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The Incidence of Vertebral Fractures in Men and Women: The Rotterdam Study

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ABSTRACT

Vertebral fractures are considered the most common fractures in osteoporosis. Nevertheless, little is known about the epidemiology of these fractures, especially in men. Therefore, the incidence of vertebral fractures was studied in 3469 men and women from the Rotterdam Study. Spinal radiographs were obtained at baseline and again after a mean follow-up of 6.3 years. The follow-up radiographs were scored for vertebral fractures using the McCloskey-Kanis assessment method. Whenever a vertebral fracture was detected, the radiograph was compared with the baseline radiograph. If this fracture was not already present at baseline, it was considered an incident fracture. The incidence increased strongly with age, ranging from 7.8/1000 person years (PY) at ages 55–65 years to 19.6/1000 PY at ages over 75 years for women, and 5.2–9.3/1000 PY for men, respectively. Analyses repeated in strata of presence or absence of prevalent vertebral fractures showed that both in men and in women, the increase in incidence with age was almost exclusively observed in subjects with one or more prevalent fractures present at baseline. For both genders, the incidence of vertebral fractures doubled per SD decrease in lumbar spine or femoral neck bone mineral density (BMD). This study shows that overall, the incidence of vertebral fractures is higher in women than in men. In both genders, the incidence increases with age. Furthermore, the presence of a prevalent vertebral fracture and a low BMD are strong independent predictors of incident vertebral fractures in men and women. (J Bone Miner Res 2002;17: 1051–1056)

Key Words: **incidence, vertebral, fracture, population-based, men**

INTRODUCTION

VERTEBRAL FRACTURES are the most common and yet least well-investigated fractures in osteoporosis, especially in men.[1–4] In part, this is caused by the fact that only about one-third of vertebral fractures come to medical attention, whereas the majority remains unnoticed.[5] Vertebral fractures can be very debilitating; they are associated with increased functional impairment,[6] back pain, and kyphosis.[7,8] Furthermore, even in subjects without symptoms, vertebral fractures are associated with a decreased quality of life, which is not only the result of back problems, but also of other conditions such as depression.[9,10] Several studies have shown that the presence of a vertebral fracture is associated with an increased mortality risk.[11,12] Further-

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more, subjects with vertebral fractures have an increased risk of both new vertebral and nonvertebral fractures such as hip fractures.[13–17] A limited number of other studies investigated the incidence of vertebral fractures. Cooper et al. studied the incidence of clinically detected vertebral fractures in Rochester, MN.[5] In the same population, Melton et al. estimated the incidence of all vertebral fractures from the prevalence.[3] Furthermore, some studies have shown cumulative incidence of vertebral fractures in women.[13,15,16] Several studies have investigated the prevalence of vertebral fractures.[18–21] The largest of those, the European Vertebral Osteoporosis Study, is currently also studying the incidence of vertebral fractures in European countries.

To our knowledge, this study is the first single-cohort study in both men and women to investigate the incidence of vertebral fractures in nearly 3500 subjects aged 55 years and over during more than 6 years of follow-up.

MATERIALS AND METHODS

Study population

The Rotterdam Study is a prospective population-based cohort study of men and women aged 55 years and over and has the objective to investigate the incidence of and risk factors for chronic disabling diseases. Both the rationale and the study design have been described previously.[22] The focus of the Rotterdam Study is on neurological, cardiovascular, ophthalmologic, and locomotor diseases. All 10,275 inhabitants of Ommoord, a district in Rotterdam, The Netherlands, were invited to participate. Of these, 7983 (4878 women) participated in the study (resulting in a response rate of 78%). The Medical Ethics Committee of the Erasmus University Medical School has approved the Rotterdam Study.

Clinical examination

Between 1990 and 1993, an extensive baseline home interview on medical history, risk factors for chronic diseases, and medication use was performed on all participants by trained interviewers. After the home interview, the participants were invited to come to the research center for clinical examination and laboratory assessments. Bone mineral density (BMD) measurement of the femoral neck and lumbar spine was performed by dual-energy X-ray absorptiometry (DXA) (Lunar DPX-L densitometer; Lunar Corp., Madison, WI, USA) as described previously.[23]

Vertebral deformity assessment

Both at baseline, between 1990 and 1993, and at the second follow-up visit, between 1997 and 1999, a trained research technician obtained lateral radiographs of the thoracolumbar spine of subjects who were able to come to the research center. At baseline, there were two research technicians available, and one of them took all the radiographs at the follow-up visit. All radiographs were taken following a standard protocol, with a distance between source and plate of 120 cm, using a Solarize FV (General Electric CGR; General Electric, Utrecht, the Netherlands). The follow-up radiographs were available for 3549 individuals (2022 women) who survived after an average 6.3 years after their baseline center visit and who were still able to come to our research center. The fact that all subjects had to survive to this point and still had to be mobile enough to visit the center caused a health selection bias in our study population, with participants being younger than nonparticipants (mean age, 65.5 years [SD 6.6] in participants and 74.5 years [SD 10.0] in nonparticipants, respectively). Overall, participants generally were more healthy than nonparticipants. All follow-up radiographs were evaluated morphometrically in Sheffield, UK, by the McCloskey-Kanis method as described previously.[24] If a vertebral fracture was detected, the baseline radiograph was evaluated as well. If the fracture was already present at baseline, it was considered a baseline prevalent fracture. However, if the vertebra was determined to be normal at baseline and any of the three vertebral heights (anterior, central, or posterior) showed a minimum decrease of at least 4.6 mm and 15% in absolute height on the later film, it was considered an incident fracture. All vertebral fractures were confirmed by visual interpretation by an expert in the field to rule out artifacts and other etiologies, such as pathological fractures. We excluded 80 individuals who had not attended the baseline visit. Therefore, the population for analysis consisted of 3469 individuals (1971 women) with information on incidence of vertebral fractures.

Statistical analysis

Differences in baseline characteristics were compared using Student's *t*-test for continuous variables and χ^2 for categorical variables. Because we have no information on the exact date of fracture, we estimated this date by using the date halfway between the baseline and follow-up radiograph dates. This date also was used to estimate the average age during follow-up for both cases and noncases. For the calculation of follow-up time, the time between the two radiographs was used for noncases, whereas for cases we used the time between the date of the first radiograph and the date halfway between the baseline and follow-up radiograph, the estimated date of fracture. In a first analysis, we calculated overall incidence rates for men and women separately. Analyses were repeated in 5- and 10-year age strata and we estimated an exponential curve through the incidence rates. Analyses also were repeated in strata of presence or absence of a prevalent vertebral fracture at baseline. To analyze the gender difference in vertebral fracture incidence, we calculated age adjusted odds ratios (ORs) with 95% CIs for the risk of an incident vertebral fracture for women compared with men with logistic regression analysis. Additionally, we adjusted for lumbar spine BMD. To assess whether BMD measured at another site equally predicts incident vertebral fracture risk, we compared OR with 95% CI for incident vertebral fractures per SD decrease in lumbar spine and femoral neck BMD.

For men and women separately, we modeled the association between lumbar spine BMD and incident vertebral fractures, adjusting for age and the presence of prevalent vertebral fractures, using logistic regression.

TABLE 1. BASELINE CHARACTERISTIC FOR SUBJECTS WITH AND WITHOUT INCIDENT VERTEBRAL FRACTURES FROM THE ROTTERDAM STUDY

	No incident vertebral fracture	*Incident vertebral fracture*	p *Value*
Number (% women)	3293 (55.9)	176 (73.3)	<0.001
Age (SD)	65.4 (6.6)	67.9 (6.9)	<0.001
Weight (SD)	74.7 (11.7)	70.7 (12.3)	<0.001
Height (SD)	168.3 (9.1)	165.6 (9.6)	<0.001
BMD femoral neck (SD)	0.86 (0.13)	0.77 (0.13)	<0.001
BMD lumbar spine (SD)	1.10 (0.19)	0.95 (0.17)	<0.001
Smoking (%)			
Current	683 (21.0)	49 (28.0)	0.039
Former	1500 (46.1)	66 (37.7)	
Never	1069 (32.9)	60 (34.3)	
Prevalent vertebral fracture (%)	205 (6.2)	48 (27.3)	<0.001
Use of walking aid (%)	181 (5.5)	16 (9.1)	0.045

Values are means with SDs or numbers with percentages.

SPSS 9.0 for windows was used for all analyses (SPSS, Inc., Chicago, IL, USA).

RESULTS

During an average follow-up period of 6.3 years, 240 new vertebral fractures occurred in 176 individuals, 129 of which were women. The study generated a total of 22,046 person years (PY; 12,461 for women). Table 1 shows the baseline characteristics for subjects with and without incident vertebral fractures. Individuals with incident fractures are older, thinner, and are more often current smokers. In addition, they are significantly shorter at baseline. In subjects with incident vertebral fractures, BMD was significantly lower than in subjects without these fractures, at both the femoral neck and the lumbar spine.

The numbers of individuals with one or more incident vertebral fractures stratified according to the presence or absence of a baseline prevalent vertebral fracture are shown in Table 2. Women without a vertebral fracture present at baseline had a lower incidence of vertebral fractures than did women with one or more prevalent vertebral fractures (4.9% and 26.2%, respectively; $p < 0.001$). An increased incidence was observed also in men with prevalent fractures but this was less pronounced (2.7% and 8.7%, respectively; $p = 0.004$).

Figure 1 shows the distribution of incident vertebral fractures within the spines of both men and women. In both sexes, there are two peaks of incidence in the midthoracic spine and at the level of the thoracolumbar junction. Th12 and L1 are the most frequent vertebrae affected in both men and women.

The overall incidence of vertebral fractures was 10.9/1000 PY; the incidence was higher for women than for men (14.7/1000 PY and 5.9/1000 PY, respectively), resulting in a woman/man ratio of 2.5. In Table 3, incidence rates per 1000 PY, according to 10-year age strata and absence or presence of a baseline prevalent fracture are shown. Both in men and in women, the incidence of vertebral fractures increases with age, even though this is most pronounced in

TABLE 2. NUMBERS WITH PERCENTAGES OF INDIVIDUALS WITH INCIDENT VERTEBRAL FRACTURES IN STRATA OF ABSENCE OR PRESENCE OF A BASELINE PREVALENT VERTEBRAL FRACTURE

	Men	*Women*
Prevalent vertebral fracture absent		
No incident fracture	1356 (97.3)	1732 (95.1)
One incident fracture	35 (2.5)	72 (3.9)
More than one incident fracture	3 (0.2)	18 (1.0)
Prevalent vertebral fracture present		
No incident fracture	95 (91.3)	110 (73.8)
One incident fracture	5 (4.8)	24 (16.1)
More than one incident fracture	4 (3.9)	15 (10.1)

Values are numbers with percentages in parentheses.

women. This is again shown in 5-year age strata in Fig. 2. The increased incidence with age in women primarily is observed in those with a baseline prevalent fracture present. In men, a similar pattern is observed although the incidence rates were significantly lower than in women. At ages of 75 years and over, the incidence rate ratio between subjects with and without a prevalent vertebral fracture at baseline was very similar for both genders, ~6 for men and 8 for women.

After adjustment for age, the risk of an incident vertebral fracture was higher in women than in men (OR, 2.1; 95% CI, 1.5–3.0). After adjustment for age and lumbar spine BMD, these risk estimates dropped and were no longer statistically significant (OR, 1.3; 95% CI, 0.9–1.8). When adjustment was made for femoral neck BMD instead of lumbar spine BMD, ORs again dropped but remained higher and were still statistically significant (OR, 1.6; 95% CI, 1.1–2.3). Further adjustment for the presence or absence of baseline prevalent vertebral fractures essentially did not change these risk estimates.

Especially in men, the age-adjusted relative risk of an incident vertebral fracture was higher per 1 SD decrease in

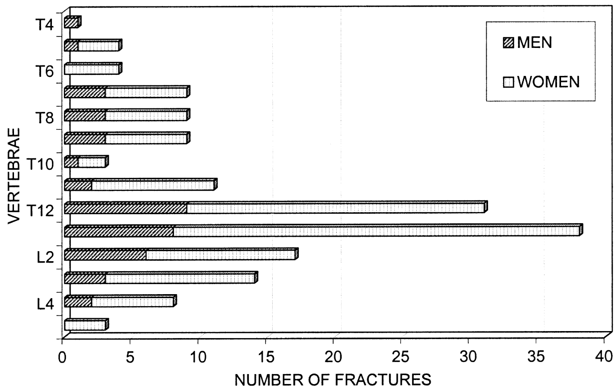

FIG. 1. Distribution of incident vertebral fractures within the spine in men and women.

lumbar spine BMD than per SD decrease in femoral neck BMD (OR, 2.6; 95% CI, 1.8–3.7 and 1.8; 95% CI, 1.3–2.4, respectively; $p = 0.061$). A similar but less obvious trend was observed for women (OR, 2.2; 95% CI, 1.7–2.7 and 1.9; 95% CI, 1.6–2.4, respectively; $p = 0.225$). Figure 3 shows the ORs for incident vertebral fractures by absolute values of lumbar spine BMD for men and women separately. Adjustment was made for age and the presence of prevalent vertebral fractures at baseline. Especially for the higher BMD values, the lines completely overlapped for men and women. At very low BMD levels, the line for men was somewhat higher than for women. This is probably caused by the low numbers of men at very low BMD levels.

DISCUSSION

In this large population-based cohort study, we found that both in men and in women, the incidence of vertebral fractures strongly increased with age. This increase with age occurred mainly in subjects who had a prevalent vertebral fracture present at baseline. At higher ages, the incidence rate ratio between subjects with and without prevalent vertebral fractures was almost similar for men and women.

The absolute incidence of vertebral fractures is lower in men than in women, but after adjustment for age and the presence or absence of prevalent vertebral fractures, the risk of an incident vertebral fracture is similar at any given level of lumbar spine BMD in men and women. Therefore, the difference in absolute incidence in men and women may be caused by the fact that overall men have a higher peak BMD and loose bone at a lower rate than women do.[25] In line with this finding, Lunt and colleagues also suggested that BMD together with age explain much of the differences in risk of vertebral fractures between men and women in a cross-sectional analysis.[26]

For both men and women, the presence of prevalent vertebral fractures as well as a low BMD were strong independent risk factors for incident vertebral fractures. Ross et al. already showed prevalent vertebral fractures to be a strong risk factor for incident vertebral fractures in women.[13] This study shows that prevalent vertebral fractures also are important predictors for incident vertebral fractures in men.

A limited number of other studies investigated the incidence of vertebral fractures. Cooper et al. studied the incidence of clinically detected vertebral fractures during a 5-year period in the population of Rochester, MN.[5] For women, these incidence rates were about one-third of our incidence rates. This is similar to what could be expected from earlier studies, because it was estimated that only about one-third of all vertebral fractures spontaneously come to clinical attention.[27] For men, this was less obvious, probably because of low numbers. In a sample from the same study population, Melton et al. estimated the incidence of all vertebral fractures in women from the prevalence using the method of Leske et al.[3,28] Their estimated incidence is similar to our incidence at lower ages, but from around age 70 years their incidence rates are higher than ours are. However, to estimate the incidence from the prevalence, it is assumed that subjects with vertebral fractures have a similar risk of mortality as subjects without vertebral fractures. Several recent studies have shown that prevalent vertebral fractures are associated with an increased mortality risk.[11,12] Because the absolute mortality risk increases with age, this could explain why results deviate at higher ages. Furthermore, some other studies reported the cumulative incidence of vertebral fractures in women.[13,15,16] The Study of Osteoporotic Fractures showed a vertebral fracture cumulative incidence of 5.4% over an average follow-up time of 3.7 years in women aged 65 years and over,[16] whereas this was 6.8% over 4.7 years in postmenopausal Japanese-American women.[13] Comparison with these studies is hampered by the fact that different methods for defining vertebral fractures are used and that large differences in duration of follow-up and age distribution of the subjects exist.

The absence of consensus about the definition of a vertebral fracture is indeed the major problem in studying the incidence of vertebral fractures.[24,29–32] Several methods have been developed for the evaluation of spinal radiographs. For this study, we used the McCloskey-Kanis method, which is a method that is developed especially for assessing both the prevalence and the incidence of vertebral osteoporosis in the population and in prospective studies. In contrast to other methods, this method predicts vertebral heights and ratios for the individual patient rather than comparing them exclusively to a reference population, resulting in a lower false positive rate.[24]

Even though this is a large population-based cohort study there are some weaknesses. There is a selection bias in our study population because in order to be eligible for this study, subjects had to be able to come to our third center visit. Therefore, only the subjects who survived over 6 years of follow-up and were still mobile enough were included in this study. Because of this selection bias, our incidence rates probably are an underestimation of the true incidence in the population. However, because vertebral fractures only come to medical attention in one-third of all cases, this is the only way to estimate the real incidence of vertebral fractures. Our assessment of vertebral deformities was based solely on morphometry, which is not used commonly in clinical prac-

TABLE 3. INCIDENCE PER 1000 PY OF VERTEBRAL FRACTURES IN ELDERLY MEN AND WOMEN

	Men			*Women*		
	No. of fractures	*PY*	*Incidence*	*No. of fractures*	*PY*	*Incidence*
Overall						
55–65 years	17	3294	5.2 (3.2–8.3)	33	4210	7.8 (5.6–11.0)
65–75 years	24	4682	5.1 (3.4–7.7)	99	5811	17.0 (14.0–20.7)
75+ years	16	1736	9.3 (5.7–15.1)	51	2598	19.6 (14.9–25.8)
No vertebral fracture present						
55–65 years	16	3156	5.1 (3.1–8.3)	32	4064	7.9 (5.6–11.1)
65–75 years	17	4359	3.9 (2.4–6.3)	61	5358	11.4 (8.8–14.6)
75+ years	9	1534	5.9 (3.1–11.3)	26	2327	11.2 (7.6–16.4)
Vertebral fracture present						
55–65 years	1	138	7.2 (1.0–51.3)	1	146	6.9 (1.0–48.7)
65–75 years	7	323	21.6 (10.3–45.4)	38	454	83.7 (60.9–115.0)
75+ years	7	193	36.4 (17.3–76.3)	25	271	92.4 (62.4–136.7)

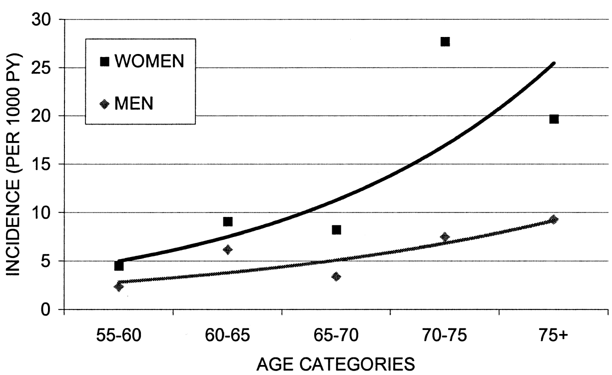

FIG. 2. The incidence of vertebral fractures per 5-year age strata in men and women.

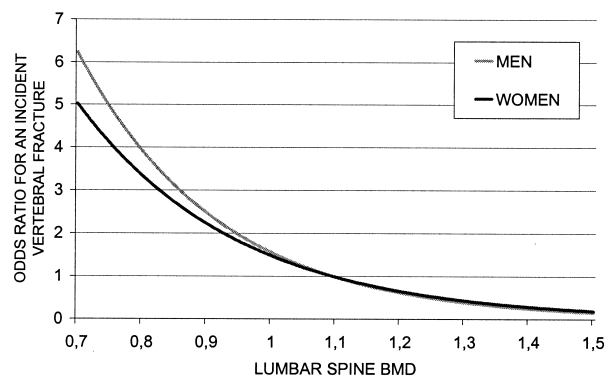

FIG. 3. ORs for incident vertebral fractures by lumbar spine BMD in men and women, age and previous vertebral fracture adjusted.

tice. Because at older ages most vertebral fractures occur after minor or no trauma,[5] we assumed that most incident vertebral fractures in this group of elderly participants were caused by osteoporosis.

Altogether, we show that the incidence of vertebral fractures increases strongly with age in both men and women. Subjects with a prevalent vertebral fracture present at baseline primarily accounted for this increase of incidence with age. Even though overall incidence rates are higher in women than in men, the risk of an incident vertebral fracture at any given level of absolute BMD is similar for men and for women. The presence of a prevalent vertebral fracture and a low BMD are strong and independent risk indicators for incident vertebral fractures in both men and women.

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