.* 2004;15:38-42.
39. Clayton RA, Gaston MS, Ralston SH, Court-Brown CM, McQueen MM. Association between decreased bone mineral density and severity of distal radial fractures. *J Bone Joint Surg Am.* 2009;91:613-9.
40. Owen RA, Melton LJ 3rd, Ilstrup DM, Johnson KA, Riggs BL. Colles' fracture and subsequent hip fracture risk. *Clin Orthop Relat Res.* 1982;171:37-43.
41. Earnshaw SA, Cawte SA, Worley A, Hosking DJ. Colles' fracture of the wrist as an indicator of underlying osteoporosis in postmenopausal women: a prospective study of bone mineral density and bone turnover rate. *Osteoporos Int.* 1998;8:53-60.
42. Black DM, Cummings SR, Karpp DB, Cauley JA, Thompson DE, Nevitt MC, Bauer DC, Genant HK, Haskell WL, Marcus R, Ott SM, Torner JC, Quandt SA, Reiss TF, Ensrud KE. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. *Fracture Intervention Trial Research Group.* *Lancet.* 1996;348:1535-41.
43. Black DM, Delmas PD, Eastell R, Reid IR, Boonen S, Cauley JA, Cosman F, Lakatos P, Leung PC, Man Z, Mautalen C, Mesenbrink P, Hu H, Caminis J, Tong K, Rosario-Jansen T, Krasnow J, Hue TF, Sellmeyer D, Eriksen EF, Cummings SR; HORIZON Pivotal Fracture Trial. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. *New Engl J Med.* 2007;356:1809-22.
44. McClung MR, Geusens P, Miller PD, Zippel H, Bensen WG, Roux C, Adami S, Fogelman I, Diamond T, Eastell R, Meunier PJ, Reginster JY; Hip Intervention Program Study Group. Effect of risedronate on the risk of hip fracture in elderly women. *Hip Intervention Program Study Group.* *New Engl J Med.* 2001;344:333-40.
45. Orwoll E, Ettinger M, Weiss S, Miller P, Kendler D, Graham J, Adami S, Weber K, Lorenc R, Pietschmann P, Vandormael K, Lombardi A. Alendronate for the treatment of osteoporosis in men. *New Engl J Med.* 2000;343:604-10.
46. Freedman KB, Kaplan FS, Bilker WB, Strom BL, Lowe RA. Treatment of osteoporosis: are physicians missing an opportunity? *J Bone Joint Surg Am.* 2000;82:1063-70.
47. Penning-van Beest FJ, Erkens JA, Olson M, Herings RM. Determinants of non-compliance with bisphosphonates in women with postmenopausal osteoporosis. *Curr Med Res Opin.* 2008;24:1337-44.
48. Penning-van Beest FJ, Erkens JA, Olson M, Herings RM. Loss of treatment benefit due to low compliance with bisphosphonate therapy. *Osteoporos Int.* 2008;19:511-7.
49. Cramer JA, Amonkar MM, Hebborn A, Altman R. Compliance and persistence with bisphosphonate dosing regimens among women with postmenopausal osteoporosis. *Curr Med Res Opin.* 2005;21:1453-60.
50. Lyles KW, Colón-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C, Hyldstrup L, Recknor C, Nordsletten L, Moore KA, Lavecchia C, Zhang J, Mesenbrink P, Hodgson PK, Abrams K, Orloff JJ, Horowitz Z, Eriksen EF, Boonen S; HORIZON Recurrent Fracture Trial. Zoledronic acid and clinical fractures and mortality after hip fracture. *New Engl J Med.* 2007;357:1799-809.
51. Boonen S, Black DM, Colón-Emeric CS, Eastell R, Magaziner JS, Eriksen EF, Mesenbrink P, Haentjens P, Lyles KW. Efficacy and safety of a once-yearly intravenous zoledronic acid 5 mg for fracture prevention in elderly postmenopausal women with osteoporosis aged 75 and older. *J Am Geriatr Soc.* 2010;58:292-9.